This 2003 Annual Meeting abstract supplement contains all of the abstracts to be presented at the APSS 17th Annual Meeting on June 3-8 in Chicago, Illinois. This year we experienced the largest increase in submitted abstracts that has ever occurred, with 1148 submissions. This represents a 51% increase over that submitted in 2002. This likely reflects the combined meeting with the World Federation of Sleep Research Societies, the 50th anniversary of the discovery of REM sleep being celebrated at the meeting, and the sustained increase in science addressing sleep and its disorders. Thus, more science will be presented in Chicago this year than has been presented at any previous meeting addressing this topic.

Of the 1148 abstracts, 169 will be presented in oral format, 51 in poster symposiums, and the remainder as posters. With this number of abstracts being presented as posters, the Program Committee had to make some hard decisions as to how best to handle this. They elected to:

1) Thematically group the posters.
2) Posters will be up for only one day during the meeting, but will be up the entire day.
3) Most importantly, there will be a 90 minute block of time each day (Thursday, Friday, and Saturday, June 5,6, and 7) between 1:30pm and 3:15pm that poster viewing will be unopposed by any other scientific presentation.

Each poster will have a unique 4 digit number within the appropriate category (listed below) which should allow for easy identification.

The categories for this year's science have not changed from last year and are listed here:

A. Basic Neuroscience
B. General Physiology
C. Clinical Pharmacology
D. Dreams
E. Circadian Rhythms
F. Phylogeny
G. Pediatrics
H. Aging
I. Sleep Deprivation
J. Sleep Disorders - Breathing
K. Sleep Disorders - Narcolepsy
L. Sleep Disorders - Insomnia
M. Sleep Disorders - Parasomnias
N. Sleep Disorders - Movement Disorders
O. Sleep Disorders - Neurologic Disorders
P. Sleep in Medical Disorders
Q. Sleep in Psychiatric Disorders
R. Instrumentation & Methodology
S. Sleep Education
T. Molecular Biology & Genetics
U. Sleep & Behavior

Despite the troubled times in America and abroad, we expect this will be the largest APSS meeting to date. It is our hope that this year's Annual Meeting will provide the opportunity for the meaningful exchange of both clinical and basic science related to sleep and its disorders.

David P. White, M.D.
Editor-in-Chief

0001.A

Neostigmine-Induced REM Sleep Enhancement In C57BL/6J (B6) Mouse Is Concentration-Dependent And Blocked By Atropine

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Introduction: Microinjection of the acetylcholinesterase inhibitor neostigmine bromide (Neo) into the pontine reticular formation (PRF) of B6 mouse causes a REM sleep-like state (REM-Neo) characterized by motor atonia, EEG activation, and disordered breathing (Sleep 25: 835, 2002). The present study is testing the hypothesis that REM-Neo is concentration-dependent and can be blocked by the muscarinic antagonist atropine sulfate.
Methods: Four mice each received PRF microinjections of saline (50 nl), four concentrations of Neo (1.33, 13.3, 133, 1330 ng/50 nl), and 13.3 ng Neo + 10 ng atropine/50 nl. Dependent measures included %REM sleep, %Wake, %NREM sleep, REM latency, REM epoch duration, and number of REM epochs, which were quantified during 4 hours of EEG and EMG recording.
Results: ANOVA revealed a significant ($p<0.0001$) concentration-dependent enhancement of %REM sleep (+1468.9% with 1330 ng). Neo significantly ($p<0.01$) decreased %Wake (-63.6%), %NREM sleep (-92.8%), and REM sleep latency (-92.3%). Neo significantly ($p<0.01$) increased REM epoch duration (+494.4%) and number of REM epochs (+153.6%). Atropine significantly ($p<0.001$) blocked the REM sleep enhancement caused by Neo.
Conclusions: The finding that the effects of Neo on sleep were concentration-dependent and blocked by atropine supports the conclusion that cholinergic REM sleep enhancement in B6 mouse is mediated by muscarinic receptors in the PRF.

Research supported by HL65272, HL40881, HL57120, MH45361, and Department of Anesthesiology

0002.A

The Effects of Serotonergic Activation on Wakefulness and NREM Sleep of Rats Depend on Circadian Phase

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Introduction: Extensive experimental data and clinical observations suggest that serotonin (5-HT) promotes wakefulness *per se*, but is necessary for sleep because it induces the synthesis and/or release of sleep-inducing factor(s). As such, the impact of serotonergic activation on waking and sleep may differ depending on the circadian phase during which the activation occurs. Because their sleep-wake behavior is differentially distributed between the light and dark periods of the daily cycle, we used rats to test the hypothesis that the impact of serotonergic activation on wakefulness and NREM sleep depends on the timing of activation. To that end we injected the 5-HT precursor L-5-hydroxytryptophan (5-HTP) into freely behaving rats at either dark or light onset.
Methods: Male Sprague-Dawley rats (250-275 g) were maintained on a 12:12 h light:dark cycle at 21 ºC. Animals were anesthetized and instrumented for standard polygraphic recordings. 5-HTP (25, 50, 75 and 100 mg/kg) was dissolved in pyrogen-free saline and injected intraperitoneally into freely behaving rats 15 min prior to either dark or light onset. Each rat was injected with both vehicle and at least one dose of 5-HTP, therefore serving as its own control. Experimental manipulations were randomly scheduled with an interval of at least three days.
Results: When 5-HTP was administered at dark onset, wakefulness and NREM sleep were affected in a dose- and time-dependent manner. Wakefulness was initially and briefly enhanced in post-injection hours 1-2 by the two lowest 5-HTP doses. The two highest 5-HTP doses induced a delayed and long lasting increase in NREM sleep in post-injection hours 3-12. Each dose of 5-HTP increased wakefulness when administered at light onset. Wakefulness was increased and NREM sleep suppressed for the first two post-injection hours. In contrast to responses during the dark period, there were no subsequent increases in NREM sleep.
Conclusions: These results demonstrate that serotonergic activation enhances wakefulness or NREM sleep of rats depending on the timing of activation. Serotonergic activation at the beginning of the dark period primarily enhances NREM sleep, whereas serotonergic activation prior to light onset increases wakefulness and inhibits NREM sleep. These data provide additional support for the hypothesis that 5-HT promotes wakefulness and induces NREM sleep through actions on other NREM sleep-inducing factors. The factors mediating 5-HT effects on NREM sleep remain to be elucidated.

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0003.A

Neuroanatomical Substrates of Sleep-Wake Behavior and Analgesia: Modulation by Anesthetics

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Introduction: Anesthetics that antagonize the NMDA receptor (e.g. ketamine, phencyclidine and nitrous oxide) produce amnesia and analgesia but do not induce complete loss of consciousness. GABA agonist anesthetics (e.g pentobarbital, chloral hydrate, muscimol and ethanol) produce amnesia, analgesia and unconsciousness. Similarities and differences between the mechanisms of NMDA receptor antagonist and GABAA receptor modulated analgesia, anesthesia and modifications of sleep-wake behavior raise question regarding common sites of action.
Methods: We examined c-Fos immunoreactivity (ir) in the sleep-wake system and supraspinal noradrenergic descending inhibitory pathways following administration of anesthetics. Next we lesioned the pontine descending noradrenergic cell groups using 6-hydroxydopamine and the ventrolateral PAG using the excitotoxin ibotenic acid to assess whether antinociceptive responses to the anesthetics are mediated, at least in part, by the A5, A6 (locus coeruleus), A7 cell groups, or the PAG.
Results: We found that subanesthetic doses of ketamine induced strong arousal behaviors and both sub-anesthetic and anesthetic doses increased fast theta EEG (4-7 Hz). In contrast, GABAergic agents produced slow delta EEG and sedation. Ketamine induced c-Fos expression in cholinergic, monoaminergic and orexinergic arousal systems and completely suppressed c-Fos immunoreactivity (ir) in sleep promoting ventrolateral preoptic nucleus (VLPO) whereas GABAergic agents suppressed Fos expression in arousal promoting systems and increased it in the VLPO. All anesthetics tested, with exception of pentobarbital induced c-Fos in the spinally projecting noradrenergic cell groups (A5, A6 and A7). 6-hydroxydopamine lesions of A5-7 or ibotenic acid lesions of the ventrolateral periaqueductal gray (PAG) attenuated antinociceptive responses to noxious termal stimulation (tail-flick test) by both types of anesthetics.
Conclusions: We hypothesize that a) the neural substrates of sleep-wake behavior are also involved in anesthetic-induced sedative effects and b) the descending noradrenergic cell groups regulate analgesic effects of

both NMDA receptor antagonist and GABAA receptor agonist anesthetics.

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0004.A

Corticotropin-Releasing Hormone (CRH) Mediates Amygdaloid-Kindling Induced Sleep-Wake Alteration in the Rat

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Introduction: We have previously hypothesized that corticotropin-releasing hormone (CRH) are involved in the regulation of physiological sleep-wake activity, based in part on observations that central or systemic administration of CRH receptor antagonists reduce spontaneous waking. Other observations indicate that CRH mRNA expression is up-regulated by kindling, which resembles temporal lobe epilepsy. Sleep disturbance is common, but is frequently overlooked in patients with epilepsy. The present study was designed to further elucidate the role of CRH in amygdaloid-kindling induced sleep-wake alteration.
Methods: Male Sprague-Dawley rats (250-300 g) were surgically implanted with EEG recording electrodes, a chronic guide cannula directed into the lateral cerebral ventricle and a bipolar electrode placed in central nucleus of amygdala, and were allowed a minimum of a one week recovery period. These rats were kept on a 12:12 h Light:Dark cycle at 23 $\pm$ 1 Celsius degree. After recovery, 24-h baseline recordings were obtained from undisturbed animals. Rats were then habituated, with daily kindling manipulation, by daily handling and ICV injections of pyrogen-free saline (PFS) timed to coincide with scheduled experimental administrations until kindling seizure (Racine's stage 5 seizure) was apparent. The kindling stimulus was a train of biphasic pulses (1 milliseconds duration each) of 50 Hz for 1 second. The intensity for each stimulus, ranging from 50 to 200 microAmp, was determined as a threshold for the first appearance of the concurrent afterdischarge. The afterdischarges should more than 2 Hz spikes and have a voltage at least three times higher than the pre-stimulation baseline EEG. After Racine's stage 5 seizure was apparent, 24-h EEGs were recorded beginning at the light onset, given PFS injection and kindling stimulation prior to the light (rest) period. Rats were then received two CRH receptor antagonists, astressin (0.5, 2.5 or 12.5 microgram) or alpha-hCRH (1, 5 or 25 microgram), instead of vehicle. Circulating corticosterone concentrations were determined by radioimmunoassay.
Results: Our results indicate that amygdaloid-kindling, given prior to the light (rest) period, decreases slow-wave sleep (SWS) and rapid eye movement sleep (REMS) and increases wakefulness during light (rest) period. Slow-wave activity (SWA) during SWS is also enhanced by amygdaloid kindling during the light (rest) period. In addition, circulating corticosterone concentrations are increased at 2-h after kindling stimulation. ICV administration of astressin dose-dependently blocks kindling's effects on SWS and wakefulness. alpha-hCRH ICV administered into rats also reverses sleep-wake alteration induced after kindling. Both high doses of astressin (12.5 microgram) and alpha-hCRH (25 microgram) statistically reduce kindling-induced increase of circulating corticosterone concentrations. However, the increase of SWA during SWS is not altered by either astressin or alpha-hCRH.
Conclusions: Our results suggest the involvement of CRH in the sleep-wake alteration induced by amygdaloid kindling when kindling stimulation manipulated at the beginning of the light (rest) period. However, kindling-induced decrease of REMS and increase of SWS during SWS are not mediated by CRH.

0005.A

Rest-Activity Cycles in Childhood and Adolescent Depression

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Introduction: There is clear evidence that circadian and ultradian rhythms are abnormal in adults with major depressive disorder (MDD), but few studies examine these rhythms in children and adolescents with MDD. Moreover, few studies evaluate potential gender differences in biological rhythms. The present study examined circadian rest-activity cycles, based on actigraphy in 100 children with MDD and in healthy normal controls (NCs), 8-17 yrs of age.
Methods: Fifty-nine (28 females, 31 males) symptomatic and unmedicated depressed outpatients and 41 (20 females, 21 males) normal controls participated in study. All participants underwent full psychiatric and medical evaluations to determine eligibility. Regularized sleep schedules were established prior to study commencement. Actigraphs were worn 24 hours per day and recorded motion and light exposure over a minimum of five consecutive days. Thresholds, sensitivities, scaling and epoch length were held constant across all individuals. Sleep diaries and habits questionnaires were also completed daily throughout the study. Circadian amplitude and period length of activity cycles were quantified using power spectral analysis of activity counts across the entire recording period. In addition, total activity count, average light exposure and time spent in >1000 lux light were computed for each participant. All data were then coded for group (MDD vs NC), gender and age using a cutpoint of 12 years. ANOVAs contrasted between-group differences testing the 3-way interaction first, followed by multiple comparisons.
Results: Significant group by gender by age interactions were obtained on nearly all rest-activity measures. Although the period length did not differ between patients and NCs, circadian amplitude was significantly blunted in the MDD group, particularly among girls. Adolescent boys with MDD also showed blunted circadian amplitude, but not those under 13 years of age. Moreover, the MDD groups spent significantly less time in bright light and had lower light exposure overall, compared to NCs ($p<.05$). This group difference was particularly pronounced in those over 13 years of age. Both adolescent girls and boys with MDD showed significantly less total daily activity, whereas the same results were evident only in girls in the 8-12 year group. Age-related changes in most rest-activity measures were larger in boys with MDD than in any other group. Finally, the gender differences in the group with MDD were 3-5 times greater than those observed in NCs.
Conclusions: These findings are consistent with a weak brain oscillator in early onset MDD, but one that is strongly influenced by gender and age. These results are also consistent with quantitative sleep EEG findings in childhood depression suggesting that impaired temporal organization of sleep EEG may relate to rest-activity cycle abnormalities. Further, the very large gender differences in the MDD group support a divergent pathophysiology of this disease in males and females, but unlike previous work, suggest they are evident even before puberty.

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0006.A

Dopamine Effect on Muscle Activity is Mediated by Medullary Magnocellularis Nucleus

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Introduction: Nucleus magnocellularis (NMC) of the medulla is a het-

erogeneous nucleus containing serotonergic, GABAergic, glycinergic, cholinergic and glutamatergic neurons. The NMC receives axonal projections from neurons in the dorsal and intermediolateral column of the spinal cord, as well as the upper central nervous system including cortex, thalamus, and the ventral mesopontine junction (VMPJ). Neurons in the NMC have been shown to project to the dorsal and ventral horns and intermediolateral column of the spinal cord, thalamus and cortex. Physiologically, the NMC plays an important role in sensory-motor integration. Somatic and visceral noxious and innocuous afferent pathways converge on the NMC. Activation of the NMC powerfully inhibits motoneuron activity. The VMPJ includes the caudal portion of the dopaminergic (DA) retrorubral nucleus (A8), ventral tegmental area (A10), serotonergic supralemniscal area (B9) in the caudoventral midbrain and rostroventral paralemniscal tegmental field in the pons. Glutamatergic and GABAergic neurons are also found in the VMPJ. Our previous work demonstrated that 6-OHDA lesions in the VMPJ, which specifically damages to the DA neurons, produce periodic muscle twitches during sleep and insomnia in the cat. These results indicate that DA neurons in the VMPJ play an important role in the regulation of sleep and muscle activity during sleep. Since anatomical studies have shown that DA neurons in the VMPJ do not project to the spinal cord and physiological studies have demonstrated that dopamine release in the motor nuclei is not changed during pontine inhibitory area (PIA) and NMC stimulation-induced muscle tone suppression, we hypothesize that the VMPJ dopamine effect on muscle activity is mediated through the caudal brainstem. In the current study, we tested this hypothesis using microinjection technique.

Methods: Experiments were performed in 6 cats decerebrated at the post-mammillary-pre-collicular level. Decerebration was performed under haloxane-oxygen anesthesia and anesthesia was discontinued immediately after decerebration. Bipolar stainless steel electrodes were implanted into the genioglossus and both sides of neck muscle to record EMG activity. A half microliter of dopamine receptor agonists was microinjected into the PIA and NMC to evaluate muscle response to dopamine receptor subtype activation. All agonists were dissolved in artificial CSF and the concentration used was SKF 38393 (a D1 agonist, Sigma): 8 mg/mf^al; quinpirole (a D2 agonist, Sigma): 4 mfÝg/mfÝl.

Results: We found that SKF 38393 microinjected into the PIA (102.7% $\pm$ 7.9% of the baseline) and NMC (97.4% $\pm$ 6.8% of the baseline) failed to change muscle tone. In contrast, dopamine D2 receptor agonist, quinpirole, microinjected into the NMC (48.5% $\pm$ 10.6% of the baseline), but not the PIA (96.2% $\pm$ 8.4% of the baseline) suppressed muscle tone in both the genioglossus and neck. The latency and duration of NMC-quinpirole-induced atonia were 18.2 sec and 4.8 min, respectively, which are comparable to those after glutamate injections in this region (Lai and Siegel, 1988, latency: 18.1 sec, duration: 4.2 min).

Conclusions: Our result indicated that activation of dopamine D2, but not D1 receptor in the NMC induces muscle tone suppression in both tongue and nuchal musculature. The VMPJ dopaminergic effect on muscle activity during sleep may be mediated through the dopamine D2 receptor in the NMC. We hypothesized that 6-OHDA lesions in the VMPJ eliminate dopamine effect on neuronal activity in the NMC, which in term generate muscle hyperactivity in sleep similar to that seen in human RLS/PLMD patients.

This work supported by NIH grants HL41370 and HL60296 and a research grant from the Restless Legs Syndrome Foundation.

0007.A

Pontine Phasic Activity is Phase-Locked to Hippocampal Theta Wave During REM Sleep in Rats

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Introduction: In cats, ponto-geniculo-occipital wave (PGO wave) is observed in pons, lateral geniculate nucleus, and occipital cortex during REM sleep. We showed that the PGO wave was phase-locked to hippocampal theta wave which is characterized by its sinusoidal slow field potential (about 5 Hz). In rats, a PGO wave-like phasic field potential has been recorded from the pons and the cerebellum, which is referred to as a pontine wave (P wave). In this study, we investigate phase-relationship between P wave and hippocampal theta wave of rats, which is compared with the results from the cats.

Methods: Five Sprague-Dawley rats (400-550g) were used in our experiments. Stainless bipolar electrodes (diameter 0.1 mm) were implanted in the pons (AP -0.4 (intraaural zero), ML 1.0, DV 7.0) and in the anterior lobe of the cerebellum (AP -2.6 (intraaural zero), ML 0.0, DV 7.0) for recording P wave. Stainless monopolar electrodes (diameter 0.1 mm) were implanted bilaterally in the hippocampus (AP -2.0 (bregma), ML 2.5, DV 2.0) for recording the theta wave. The phase relationship between the P wave occurrence and the hippocampal activity was analyzed. This analysis was applied to a single PGO and a first event in a cluster PGO (first PGO), respectively. All experimental procedures involving these animals were performed in accordance with protocols approved by the Institutional Animal Care and Use Committee.

Results: The P waves were observed in all rats and the theta waves were recorded in four of five. The single P waves tended to occur just after the positive peak of the hippocampal theta wave in all the rats. To almost the same degree as the single, the first P waves were phase-locked to the hippocampal theta waves.

Conclusions: We showed that the P waves were phase-locked to the hippocampal theta wave in the rats. This result suggests that the pontine P wave generator is under modulation by theta-related activities. In cats, the first PGO wave in a cluster was less tightly phase-locked to the theta wave than the single PGO waves. This was attributed to possible differences in contributors to generating single and cluster PGO. In contrast, the result here suggests that the generation mechanism of the cluster P wave of rats is similar to that of the single.

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0008.A

GABAergic Mechanisms In The REM Sleep Induction Zone Of The Rat

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Introduction: The caudal aspect of the nucleus pontis oralis (PnOc) in the rat has been referred to as a REM sleep induction zone based on the findings that unilateral injection of a variety of neurotransmitter agonists into this region elicit a long-lasting increase in the expression of REM sleep. Recent studies implicate a role for the GABAergic system in the REM sleep induction zone of the cat inasmuch as injection of GABAa receptor antagonists result in a short-lasting REM sleep induction and GABAa agonists increase wakefulness. In the rat, it has been found that c-fos expression in GABAergic interneurons of the PnOc is reduced during the rebound from REM sleep deprivation. This is consistent with a reduction in GABA transmission during periods of high propensity for REM sleep. In this preliminary report, we sought to determine the action of GABA-receptor ligands in the PnOc of the rat as well as to determine levels of GABA during different states of arousal.

Methods: Under anesthesia, Long-Evans Hooded rats were surgically prepared for chronic sleep recording and additionally implanted with guide cannulae aimed at medial sites in the PnOc. After recovery, one group received multiple unilateral injections (60 nl) of the GABAa

antagonist, bicuculline methiodide (1 mM), the agonist, muscimol (0.68 mM), and four saline vehicle injections, all one week apart and within 1 hr after lights-on. Each injection was followed by 6 hrs of recording. In a separate group, a pin-style microdialysis probe (BR-2, BAS) was perfused at 2 or 4 ul/min to obtain dialysate samples in PnOc during identified states of wake, slow wave and REM sleep in freely moving animals. GABA was assayed by derivatization and HPLC-EC.
Results: Compared to mean control values, bicuculline induced a short-lasting increase in REM sleep, significant in the third hour after injection. This was followed by a tendency towards decreased REM sleep amounts. Muscimol-injection resulted in continuous wakefulness for the first three hours. GABA levels in PnOc were highly related to state. Values for REM sleep were almost half that of wake (REM, SW, AW: 0.11, 0.14, 0.20 pmol/ul, respectively).
Conclusions: These data are consistent with a role for GABA in the PnOc in the control of REM sleep and wakefulness. High GABA inhibitory tone may maintain the localized, sensory- and motor-related excitation observed in the reticular formation during wakefulness. Low levels of GABA during REM sleep may not only permit the more generalized tonic facilitation characteristic of this state, but also may be responsible for disinhibiting the propagation of excitation throughout the reticular formation. The long-lasting effect to increase REM sleep by various agents injected into the PnOc may act commonly to induce a long term inhibition of GABA transmission in the REM sleep induction zone.

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0009.A

Tetrodotoxin Inactivation Of Pontine Regions Suppresses REM Sleep

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Introduction: Studies using various methodologies have implicated n. subcoeruleus (SubC) and n. reticularis pontis oralis (RPO) in the generation of REM. In rats, electrolytic lesions in these regions may give rise to the phenomena of REM without atonia (REM-A) in which the electrophysiological features of REM are normal, except for the absence of muscle tone. However, electrolytic lesions damage both cell bodies and fibers of passage, and the neural reorganization and adaptation that can occur post-lesion can complicate interpretation. Tetrodotoxin (TTX) is a sodium channel blocker that temporarily inactivates both neurons and fibers of passage, and thus may be functionally equivalent to an electrolytic lesion, but without allowing time for neural adaptation. In this study, we examined the influence of microinjections of TTX into SubC and RPO on sleep in freely behaving rats.
Methods: Rats (90 day old male Sprague-Dawley) were implanted with electrodes for recording EEG and EMG. Guide cannulae were implanted aimed into SubC (n=6) or RPO (n=2). Each animal received two bilateral microinjections of TTX (TTX1: 2.5 ng/0.1 µl; TTX2: 5.0 ng/0.2 µl) and control microinjections of saline alone (SAL). The injections were made 2 h following lights on and sleep was recorded for the subsequent 22 h. Sleep was scored from computerized records in 10 s epochs. Recordings from the 10 h light period and the 12 h dark period were examined separately.
Results: Compared to SAL, TTX in SubC increased REM latency (SAL: 75±7.7; TTX1: 395±118, p<.047; TTX2: 554±76, p<.004) and reduced light period REM (TTX1: -44±23.3%, p = .08; TTX2: -83±13%, p<.024) relative to SAL. Compared to SAL, TTX in RPO increased REM latency (Range [TTX1: +77 to 368 min; TTX2: +141 to 504 min]), and reduced light period REM (TTX1: -33%; TTX2: -52%). A small dark period REM rebound occurred after microinjections into RPO (TTX1: +22%; TTX2: +24%), but not SubC. TTX produced smaller reductions in light period NREM% (SubC: -19 to 23%; RPO: -6 to 13%).
Conclusions: TTX inactivation of SubC and RPO suppressed REM sleep with smaller effects on NREM. The results complement studies that have implicated SubC and RPO in REM generation. REM-A was not observed. In animals, post-lesion REM-A often fully manifests over time. This suggests that neural reorganization and adaptation that occurs in response to damage and consequent altered functionality may play a role in REM-A produced by electrolytic lesions, though other lesion sites that produce REM-A need to be examined. Interestingly, specific lesions in the brain are rarely found in human REM behavior disorder (RBD). Instead, RBD is often associated with diseases that are characterized by widespread neural atrophy that also occurs over time.

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0010.A

Effects Of Auditory Stimulation During Different Stages Of REM Sleep

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Introduction: REM sleep is not an uniform phenomenon. It includes two different stages: phasic and tonic. The former one is characterized by the presence of phasic phenomena (eye movements, muscle twitches, PGO-waves), hippocampal theta-rhythm and desynchronized neocortical EEG. During the second stage (tonic)phasic phenomena and hippocampal theta-rhythm are dramatically reduced, alpha-like activity appears in the neocortical EEG. The muscle tone during both these stages is the lowest compared to another sleep-wake states. It is known that auditory stimulation increases REM sleep duration in rats, cats and humans. However these studies have been conducted without special attention to the heterogeneity of REM sleep. In this study we examined the effects of auditory stimulation on the behavioral and polygraphic phenomena during different stages of REM sleep.
Methods: Under nembutal anesthesia seven adult cats were implanted with electrodes for polygraphic sleep monitoring (neocortical and hippocampal EEG, EMG, EOG). After adaptation to the experimental conditions ten 3-hour control polygraphic recordings of sleep-waking cycle were conducted. During the first series of experiments, thresholds for behavioural arousal induced by auditory stimulation (tone 1 kHz, 5 s) during phasic and tonic stages were defined. During the second series of experiments the effects of subthreshold auditory stimulation (80% of threshold intensity) upon polygraphic parameters of two REM sleep stages were analysed. The results were statistically evaluated according to the Student‘s t-test.
Results: The threshold for behavioral arousal in response to auditory stimulus was found to be 26% higher in phasic stage than in tonic one. Subthreshold stimulation in phasic stage in 72% of analysed cases caused the transition to tonic stage with latency not more than 10 s. Subthreshold stimulation in tonic stage resulted in the increase of duration of this stage
Conclusions: The results show that sleep depth decreases during tonic stage of REM sleep compared to the phasic one. The same differences in the threshold for behavioral arousal between these two stages we found previously in response to posterior hypothalamus electrical stimulation (Suntsova et al., 2000). Both auditory and posterohypothalamic stimulations during phasic stage provoke the transition to the tonic one, whereas the stimulation during tonic stage increases its duration. In addition, it has been shown (Dergachyova, Suntsova, 2001) that the activity of posterohypothalamic wake-active neurons during tonic stage is higher than during phasic one. These data suggest that one of the mechanisms underlying the prolongation of REM sleep in response to auditory stimulation is the increase of the percentage of more superficial tonic stage.

0011.A

Inhibition of Rostral Basal Forebrain Neurons Promotes Wakefulness and Induces FOS in Orexin Neurons

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Introduction: The factors regulating the activities of orexin-containing neurons have been examined from the aspect of feeding and metabolism. On the other hand, a circadian variation in the activites of orexin neurons has been demonstrated by use of FOS immunohistochemistry, which raises the possibility that the activities of the neuronal elements regulating sleep-wake states might also influence the activities of the orexin-containing neurons. However, this possibility has not been examined well. The ventromedial portion of the rostral basal forebrain is thought to contain the neuronal elements regulating the sleep-wake states, since the application of several neuroactive compounds in this brain region altered the sleep/wake states of an animal. Thus, we investigated whether the activities of the rostral basal forebrain neurons alter the activities of the orexin neurons.

Methods: Adult male rats of the Sprague-Dawley strain were used. They received the surgical operations monitoring EEG, EOG, and EMG as well as those implanting the microdialysis probes in the ventromedial part of the rostral basal forebrain. After an enough recovery period, we performed following studies in accordance with the Japanese Neuroscience Society Guide for Animal Care and Use of Laboratory Animals. Firstly, we performed microdialysis-perfusion of the ventromedial portion of the rostral basal forebrain of rats with muscimol to make a focal inactivation in this brain region, and then examined its influence on their behavioral state. Secondly, we performed double immunohistochemistry to detect FOS and orexin to examine how this focal inactivation of the rostral basal forebrain neurons influences the activities of orexin neurons. Thirdly, we studied the expression pattern of FOS following the unilateral perfusion of muscimol to examine whether the change in the expression of FOS is simply a consequence of the change in the behavioral state.

Results: Bilateral-perfusion with muscimol (5, 15, and 50 μM) produced a dose-dependent decrease in the amount of sleep. This perfusion with muscimol at 50 μM produced FOS-like immunoreactivity in 37 % of the orexin neurons located in the tuberal part of the hypothalamus, whereas the FOS-like immunoreactivity was sparse in orexin neurons of the sleeping control rats ($p=0.001$ by Mann-Whitney U-test). Unilateral-perfusion with muscimol (50 μM) also suppressed sleep. In this case, FOS-like immunoreactivity was seen in 40 % of the orexin neurons on the side ipsilateral to the perfusion site but only in 10 % of them on the contralateral side ($p=0.018$ by Wilcoxon signed rank test).

Conclusions: These functional data suggested that a sleep-generating element in the ventromedial part of the rostral basal forebrain provide an inhibitory influence on the activities of the orexin neurons in the tuberal part of the hypothalamus.

0012.A

Interactions Between GABAergic and Cholinergic Pontine Reticular Mechanisms in the Control of Active Sleep and Wakefulness

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Introduction: Cholinergic systems within the nucleus pontis oralis (NPO) play a critical role in the generation of active (REM) sleep. We have recently reported that microinjections of GABA antagonists into the NPO produce active sleep, whereas microinjections of GABA agonists produce wakefulness (Xi et al., 2001). These findings indicate that a GABAergic system in the NPO plays an important role in the control of behavioral states of active sleep and wakefulness. We therefore suggest that the generation of active sleep depends on an interaction between pontine cholinergic and GABAergic systems. Specifically, we hypothesize that the excitatory cholinergic control of NPO neurons is gated by a pontine GABAergic inhibitory system. To test this hypothesis, we examined the behavioral responses of chronic, unanesthetized cats following the injection, into the NPO, of cholinergic and GABAergic receptor agonists and antagonists.

Methods: Experiments were performed on three adult cats that were prepared for monitoring behavioral states and for drug administration. The effective NPO region was defined by the stereotaxic coordinates at which an injection of carbachol (0.25 ml, 22 mM) induced active sleep with a latency shorter than 4 min. In experimental sessions, microinjections of carbachol and muscimol, a GABAsAs receptor agonist (0.25 ml, 10 mM), or scopolamine, a muscarine receptor antagonist (0.25 ml, 10 mM) and bicuculline, a GABAsAs receptor antagonist (0.25 ml, 10 mM), were carried out. In all cats, control solutions of saline (0.25 ml) were injected into the same site that received the injection of drugs.

Results: Microinjections of carbachol (n=5) or bicuculline (n=3) into the NPO elicited, with a short latency, active sleep and induced an increase in the time spent in this state. However, muscimol, when it was injected into the same area of the NPO 20-30 minutes prior to the injection of carbachol, completely blocked the active sleep-inducing effects of carbachol; the increase in active sleep induced by carbachol was also abolished (active sleep: 3.1±4.3%, n=4, [muscimol+carbachol] vs. 60.1±5.4%, n=3, [saline+carbachol], $P<0.05$). The induction of active sleep by carbachol was also suppressed by a subsequent injection of muscimol (n=3). On the other hand, the microinjection of scopolamine, followed by bicuculline, did not block the induction of active sleep induced by bicuculline (scopolamine+bicuculline: 51.4±5.7%, n=4).

Conclusions: The present results demonstrate that interactions between cholinergic and GABAergic neurotransmitters exist in the NPO and that they play a critical role in the generation of active sleep. We conclude that the excitatory cholinergic control of the activity of NPO neurons that are involved in the generation of active sleep is gated by a pontine GABAergic inhibitory system. This gate mechanism exerts its effects postsynaptically by direct GABAergic inhibitory control of NPO neurons.

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0013.A

Glycinergic Mechanisms in the Control of Hypoglossal Motor Outflow to Genioglossus Muscle in Natural REM Sleep

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Introduction: Glycine is primarily responsible for inhibition of postural motoneurons in rapid-eye-movement (REM) sleep but its role in the control of respiratory motoneurons is unclear. The hypoglossal motor nucleus innervates the genioglossus (GG) muscle of the tongue, a respiratory muscle important for the maintenance of an open airway and effective breathing. REM sleep recruits powerful neural mechanisms that can abolish GG activity, even during strong reflex respiratory stimulation by elevated CO2 (Horner et al., J Appl Physiol. 2002; 92: 878-887); an effect that predisposes to obstructive sleep apnea in humans. Studies in the pharmacologically induced REM-like state produced by pontine carbachol in reduced animal preparations suggest that both postsynaptic glycinergic inhibition (Yamuy et al., Neuroscience 1999; 94: 11-15) and withdrawal of excitatory neurotransmitters (Woch et al., J

Physiol. 1996; 490: 745-758) may potentially contribute to suppression of GG activity. However, the physiological role of glycinergic inhibition in mediating suppression of hypoglossal motor output to GG muscle in natural REM sleep has not been determined. We developed an animal model to chronically manipulate neurotransmission at the hypoglossal motor nucleus using microdialysis across natural sleep-wake states in rats (Jelev A, Sood S et al., J Physiol. 2001; 532: 467-481). The present study tests the hypothesis that glycine contributes significantly to the suppression of GG activity in REM sleep during room air and CO2-stimulated breathing.

Methods: Ten male Wistar rats were implanted with electroencephalogram and neck muscle electrodes to record sleep-wake states, and GG and diaphragm wires to record respiratory muscle activities. Microdialysis probes were implanted into the hypoglossal motor nucleus, with sites verified by histology, and were perfused with artificial-cerebrospinal-fluid (ACSF) or 0.1mM strychnine (glycine receptor antagonist) during room air and CO2-stimulated breathing (6-8% inspired CO2). We have shown that this dose of strychnine effectively reverses glycine-mediated inhibition of hypoglossal activity (Morrison JL et al. J Appl Physiol. 2002; 93: 1786-1796).

Results: Strychnine at the hypoglossal motor nucleus increased respiratory-related GG activity during room air (P=0.010) but not CO2-stimulated breathing (P=0.221) with the effect in room air being independent of sleep-wake states (P=0.625), i.e., a non-specific release from inhibition. Nevertheless, GG activity was minimal in those REM sleep periods without GG twitches, with GG suppression from non-REM being >85% regardless of ACSF or strychnine at the hypoglossal motor nucleus and room air or CO2-stimulated breathing. GG activation in response to microdialysis perfusion of serotonin at the end of the experiments confirmed an intact hypoglossal motor nucleus in all rats.

Conclusions: The results show that although inhibitory glycinergic mechanisms are present at the hypoglossal motor nucleus, such mechanisms make a minimal contribution to the marked suppression of GG activity and reflex responses in natural REM sleep suggesting different control of postural and respiratory motoneurons.

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0014.A

Sleep Spindles and Slow Waves During Light NREM Sleep Activate Memory

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Introduction: Recent neurophysiolgy hypothesizes that sleep spindles and slow waves during NREM sleep are profoundly associated with learning, especially with memory consolidation during wakefulness before sleep. By recording EEG and fMRI simultaneously during light NREM sleep and followed by an analysis of fMRI data accompanying the occurrence of slow waves and sleep spindles, we succeeded in getting robust activation in several cortical and subcortical areas most of which are associated with memory processing.

Methods: Six normal volunteers (25-47 years old) participated in the experiments. Subjects were instructed to fall and remain asleep in an MR magnet. EEGs (Oz, Pz, Cz, and Fz) and ECG were recorded inside the MR scanner. After removing artifacts caused by magnetic field from EEG, the power spectra of EEGs during the MR scan interval were computed. The power spectrum was divided into the delta, theta, slow alpha, fast alpha and sigma (12-16 Hz) bands, and average powers in each frequency band were calculated. The fMRI data were acquired on a 1.5 T MR scanner. Five hundreds volumes — each consisting of 30 slices (voxel size: 4x4x5 mm; TE: 66 ms, FA: 90 ‹, TR: 8 s.) — were acquired continuously over a period of 66 minutes. During the scans, the MR magnet room was kekept absolutely dark and no stimulus was presented except for MR scan noise. The fMRI data were analyzed using SPM99. We entered the time series of theta-band and sigma-band as user-specified regressors in the design matrix to find activation areas accompanying occurrence of theta waves and sleep spindles, respectively.

Results: In spite of the unusual sleeping conditions, all the subjects reached sleep stage 2. Though the subjects did no task, several brain areas were activated accompanying increases in slow waves and occurrence of sleep spindles. The hippocampus, parahippocampal gyrus, lingual gyrus and BA 10 were activated accompanying slow waves during light NREM sleep. The thalamus, pulvinar, and retrosprenial cortex were activated accompanying occurrence of sleep spindles. As for the posterior temporal, posterior cingulate and putamen, these areas were activated accompanying occurrences of either sleep spindles or slow waves, or both.

Conclusions: Neuropsychological and brain imaging studies suggest that not only the hippocampus and parahippocampal gyrus, but also the lingual gyrus, retrosplenial cortex and BA 10 play an important role in memory processing. Recent neurophysiology hypothesizes that sleep spindles and slow waves relate to memory reprocessing for consolidation during NREM sleep. This hypothesis is based on animal studies in which neural structures (place cell in the hippocampus and only a few neocortical neurons) engaged in the process of learning during waking could be re-activated for memory consolidation during subsequent NREM sleep. Taken together, the result of the present study suggests that memory reprocessing for consolidation occurs during light NREM sleep involving several cortical and subcortical areas in human brain.

0015.A

Inhibitory Control Of REM Sleep By Medial Septal Neurons In Rats

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Introduction: A number of basal forebrain structures including septum have been implicated in the regulation of sleep-wakefulness (S-W). Neuronal activity of septum is correlated with S-W. Electrolytic lesion studies of the medial septal (MS) area indicate that hippocampal theta wave is dependent on the integrity of this area. However, cell specific lesion studies to find out the involvement of the MS in sleep are lacking. This study was hence undertaken to find the role of the MS neurons in sleep.

Methods: The study was carried out in 6 adult male Wistar rats (180-250g) with chronically implanted electrodes for recording sleep parameters i.e. EEG, EMG and EOG, continuously for 24 hrs. All the recording electrodes were connected to an IC socket and the whole assembly was fixed to the skull with dental cement. After post-operative recovery, all the parameters were recorded for 24 hrs. The cell specific neurotoxin NMDA (5ml in 0.2ml saline) was injected intracerebrally to destroy the MS neurons and all the parameters were recorded again for 24 hrs on days 7th and 21st. S-W was assessed on the basis of EEG, EOG and EMG recordings taking 30 sec epochs and calculated into stages i.e. wakefulness (W), slow wave sleep (S1, S2), and rapid eye movement sleep (REM). The comparison of these components of the S-W of rats was made between the prelesion (control) with postlesion values i.e. day 7th and 21st of MS lesion, using Friedman's two way ANOVA. At the completion of the experiment, the lesion sites were confirmed histologically using cresyl violet staining.

Results: The lesion in the MS produced an increase in wakefulness and a decrease in S1 as well as S2 when compared with the control values. There was an increase in REM sleep when compared with the control values. The percentage of REM sleep (ratio of REM sleep time and total sleep time) on both postlesion days showed a marked increase (16.5% and 15.7%) when compared with the prelesion values (11.1%). There was decrease in percentage of slow wave sleep on day 7th (83.5%) and 21st of lesion (84.3%) compared to prelesion control (88.9%). Although, the data did not reach statistical significance but increase in REM sleep and decrease in slow wave sleep were very evident in this study. This is

in contrast to the earlier reports on the role of other basal forebrain areas on S-W.
Conclusions: The present findings suggest that the MS may be involved in the regulation of SWS and the inhibition of REM sleep.

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0016.A

Orexin A and B Levels Change in the Hypothalamus During the Estrus Cycle and Ageing in Female Rats

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Introduction: Orexins A and B are novel hypothalamic neuropeptides which have been shown to regulate food intake, energy balance, autonomic nervous system, vigilance states and secretion of several hormones. Infusions of orexin A have been shown to increase wakefulness and decrease sleep. These observations suggest that orexins may play a role in the regulation of vigilance states. Orexin cells in the lateral hypothalamus send projections to several brain areas, including the nuclei, which regulate vigilance states and the hypothalamus. We have previously shown that orexin gene expression and the brain levels of both orexin A and B decrease in the course of ageing in male rats. Sleep varies across the menstrual cycle in women and across the estrus cycle in female rats. In female rats both non-REM sleep and EEG power density in the delta band were lower in proestrus than in other phases of the estrus cycle. We hypothesised that changes in hypothalamic orexin levels may at least partially explain the changes in nonREM sleep during the estrus cycle.
Methods: 40 young (3-4 mo) and 30 middle aged (7-8 mo) female rats were inspected for vaginal smears for at least 5 cycles. Of the young rats 6.6% had irregular cycles, while more than 60% of the one year old rats had irregular cycles. Rats were decapitated at different phases of their estrus cycle, and brain tissues and trunk blood were collected. Orexin A and B were measured from the hypothalamic tissue using radioimmunoassay.
Results: Both orexin A and B were higher during the proestrus day than on other days of the estrus cycle in young and old rats. Both orexin A and B levels in the hypothalamus were lower in old than young animals regardless of the cycle day.
Conclusions: Since orexin A increases waking and decreases sleep, the increase in orexin content during proestrus could at least partially explain the decrease in sleep during the proestrus day. The physiological significance of increased vigilance is obvious, since the females prepare to mate. As in males, also in females the amounts of both orexin A and B peptides decrease during ageing. The decrease in non-REM sleep during proestrus can at least partially be explained by increased orexin levels.

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0017.A

Effect Of The Wake-Promoting Agent Modafinil On Sleep-Promoting Neurons From The Ventrolateral Preoptic Nucleus: An In Vitro Pharmacological Study

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Introduction: A large body of experimental and clinical data suggest that the pharmacological profile of modafinil, an increasingly popular wake-promoting drug used in the treatment of narcolepsy, differs from those of classical psychostimulants such as amphetamine. The brain targets on which modafinil acts to induce wakefulness are however still a matter of debate. We made the hypothesis that modafinil could increase waking by inhibiting the GABAergic sleep-promoting neurons from the ventrolateral preoptic area (VLPO). Such action could be direct or indirect via the potentiation of an inhibition induced by a waking neurotransmitter. To test this hypothesis, we studied the effect of modafinil application on the membrane potential and firing rate of VLPO neurons recorded in rat brain slices. We also determined whether a modafinil pretreatment modify the effect of noradrenaline, carbachol, serotonin, histamine, dopamine, and clonidine application on VLPO neurons activity.
Methods: Brain slices containing the VLPO were obtained from 15-20 days old rats (OFA) according to standard procedures. Individual 300 or 400mm thick slices were transferred to a thermoregulated (32°C) chamber, under either a dissecting microscope for sharp intracellular recordings or a Zeiss Axioscop with an infrared camera for juxtacellular recordings of identified cells. Slices were maintained immersed and continuously superfused at 3-5 ml/min with oxygenated ACSF. Two parameters of the drug responses were systematically quantified: 1) the amplitude corresponding to the maximal change in firing rate (in Hz or percentage of the basal firing rate) and 2) the duration of the effect (in min). Amplitude and duration of the effect were compared between control, drug and wash conditions using a paired Student's t test.
Results: Pretreatment with modafinil (20, 60, 100, 200 mM) specifically increased the inhibition of VLPO neurons induced by noradrenaline (0.5, 1, 10, 100mM) but had no effect when applied alone or in combination with serotonine (100 mM), carbachol (5 mM) or histamine (100 mM). Furthermore, pretreatment with modafinil did not increase the inhibition induced by dopamine (10, 100 mM) and clonidine (0.05 mM). Pretreatment with nisoxetine (10 mM), a selective noradrenaline reuptake blocker, similarly increased the noradrenaline-induced inhibition of VLPO cells. Further, the potentiation by modafinil was occluded when modafinil and nisoxetine were co-applied.
Conclusions: These results suggest that modafinil blocks the reuptake of noradrenaline by the noradrenergic terminals on sleep-promoting neurons from the VLPO. Such mechanism could at least partially be responsible for the waking effect of modafinil, through the potentiation of the tonic noradrenaline inhibition, present during waking, on GABAergic sleep-promoting neurons from the VLPO.

0018.A

Changing Photic Stimulation Induces Phase-Locking Between Visual Units and Theta Rhythm in Wakefulness and Sleep

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Introduction: The hippocampal theta rhythm (q) was shown to be associated with movements, attention, auditory processing, autonomic functions, learning and memory and has been postulated as an associator of discontiguous events. We had reported phase-relationships between q rhythm and visual/auditory unit firing with both spontaneous and evoked activity during wakefulness, slow wave and paradoxical (REM) sleep. It is our tenet that the described phase-locking contribute to the information processing during wakefulness and even during sleep. The dynamic of the visual units temporal correlation with q rhythm is our present research target looking for phase-locking induced fluctuations.
Methods: Guinea-pigs were implanted with conventional electrodes for sleep-wakefulness control. A craniotomy over the lateral geniculate (LGn) region was made and left open for glass microelectrode access. Two metal bars attached to the skull permitted the stereotaxic position reproduction. Visual stimuli consisted of flashes of light at different frequencies. The visual evoked extracellular unitary activity was analyzed with peri-stimulus time, interval and autocorrelation histograms. The hippocampal electrogram (bipolar recording) was studied using wave-

form autocorrelation and power spectra. The crosscorrelation between hippocampal q field activity and spikes was obtained by spike-triggered averaging and was considered significant when it became flat calculated with the same data after "shuffling" the spike series. Our aim was to compare the temporal correlation between the unit and the hippocampal q before and after sudden frequency light flashes shifts. This paradigm was applied both in wakefulness and sleep.
Results: In wakefulness as well as in slow wave sleep q rhythm periodically appears well organized in the hippocampal electrogram for 6-8s epochs while the probability of phase-locking between the LGn unitary and the q rhythm increased. This event sequence was observed several times throughout recording sessions with continuous and regular photic stimulation. On the other hand, after a sudden change in flash frequency, q waves amplitude and power increased while the unit firing phase-locking probability was enhanced for about 4-6 seconds. This induced temporal correlation was observed in wakefulness and slow wave sleep.
Conclusions: The phase-locking between visual units and q rhythm is a time fluctuating phenomenon. This changing temporal correlation may be present without any known provoking factor and/or during regular photic stimulation; it could be the result of attention shifts in wakefulness. The induced phase-locking -by modifying the stimulus condition- is a phenomenon that appears during waking and also slow wave sleep, thus, assuming that the visual processing may be present in both states. We hypothezise that q rhythm could contribute introducing a temporal dimension to the processing of visual information in sleep and waking.

0019.A

Sleep Responses to 5-Hydroxytryptophan (5-HTP) Are Altered in Interleukin (IL)-6 Deficient Mice

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Introduction: Serotonin is a neurotransmitter whose effects on arousal state have been studied for nearly four decades. In an attempt to synthesize seemingly paradoxical observations of the effects of serotonin on sleep, it has been proposed that serotonin itself promotes wakefulness, but induces the release of distinct, sleep-promoting substances that initiate subsequent sleep. These purported sleep-promoting substances remain to be identified. Cytokines such as IL-1 and IL-6 are immunomodulatory molecules known to influence sleep-wake behavior. Serotonin promotes the release of IL-1, which in turn induces the synthesis and release of IL-6. IL-6 promotes NREM sleep in rats. To test the hypothesis that IL-6 mediates the increases in NREM sleep observed following serotonergic activation, we determined sleep-wake behavior from IL-6-deficient mice after administration of 5-HTP, a serotonin precursor known to enhance serotonergic activity.
Methods: C57BL/6J (B6) and B6.129S6-Il6tm1Kopf (IL-6 KO) mice (Jackson Labs) were surgically implanted with transmitters (DSI ETA F20) to measure core body temperature and the electroencephalogram (EEG). Activity was monitored with infrared motion detectors. The mice were maintained on a 12:12 h L:D cycle at 27°C. On separate days, animals received intraperitoneal injections of vehicle, 50 or 100 mg/kg 5-HTP (Sigma Chemicals) 15 min prior to dark onset. Animals were recorded for 24 h beginning at dark onset. Polygraphic signals were digitized and stored for subsequent determination of arousal state.
Results: Temperature: Both strains responded to 50 mg/kg 5-HTP with a hypothermic response that lasted 2 h (B6:-0.70 $\pm$ 0.10 ºC; IL-6 KO: -0.62 $\pm$ 0.07 ºC). The hypothermic response to 100 mg/kg 5-HTP was more pronounced and lasted longer (B6:-0.79 $\pm$ 0.08 ºC; IL-6 KO: -1.20 $\pm$ 0.11 ºC). NREM sleep: 50 mg/kg 5-HTP produced a transient reduction in NREM sleep of both strains for ~2 h, but had no significant effects on sleep-wake behavior thereafter. NREM sleep of B6 mice was not altered by 100 mg/kg 5-HTP (vehicle: 28 $\pm$ 4%; 5-HTP: 32 $\pm$ 5%). In contrast, NREM sleep of IL-6 KO mice increased for 6 h after 100 mg/kg 5-HTP (vehicle: 22 $\pm$ 4%; 5-HTP: 39 $\pm$ 3% $p < .01$).
Conclusions: Though the sleep responses of IL-6 KO mice to 5-HTP differ from those of control mice, these data do not support the hypothesis that IL-6 mediates the sleep-promoting effects of serotonin. The hypothermic responses to 5-HTP indicate biological activity in this system. However, the increase in NREM sleep of IL-6 KO mice after 5-HTP suggests that the absence of IL-6 decreases the sensitivity to the NREM sleep-suppressing effects of 5-HTP, thereby unmasking the effects of a putative sleep-promoting substance induced by 5-HTP. Additional studies to elucidate mechanisms mediating these responses are underway.

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0020.A

Anandamide Enhances Extracellular Levels Of Adenosine And Induces Sleep In Rats

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Introduction: Marijuana has been used for social and religious purposes for many years.There is increasing evidence that marijuana has medicinal value also. It is given to suppress nausea and vomiting and improve appetite during chemotherapy treatment. The principal component of marijuana, delta-9-tetrahydrocannabinol (delta9-THC) increases sleep in humans (3). Endogenous cannabinoids, such as anandamide (ANA), also increase sleep (2). The mechanism by which the cannabinoids promote sleep is not known but could be linked to an induction of endogenous sleep factors such as adenosine (AD). To test this hypothesis we measured sleep and extracellular levels of AD in the basal forebrain after injection of ANA and the cannabinoid CB1 receptor antagonist, SR141716, alone or in combination with the endocannabinoid, ANA.
Methods: Three-month-old male F344 rats (n=6) were implanted with sleep recording electrodes and a microdialysis guide cannula (IC guide, BAS) into the basal forebrain cholinergic neurons (MCPO; A= -.35; L= 2.0; H= 8.5). Animals were then placed in a cage with unrestricted mobility with food and water ad lib and housed at constant temperature (21 $\pm$ 1oC) and under controlled light-dark cycle (lights on: 07:00 to 19:00h). ANA and the CB1 receptor antagonist SR141716 were dissolved in DMSO (40% in saline). Microdialysis sampling procedure. The microdialysis probe (BAS 1mm of length) was inserted 24h before sampling of AD levels. The following day at 07:00h, animals received DMSO as a vehicle. ANA (10mg/kg) was administered on day 3. SR141716A was administered (1mg/kg) on the fourth day. In the last day, in order to block the effects of ANA, SR141716A was injected (1mg/kg in 0.5 ml) and 15 min later ANA (10 mg/kg in 0.5 ml). Immediately after the injections (ip in 1ml), sleep recordings were obtained (from 7:00-12:00h). After injections, microdialysis samples were collected (5ul) every hour (flow rate= 0.25ul/min).Adenosine and Sleep analysis. AD levels were determined using HPLC. The EEG data recordings were scored for W, SWS and REM sleep.
Results: Levels of AD were increased during the first 3h after administration of ANA ($p<0.0001$). Combination SR141716A + ANA blocked the increase of AD. ANA caused a significant increase (54.5%) in SWS in the third hour and SR141716A + ANA abolished the increase in SWS caused by ANA ($p<0.05$).
Conclusions: An interaction between the CB1 and the AD A1 receptor has been described (1). Our results indicate that the sleep-inducing effects of endocannabinoids are mediated in a region of the brain implicated in arousal and that these effects are via a CB1 receptor. These findings identify a possible use of ANA to induce sleep in conditions where

sleep maybe severely attenuated.

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0021.A

GABAergic Control Of Orexinergic Neurons In The Regulation Of Behavioral States

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Introduction: We have shown that local perfusion of antisense oligonucleotides against orexin-II receptor in the subcoerulean reticular formation increased REM sleep and induced cataplexy-like episodes in rats whereas, microdialysis perfusion of orexin-A in the cholinergic basal forebrain increased wakefulness. These studies suggest that increased orexinergic tone induces wakefulness, whereas reduced orexinergic tone increases REM sleep. What controls the orexinergic neurons? GABA, with actions mediated via the GABA-A receptor, may be one such neurotransmitter. To further evaluate the role of GABAergic control of orexinergic neurons in the regulation of sleep-wakefulness, microdialysis perfusion of a specific GABA-A agonist, gaboxadol (THIP) in the orexinergic zone of the hypothalamus was performed and its effect on sleep-wakefulness was monitored in freely behaving rats.
Methods: Using standard surgical procedures, adult male Sprague-Dawley rats (300-400 g) were implanted with standard sleep recording electrodes to record the EEG and the EMG. In addition, guide cannula targeted toward the orexinergic zone of the hypothalamus (AP -3.3; ML = 1.5; DV = 8.5 from bregma) was also implanted. After 4 days of post-operative recovery and habituation, the microdialysis probe was inserted through the guide cannula. After 12 hours of recovery from probe insertion, the experiment was begun. CMA/11 probes were used with a 1 mm length and 0.24 mm O.D. dialyzing membrane (CMA/ Microdialysis; Acton, MA). All experiments were conducted during the light cycle, in a sound-attenuated chamber that had the same temperature and light conditions (lights on at 0700h and lights off at 1900 hours) as the animals' home cages, with food and water available ad libitum. Rats were connected to a polygraph cable for behavioral state recording and then to the probe inlet and outlet. Unilateral perfusion of artificial cerebrospinal fluid (ACSF = NaCl 147 mM, KCl 3 mM, CaCl2 1.2 mM, MgCl2 1.0 mM, pH 7.2) and/or THIP was carried out at a flow rate of 2.0 ml/min. The details of the protocol are: Time of Day Control Day Experimental Day09.30 – 11.00 hr ACSF ACSF11.00 – 14.00 hr ACSF THIP (1, 10 or 100 mM)14.00 – 15.30 hr ACSF ACSF After the completion of the experiments, the animals were sacrificed, brains removed and processed for histology and immunohistochemistry to localize the zone of perfusion.
Results: The result of our study suggests that THIP perfused in the orexinergic perifornical region of the hypothalamus significantly decreased wakefulness and increased nonREM sleep (n=7; $p<0.05$; one way repeated measure ANOVA). The maximum effect was observed with the highest dose (100 mM), where nonREM showed an increase of around 25% and wakefulness showed a decrease of about about 20%. To our surprise, we did not find any change in REM sleep.
Conclusions: Our data suggests that GABA, with actions mediated by the GABA-A, receptor may play an important role in the control of orexinergic neurons.

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0022.A

Vesicular Transporter Proteins for Glutamate (VGluT), GABA (VGAT) and Acetylcholine (VAChT) in Terminal Varicosities of Basal Forebrain Neurons Projecting to the Posterior Lateral Hypothalamus

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Introduction: The basal forebrain plays an important role in the control of wake and sleep states through projections to the cortex and also to subcortical structures, including the posterior lateral hypothalamus where significant wake-promoting neuronal systems lie (Gritti, Mainville and Jones, JCN, 1994). By retrograde transport, this descending projection was found to be composed of some cholinergic, many GABAergic and other unidentified basal forebrain neurons. Using dual and triple immunostaining combined with anterograde transport of biotin dextran amine (BDA), we examine here whether terminals of basal forebrain neurons in the posterior lateral hypothalamus and vicinity of orexin containing cells contain the vesicular transporter proteins for glutamate (VGluT2), GABA (VGAT) or ACh (VAChT).
Methods: Long-Evans rats (200-250 g) were operated under ketamine/xylazine/acepromazine (65/5/1 mg/kg, i.p.) anaesthesia. BDA (10 kDa) was applied iontophoretically through micropipettes into the region of the magnocellular preoptic nucleus (MCPO) and substantia innominata (SI) and allowed ~5 days for anterograde transport. Frozen sections were processed for dual or triple fluorescent staining. The vesicular transporter proteins were stained first using antibodies to VGluT2, VGAT or VAChT that were revealed by red fluorescent, Cy3-conjugated secondary antibodies. BDA was subsequently stained using green fluorescent, Cy2-conjugated-streptavidin. Finally, orexin was immunostained using blue fluorescent, AMCA-conjugated secondary antibodies.
Results: Clusters of basal forebrain neurons were labeled in the MCPO or SI and gave rise to BDA-labeled fibers and varicosities that were evident in the posterior lateral hypothalamus. Few BDA-labeled varicosities were double-labeled for VAChT, whereas larger numbers were double-labeled for VGAT. In addition, varicosities were double labeled for VGluT2. The transporter proteins were evident within boutons en passage and terminaux. Some were visible near orexin-immunopositive neurons in the region.
Conclusions: According to the here documented presence of GABAergic and glutamatergic beside a smaller proportion of cholinergic projecting fibers, basal forebrain neurons have the capacity to influence wake-promoting neurons of the posterior lateral hypothalamus in diverse ways. Indeed, these transmitters are contained in functionally distinct basal forebrain cell groups (Manns, Alonso and Jones, JN, 2000). Accordingly, sleep-active and wake-active basal forebrain neurons (Lee, Manns, Alonso and Jones, APSS, 2003) could respectively act by suppressing and exciting the wake-promoting cells of the posterior lateral hypothalamus, including the orexin neurons.

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0023.A

Studying Local Sleep Homeostasis with High Density EEG in Humans

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Introduction: In many species, sleep homeostasis is reflected by the amount of EEG slow-wave activity (SWA, power density 0.75-4.5 Hz) during non-rapid eye-movement (NREM) sleep. Topographical differences in SWA have been reported in both human and animal studies

(human: Werth et al., 1997; rat: Schwierin et al., 1999; mouse: Huber et al., 2000). In two studies, local differences in SWA were directly related to a use dependent recovery process (human: Kattler et al., 1994; rat: Vyazovskiy et al. 2000). High-density (256 channel) analysis of sleep EEG is a promising method to characterize local, task related EEG changes with increased spatial resolution.

Methods: Sleep in three healthy subjects was recorded during a 2-h night-time sleep episode using a Geodesics Sensor Net composed of 256 electrodes. Each subject completed two sessions separated by one week. During the hour before sleep subjects were engaged with a serial reaction time task (containing a pseudorandom or an implicitly learnable sequence), or with a visual control task. Waking EEG recordings (4 times 1-min, eyes open) were carried out before and after the tasks. For both the waking and sleep EEG a semi-automatic artefact removal based on power in two frequency bands (1-4.5 and 20-30 Hz) was performed. Power spectra of consecutive 4-s epochs (FFT routine, Hanning window) were calculated. Power maps of EEG in different frequency ranges were calculated.

Results: Inspection of the average sleep EEG power maps within each of the sessions revealed a predominance of power in the delta band (1-4 Hz) over the frontal cortex and minimum values over temporal areas of the cortex. Power in the spindle frequency range (12-15 Hz) was maximal along the midline. However, the peak in the fast spindle frequency range (14-15 Hz) differed in different subjects varying form 1.5 to 7.5 cm posterior to Cz along the midline. On average the area of increased power relative to the all-brain mean was 31.8 cm2, corresponding to 20 electrodes. Within-subject comparisons showed that the topographic power distribution between the two experimental nights were extremely similar.

Conclusions: To our knowledge this is the first time high density EEG recordings were successfully performed during sleep. Overall, the present findings are in agreement with an extensive study of sleep EEG topography by Finelli and co-workers (2001) based on 29-electrode all-night recordings. The results also confirm that the EEG power distribution is highly individual, possibly reflecting anatomical differences. Within each subject the high-density distribution of EEG power during sleep was highly reproducible in two nights separated by one week. Single-subject, high density analysis is thus a promising approach to 1) precisely characterize topographical changes in SWA that occur during sleep 2) determine whether local SWA changes are due to use or to plasticity and 3) investigate whether topographical changes in the sleep EEG are correlated with changes in waking EEG.

0024.A

Oxidative Stress and Cellular Damage After Sleep Deprivation

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Introduction: Oxidative stress occurs whenever there is an imbalance between oxidant production and antioxidant defenses, either because the former is increased and/or because the latter are decreased. At the cellular level, such imbalance can result in structural damage due to oxidative modifications of proteins, lipids and nucleic acids. It is currently unclear whether any oxidative damage occurs during sleep deprivation, nor it is known, should this be the case, whether sleep could play a protective role. The aims of this study were four: 1) measure antioxidant enzyme activity and cellular oxidant production to determine whether sleep deprivation causes, and recovery sleep relieves from, oxidative stress; 2) measure lipid peroxidation and protein oxidation to search for direct evidence of cellular damage after sleep deprivation; 3) determine whether sleep deprivation has differential effects in the brain (cerebral cortex) compared to peripheral tissues (liver, skeletal muscle); 4) compare the effects of short sleep deprivation (8 hours; gentle handling) with those of prolonged sleep loss (6-14 days; disk-over-water method).

Methods: Polygraphically recorded male WKY rats (300-450 g) were sacrificed when they met the criteria for the following 5 experimental conditions: 1) spontaneous sleep for 8 h (n=6), 2) short-term (8 h) total sleep deprivation (n=7), 3) long-term (6-14 d) total sleep deprivation (n= 11 pairs), 4) recovery sleep after long-term (7 d) total sleep deprivation (n=5 pairs) and 5) recovery sleep after long-term (7d) REM-selective sleep deprivation (n=6 pairs). Cellular oxidant production was estimated in homogenates by monitoring the rate of oxidation from DCFH to fluorescent 2'-7' dichlorofluorescein (DCF). Peroxidative damage to cellular lipids was determined by measuring malondialdehyde formation. Protein oxidation was estimated by measuring carbonyl formation using 2,4- dinitrophenylhydrazine. Superoxide dismutase activity (CuZn and Mn SOD) was determined spectrophotometrically.

Results: Long term sleep deprived rats lost 63 ± 4% (mean ± SD) of their non-REM sleep and 95 ± 4% of their REM sleep, while the yoked controls lost 28 ± 14% and 42 ± 25% of their non-REM and REM sleep, respectively. In the cerebral cortex, oxidant production increased by ~25% in short-term sleep deprived rats relative to their sleeping controls but did not change in long term sleep deprived rats relative to their yoked controls. SOD enzymatic activities, lipid peroxidation levels and protein oxidation levels in brain, liver and muscle were similar in all experimental groups.

Conclusions: This study measured the effect of total sleep loss on markers of oxidative stress (oxidant production and antioxidant enzyme activities) as well as on markers of cellular oxidative damage (lipid peroxidation and protein oxidation). The results show no evidence of oxidative damage, nor any indication of oxidative stress as a result of sleep loss, in any of the tissues examined. Therefore, our data do not support the hypothesis that prolonged waking may represent an oxidative challenge.

0025.A

Whole-cell Patch-clamp Recordings From Rat Subcoerulean Neurons In Vitro: Effects Of Carbachol And Orexins

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Introduction: The subcoeruleus region of the pontine reticular formation is an important brainstem site involved in the generation of muscle atonia during rapid-eye-movement (REM) sleep. A subpopulation of neurons in this region enhance their firing during REM, presumably in response to excitatory input from cholinergic REM-on neurons in the laterodorsal and pedunculopontine tegmentum - injection of cholinergic agonists into the subcoeruleus region elicits signs of REM sleep, including muscle atonia. One characteristic of the sleep disorder narcolepsy, which is caused by disruption of the orexin/hypocretin system, is periods of muscle weakness triggered by emotional arousal (cataplexy). We have recently shown that perfusion of antisense nucleotides directed against the type II orexin/hypocretin receptor in the subcoeruleus region of the rat leads to attacks of cataplexy. At present no data exist regarding the intrinsic membrane properties of neurons in this region or the modulation of membrane properties of these neurons by cholinergic agonists or orexins/hypocretins.

Methods: Coronal brainstem slices were prepared from 8-16 day-old rats using a vibratome. Preliminary experiments established that the extensive network of myelinated fibres made it very difficult to slice the brain tissue or obtain high-quality recordings in rats older than 16 days, whereas in rats younger than 8 days the lack of obvious landmarks made it difficult to precisely localize the subcoeruleus area. Two brain slices between -9.16 and -9.8 from bregma rostrocaudally (according to the Atlas of Paxinos and Watson) were cut from each animal and placed (after incubation for 1 hr in a prechamber) in a modified Haas-type recording chamber, where they were perfused with oxygenated (95% Os2s/5 % COs2s) artificial cerebrospinal fluid. Patch electrodes (3-6 MO, when filled with a potassium gluconate based intracellular solution) were positioned in the area of the subcoeruleus (subCA, subCD and

subCV) using a dissecting microscope. Whole-cell current-clamp recordings were obtained using the 'blind' method and drugs applied via the perfusion line.
Results: The effects of the cholinergic agonist carbachol (2 or 10) and/or the orexins (100, 200 or 500 nM) were tested in 12 neurons in the presence of the blocker of voltage-dependent sodium channels, tetrodotoxin (0.5). Carbachol caused a depolarization (5/9 neurons), hyperpolarization (3/9) or no effect (1/9). All three neurons which were hyperpolarized were located in the more dorsal portion of the subcoeruleus region. 7 of 11 neurons were excited by orexins, the other 4 neurons showed no effect. Orexins depolarized both neurons which were hyperpolarized by carbachol and those which were depolarized.
Conclusions: The lack of orexin excitation of the subcoerulean neurons (which we have shown here) in narcolepsy may be responsible for the previously reported upregulation and supersensitivity of another main input to these neurons - the cholinergic projection from the laterodorsal and pedunculopontine tegmentum.

0026.A

Chronic Hypoxia Leads to Oxidative Stress in Rat Cerebellum

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Introduction: It has recently been reported that patients with obstructive sleep apnea (OSA) showed significant gray matter loss in several brain regions including the cortex, hippocampus and cerebellum, suggesting that sleep apnea results in neuronal damage. Hypoxia is a common feature of OSA. Rats subjected to chronic hypoxia showed increased apoptosis in the CA1 hippocampal region and cortex. It is proposed that hypoxia induced damage results from oxidative stress. We therefore investigated the effects of chronic hypoxia on several markers of oxidative stress. Using biochemical assays, we measured the activities of the antioxidative enzymes superoxide dismutase (SOD), glutathione peroxidase (GPx) and glutathione reductase (GR) as well as the levels of the endogenous antioxidant, total glutathione (GSHt) and the levels of the lipid oxidation product, thiobarbituric acid reactive substances (TBARS).
Methods: Young adult (45-50d) male Sprague Dawley rats were exposed to either chronic intermittent hypoxia (CIH) or chronic sustained hypoxia (CSH) for 6h, 1d, 3d, 7d, 14d or 30d. The IH profile consisted of alternating room air with 10% oxygen every 90s during the light phase (6:00AM-6:00PM), while the SH profile consisted of 10% oxygen throughout the light phase. CIH and CSH rats were exposed to room air throughout the dark phase (6:00PM- 6:00AM), whereas control rats were placed in room air throughout the 24h cycle. Analysis of variance and linear regression was used to determine statistical significance at a level of $p<0.05$.
Results: SOD activity was significantly elevated in hypoxia exposed rats relative to controls ($F(1,54)=15.04$, $p=0.0003$). There was no significant difference in SOD activity between CIH and CSH exposed rats and no linear effect of time on SOD activity. GPx activity was also significantly increased in hypoxia exposed rats relative to controls ($F(1,54)=20.17$, $p=0.00004$). There was no significant difference in GPx activity between CIH and CSH exposed rats, but there was a significant linear trend of increased GPx activity with increased exposure time to hypoxia ($F(1,54)=31.11$, $p=0.0000008$). The level of TBARS was significantly increased in hypoxia exposed rats relative to controls ($F(1,82)=13.31$, $p=0005$). Furthermore, rats exposed to CSH showed significantly higher levels of TBARS compared to rats exposed to CIH ($F(1,82)=5.70$, $p=0.02$). Also there was a significant linear effect of increased TBARS levels with increased exposure time to hypoxia ($F(1,82)=19.61$, $p=0.00003$). No significant changes in the activity of GR nor in the levels of GSHt were observed in hypoxia exposed rats compared to controls.
Conclusions: This study provides strong evidence that exposure to chronic hypoxia results in oxidative stress, as indicated by the increased activities of SOD and GPx (antioxidative enzymes) and the enhanced levels of TBARS (lipid oxidation product). Oxidative stress may be a step in the biochemical pathway producing brain damage in sleep apnea.

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0027.A

State-Dependent Release of Glycine and GABA in Clarke's Column of the Upper Lumbar Spinal Cord

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Introduction: Evidence now exists that spinal neurons conveying proprioceptive sensory information via the dorsal spinocerebellar tract (DSCT) are subjected to dynamic suppressor influences during naturally occurring active sleep when compared to wakefulness or quiet sleep. We recently reported that microiontophoretically administered strychnine or bicuculline markedly reduced the active sleep-related suppression of spontaneous and glutamate-driven spike activities of DSCT neurons (J. Neuroscience, 22: 5777-5788, 2002) suggesting that glycine and/or GABA inhibit these neurons during active sleep. Further support for this notion as well as useful insight on the pathways underlying active sleep-related suppression of transmission through the DSCT would be provided by direct evidence for the active sleep-related release of glycine and GABA. The present study employed microdialysis techniques to measure state-dependent release of classical inhibitory amino acid neurotransmitters glycine and GABA in Clarke's column.
Methods: Two adult cats were prepared for sleep state recording and identification of Clarke's column dorsal spinocerebellar tract neurons as previously described (ibid). The location of Clarke's column at L3 was confirmed electrophysiologically by recording characteristic short-latency (2.9-3.2 ms) field potentials evoked by low-intensity stimulation of the anterior lobe of the cerebellum. The recording electrode was carefully replaced with a dialysis probe (Model A-I-40-02, Eicom, Kyoto, Japan). The probe tip was finally positioned at the same spinal cord depths where maximal amplitude field potentials were recorded and allowed to equilibrate for at least 2 hrs. Behavioral state was continuously monitored and dialysis samples (10 microliters) collected during wakefulness, quiet sleep, active sleep and re-awakening from active sleep. Dialysis samples were stored at -80 degrees C. Glycine and GABA levels in the dialysates were determined by HPLC with fluorescent detection (excitation at 340 nm and emission at 440 nm, Soma S-3350).
Results: Data obtained across 19 complete sleep wake cycles indicate glycine levels were increased in Clarke's column by ~40% during the state of active sleep when compared to preceding episode of wakefulness ($p<0.05$, repeated measures ANOVA, Tukey test). There was no significant difference in the levels of glycine between the states of wakefulness, quiet sleep or re-awakening from active sleep ($p>0.05$) GABA levels measured from 12 sleep cycles also demonstrated a similar profile and increased by ~34% during active sleep when compared to preceding episodes of wakefulness ($p<0.05$).
Conclusions: Our present study found that glycine and GABA release in Clarke's column significantly increases during the state of active sleep. These data provide additional support for the idea that dynamic inhibi-

tion during active sleep contributes to the reduction of sensory throughput to higher brain centers conveyed via the dorsal spinocerebellar tract. Glycine and GABA may be (co-)released by local segmental inhibitory interneurons and/or long projection neurons located in higher brain areas. The neurons releasing glycine and GABA onto Clarke's column DSCT neurons may be part of the same neural systems that result in glycine-mediated inhibition of motor outflow.

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0028.A

The Use of Rat Models to Investigate the Behavioral and Neurobiological Consequences of Sleep Apnea

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Introduction: The primary characteristics of obstructive sleep apnea (OSA) are intermittent hypoxia (IH) and sleep interruption (SI) (fragmentation). The IH and SI are thought to produce the symptoms/signs associated with OSA which include daytime sleepiness and various cognitive/attentional impairments. However, it is not known which symptoms are attributable to SI and which to IH because these events are difficult to separate in humans. Here we describe our preliminary work with two rat models that allow the separation of the effects of SI and IH. We hypothesize that the SI associated with OSA, but not the IH, is primarily responsible for the symptom of daytime sleepiness seen in OSA, and that this is mediated by adenosine (AD) effects (Strecker et al. Beh. Brain Res. 2000:115 p.183). In contrast, we predict that IH treated rats will sleep normally after the first 2 days of IH exposure (Gozal et al. J. Neurosci. 2001:21 p.2442). We also plan to test the hypothesis that many of the learning and memory impairments observed in patients with OSA are the result of chronic IH, acting via cell injury/apoptosis in cortical areas involved in cognitive functions.
Methods: A) SI paradigm. A rat model of the sleep fragmentation that occurs in OSA was produced using an automated rat treadmill operating on a cycle of 30s on and 90s off, 24 h/day, for 7 days (i.e., 30 brief awakenings per h). Control groups included an exercise control with equal amounts of time the treadmill is off and on, but with 10 min on and 30 min off, allowing deep sleep. B) IH paradigm. Rats were exposed to a schedule of IH to model the hypoxemia of OSA. Daily exposure (12h; 07:00 to 19:00; £ 7 days) to continuous sinusoidal cycling of inspired oxygen levels (10% O2 for 120 s : 21 % O2 for 120 s) was used. We have begun to investigate the effects of SI and IH at multiple levels, from the molecular to the behavioral.
Results: A) SI paradigm. Rats began to sleep during the 90s undisturbed periods within several h of SI onset, and they continued to awaken during the 30s treadmill operation for the 7 days tested. During the first 6 h of SI, extracellular AD levels in the basal forebrain rose steadily (~2 fold; N=2) resembling the rise previously described with total sleep deprivation, and a measure that may reflect increased sleep pressure. B) IH paradigm. The IH schedule produced a desaturation to 74 % on day 1, resembling the desaturation seen in OSA. Although severe hypoxia has been reported to increase extracellular AD levels, we found that 70 min exposure to the IH regimen produced only a modest rise in basal forebrain AD levels (140 % of baseline; N=3), which quickly returned to basal levels, even before the IH was terminated.
Conclusions: The availability of rat models of OSA will enhance our understanding of the neurobiological mechanisms underlying the symptoms of OSA, an important step toward future work on the targeted development of therapies to treat and/or prevent the symptoms of OSA.

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0029.A

Spontaneous Diurnal And Sleep Deprivation-Induced Fluctuations In Adenosine Levels In The Rat Basal Forebrain

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Introduction: The purine nucleoside adenosine (AD) has been proposed to be an endogenous sleep factor, facilitating sleepiness by inhibiting neurons of the magnocellular basal forebrain (BF). This region is thought to play an important role in the regulation of cortical arousal and the maintenance of wakefulness. Work in the cat has demonstrated that 6h of sleep deprivation (SD) led to a rise in extracellular AD in the BF and cortex. The proposed research extends these findings to the rat, a nocturnal species with a diurnal pattern of sleep-wakefulness that more closely resembles that of man. We predict that BF AD levels would rise spontaneously during the later half of the rat's active period, correlating with the homeostatic sleep drive.
Methods: In vivo samples were collected from microdialysis probes in the BF of Sprague-Dawley rats, and analyzed with a microbore high performance liquid chromatography system coupled to UV detection. Diurnal fluctuation: Rats were kept on a lights on 7 AM/off 7 PM schedule. Beginning at least 14h after probe insertion, 3h samples were collected. Sleep Deprivation: After evaluation of diurnal fluctuation of AD levels, hourly samples were collected, beginning at 10 AM on the day of SD. At 1 PM, experimenters kept animals awake for 6h by means of gentle handling, followed by 3h of recovery sleep.
Results: During the last 6h of the light cycle/sleep period spontaneous levels of BF AD reached a nadir (1 to 7 PM). As well, BF AD levels peaked during the second half of the active period (1 to 7 AM). Six h of SD produced significant increases in BF AD levels, which did not return to baseline with 3h of recovery sleep.
Conclusions: The homeostatic sleep drive occurs daily in the rat with a diurnal pattern of sleep-wakefulness, being maximal at the end of the active period and minimal at the end of the rest/inactive period. These experiments support a role for AD as an inhibitory sleep factor acting on select brain regions and arousal-related neuronal subtypes. Additional work is needed to confirm that the clear SD-induced increase in BF AD depends primarily on different sleep and activity levels, and, to a lesser extent, on a circadian influence. Understanding the site-specific mechanisms by which AD influences arousal and sleep will benefit research related to various sleep disorders including sleep apnea and insomnia.

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0030.A

AMPA-Induced Intracellular Calcium Responses are Inhibited by Interferon g in Primary Cultures of Fetal Hippocampal Neurons

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Introduction: Interferon gamma (IFN g) is a cytokine that enhances non rapid eye movement sleep (NREMS) in rabbits (Kubota et. al. 2001, J. Neuroimmunol. 119, 192-198). Although IFN g is primarily thought to act as an immune system modulator, IFN g is produced in the central nervous system by astrocytes and microglia, and IFN g receptors are found in neurons, astrocytes and oligodendrocytes. Further, IFN g-like immunoreactivity is present in some neurons. These observations suggest that IFN g may participate in the regulation of sleep. The mechanism by which IFN g affects neurons to produce brain mediated actions is not understood. In the present study we tested the hypothesis that INF

g alters the function of AMPA-type ionotropic receptors, an important mediator of synaptic activity.
Methods: Hippocampal neurons were cultured from day 18-20 fetal rats. Isolated hippocampi were washed in Hank's Balanced Salt Solution and incubated for 15-20 min at 370C. After incubation, cells were mechanically dissociated by several gentle aspirations into a 20 cc syringe through a 22 G needle. Dissociated cells were then centrifuged and resuspended into Dulbecco's Modified Eagle's Medium (DMEM) with 10% fetal calf serum. The cells were plated onto 100 mg/ml poly-l-ornithine coated 22 mm square glass coverslip in a 6-well plate. The cells (1-2 x 10cells/coverslip) were grown in DMEM supplemented with 10% fetal bovine serum for 2 days and then in DMEM with serum supplement (1 mM apotransferrin, 5 mg insulin, 60 nM sodium selenite and 100 mM putrescine) in a humidified atmosphere of CO2:air (5:95) at 37C. After 9-12 days of culture intracellular Ca++ levels were determined by ratiometric imaging techniques in single neurons by the use of fura-2.
Results: Acute exposure (2-5 min) to IFN g (10-20 ng/ml) did not alter intracellular Ca++ levels, however, calcium increases induced by AMPA (10 mM) were attenuated by 40 % in the presence of IFN g, an effect that was reversible upon IFN g washout. Chronic exposure (30 min to 24 h) to IFN g did not alter subsequent AMPA-induced calcium responses measured in the absence of IFN g. IFN g had no effect on calcium responses induced by depolarization with high K+.
Conclusions: These data suggest that IFN g may alter neuronal activity by an acute action to decrease AMPA receptor function. The relationship between this cellular action of IFN g and the NREMS inducing effects of IFN g remains to be determined.

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0031.A

Maintenance Of Wakefulness In Orexin Knockout Mice

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Introduction: The cause of sleepiness in narcolepsy is unknown but may be due to increased sleep drive, decreased wake drive, or behavioral state instability, with low thresholds to transition between states. Orexin knockout (KO) mice have a narcolepsy-like phenotype with short bouts of wakefulness, sleep fragmentation, and behavioral arrests resembling cataplexy (Cell, 1999, 98: 437). We studied orexin-KO mice under a variety of conditions to determine which of these processes is likely to underlie the sleepiness of narcolepsy.
Methods: Male, 3-4 month old, orexin-KO mice (backcrossed with C57BL/6J for 6-8 generations) and wild-type (WT) littermates were implanted with EEG and EMG electrodes and temperature/activity transmitters (TA-F20, DSI). After 2 weeks of recovery, recordings were performed on a 12:12 LD cycle (lights on 7am). Behavioral states were scored in 10 second epochs using Sleep Sign software (Kissei Comtec) followed by manual correction.
Results: Both groups of mice had similar amounts of wake and NREM sleep, but the orexin-KO mice had more REM sleep during the night, with little diurnal variation. Orexin-KO had more than twice as many bouts of wakefulness, but these were much shorter than in WT. During the dark period, a typical wake bout in WT lasted about 20 minutes whereas in orexin-KO, wake bouts usually lasted only about 5 minutes. During this period, 60% of wakefulness in WT mice occurred in bouts >21 minutes, but only 20% of wake in orexin-KO mice occurred in bouts of this length. To determine whether these short wake bouts might be due to decreased waking drive, we transferred mice to new cages at 1pm, and both groups remained awake for about 45 minutes. To determine whether orexin-KO mice might have altered sleep homeostasis, we deprived orexin-KO and WT mice of sleep for 2-8 hours using gentle handling. Both groups had normal amounts of recovery NREM sleep with a clear increase in the number and duration of NREM bouts, though orexin-KO mice still had some sleep fragmentation.
Conclusions: These experiments help define the mechanisms resulting in poor maintenance of wakefulness in orexin-KO mice. In contrast to mice lacking histamine (Jour Neurosci, 2002, 22:7695), the ability of orexin-KO mice to fully maintain wakefulness in a new environment suggests that their wake-promoting systems are relatively intact. An increase in homeostatic sleep drive also appears unlikely because orexin-KO mice have normal NREM rebound after sleep deprivation. Their normal amounts of wake and NREM sleep also makes these processes unlikely. Orexin may play an essential role in stabilizing wakefulness, and the behavior of these mice may be a consequence of behavioral state instability, with low thresholds to transition between wake and sleep.

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0032.A

Sleep Dependence Of The High Frequency (600Hz) Evoked Response In Rat Sensory Cortex

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Introduction: During the early phase of cortical evoked responses, a brief burst of low-amplitude, high frequency (300-1000Hz) spike-like wavelets are superimposed on the post-synaptic response. These wavelets most likely arise from thalamo-cortical circuits involving inhibitory feedback mechanisms within the cortical layers. Only a few investigators have looked for the high frequency component of the evoked response, and this component has not been adequately assessed in rodents across sleep states. Additionally, local neural groups may exhibit sleep like states semi-independent of each other and organism sleep state, and changes in the burst patterns could be used to measure a particular neural group's state. We expect to see state dependent changes in the burst patterns, which may be independently observable across different cortical columns.
Methods: The sleep dependence of the high frequency responses were investigated in Sprauge-Dawley rats with cortical screw electrodes over the somatosensory cortex. Stimulation pulse, EKG, respiration, neck EMG, and four cortical EEG signals were continuously recorded (5ksps) during 6h periods in the middle of the light cycle. Animals were continuously presented with 0.2ms auditory clicks at random intervals (1-2s ISI). Each evoked response was filtered (300-1000Hz) and grouped into state. Averages were performed on blocks of 60 or more seconds of each state to provide a quantitative measure of the burst pattern across state.
Results: High frequency bursts were observed during the early part of all evoked responses, regardless of sleep state. However, the peak to peak amplitude of the burst during quiet sleep was 30% larger and lasted twice as long when compared to the bursts generated during waking. Bursts during REM sleep were of similar amplitude as that during waking, but with a longer duration as seen during quiet sleep.
Conclusions: Since our electrodes were placed over the somatosensory cortex with the reference screw located caudal to the auditory cortex, we would expect any responses to result from the entire volume of the auditory cortical tissue. Thus, our results are consistent with the findings of other investigators who record evoked potentials 1 to 2mm deep to the surface. The larger burst amplitude during quiet sleep probably coincides with the larger post-synaptic potentials also occurring during this state, and may reflect reduced inhibition of the thalamic input. Similar-

ly, the longer lasting burst duration during both quiet sleep and REM sleep may result from an oscillatory circuit that is not as strongly inhibited during sleep. We propose that the circuitry responsible for generating both the post-synaptic and high frequency burst response can be influenced at the local level (e.g. cortical columns) by sleep promoting substances, and thus the particular high frequency burst patterns observed may provide a marker for the state of the individual neural groups.

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0033.A

Cardiac Cycle Influence On The Sensory Evoked Response In Rat

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Introduction: Few investigators have examined the relationship of the cardiac cycle and sensory acquisition, and those studies have created somewhat of a controversy on the behavioral significance of cardiac cycle and observed relationships. Early studies may suggest that EEG activity is related to events within the cardiac cycle, and that there may be a baroreceptor influence on the processing of sensory information. However, details of the observed relationships were not examined in depth, and it is difficult to conclude significance from these early reports. A cardiac influence on the evoked response has profound implications on the interpretation of trial based stimulation experiments, especially if the trials occur at regular intervals. We examined the temporal relationship between the cardiac cycle and evoked activity within the sensory cortex.
Methods: The relationship between the evoked response and cardiovascular activity was examined by recording whisker and auditory stimulated evoked potentials from the sensory cortex of the rat, under both ketamine/xylazine anesthesia and freely behaving conditions. An amplifier and computer data acquisition system continuously recorded eight channels (Stimulation pulse, EKG, Respiration, Neck EMG, and four cortical EEG signals at 5ksps). During the recordings, animals were continuously presented with 0.2 ms auditory clicks or contralateral whisker stimulation at random intervals (1-2s ISI). Each evoked response was grouped into 2ms time bins relative to the peak of the EKG R-wave. In chronic studies, evoked responses were also separated by sleep state.
Results: Under anesthesia, we observed a 20% reduction in the averaged evoked response to whisker stimulation, when the peak of the evoked response occurred approximately half way between EKG R-waves. In the chronic experiments, whisker stimulation is currently not possible during natural sleep states, and the chronic auditory evoked response was small (10%) compared to the whisker stimulation; thus, significant variability in the evoked potential precluded conclusive results. However, there is some suggestion that the 20% reduction in evoked potential is preserved during quiet waking, but reversed in direction during quiet sleep.
Conclusions: The observed relationship between stimulus delivery within specific time periods of the cardiac cycle, and patterns related to state could have a large impact on how evoked potential data should be most efficiently acquired in future experiments. Phase coupling of EKG with a regular ISI, or phase locking of the cardiac cycle with a regular stimulus would affect the amplitude of evoked responses. Additionally, trial by trial analysis of individual evoked potentials show a significant amount of variability, which at least in part, could be due to the phase of the cardiac-respiratory cycle during which a stimulus was presented. Previous publications have demonstrated the significance of the cardiac cycle within behavioral studies; thus, further investigation is prudent to further examine these relationships.

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0034.A

Sleep Dependence Of Auditory Evoked Potentials In Rat Sensory Cortex

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Introduction: Studies of cortical evoked responses in rat show a complex series of waveforms from population post-synaptic potentials and population spikes. Many studies have shown that the amplitude of the evoked potential is state dependent. However, the state related differences vary significantly between studies presumably based on animal model differences and electrode placement. Few studies have adequately addressed sleep related evoked potential changes in the rat model. Additionally, within a single experiment there are significant differences in the amplitude of the evoked response across stimuli. We address at least some of the variability by examining spontaneous fluctuations in the auditory evoked potential continuously across long periods of sleep/wake states and plotting the responses across time.
Methods: Continuous 3 to 6 hour recordings were acquired from freely behaving rats in their home cage with recording screws placed over the sensory cortex. Four channels of cortical EEG and one channel each of EKG, respiration and neck EMG were recorded while providing 1-2 second random interval click stimuli. Sleep state was determined by post-hoc analysis and time triggered evoked potentials were divided into state averages. Individual trials were also plotted against each other in continuous time series plots.
Results: We observed a 36% increase in the amplitude of the largest peak of the evoked potential during slow wave sleep when compared to waking. REM was not significantly different but showed an additional component at 35 ms which was not present during slow wave sleep or waking. Changes in the evoked potential across states were easily recognized by following the shape of the evoked response across continuous plots of time triggered evoked potentials. By plotting the peak amplitude of the evoked potential, we also observed spontaneous fluctuations in the auditory evoked responses of local field potentials in individual brain regions during sleep states with a period of 60 seconds. These fluctuations were different across corresponding contralateral regions and organism sleep state suggesting an independent and localized origin.
Conclusions: The differences in amplitude of the evoked potential across sleep states could be a result of relaxed thalamic control of the input to the cortex during slow wave sleep. There were significant differences in the temporal pattern of the periodic fluctuations across brain regions suggesting that the signals were unique to a particular brain area and not a product of a brain wide phenomenon. We believe that these fluctuations could represent the state changes of individual neural groups that are independent from the organism as a whole.

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0035.A

Glucocorticoids Mediate The Effects Of Sleep Deprivation On Brain Glycogen and Glucose Levels

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Introduction: Glycogen is the largest energy reserve in the brain and levels decrease in some brain regions after prolonged sleep deprivation

(SD). The variation in glycogen levels among brain regions after SD may be due in part to secretion of glucocorticoids during SD. The glucocorticoid, corticosterone (CORT), is markedly elevated during SD and glucocorticoid activity varies greatly by brain region. Because CORT inhibits glucose uptake in central and peripheral tissues, we hypothesized that elevations in CORT during SD would facilitate utilization of brain glycogen stores and that eliminating endogenous CORT would prevent reductions in brain glycogen after SD.

Methods: Adrenalectomized (ADX, n=9) and intact (n=8) 34 day old rats were subjected to a 6-h SD by gentle handling beginning at the daily time of lights-on. Rats were immediately sacrificed after SD by microwave irradiation (3.5 kW/1.7 sec). Tissue samples from the cortex, cerebellum, brainstem, hippocampus, and liver were assayed for glycogen and glucose content. Plasma was obtained to assay for CORT and glucose levels.

Results: SD reduced glycogen levels in the cerebellum and hippocampus by 23% (P<0.001) and 9% (P=0.02), respectively, in intact rats whereas ADX prevented these effects. SD did not alter glycogen levels in the cortex or brainstem of intact animals, but did increase cortical glycogen levels to 43% (P<0.001) above controls in ADX animals. SD in intact animals increased glucose levels in the cortex by 28% (P=0.03), but had no effect in the cerebellum, brainstem, or hippocampus. SD did, however, decrease glucose levels in ADX animals in all four brain regions [cortex, 23% (P=0.003), cerebellum, 32% (P>0.001), brainstem, 34% (P<0.001), hippocampus, 25% (P<0.001)]. Corticosterone increased 17-fold in intact animals during SD (P<0.001). SD increased liver and blood glucose by 55 and 15%, respectively (P<0.01), but had no effect on these measures in ADX rats. SD had no effect on liver glycogen in intact or in ADX rats.

Conclusions: Eliminating endogenous CORT attenuated reductions in brain glycogen normally observed after SD in intact animals. These results are consistent with the role of glucocorticoids in facilitating brain glycogen and glucose utilization during SD as they do in response to other energetic demands. Glucocorticoids seem to play a role in brain glucose homeostasis because ADX animals had significantly lower glucose levels in all brain regions even though blood and liver glucose levels were normal. Thus, low brain glucose levels in the presence of elevated peripheral glucose levels in ADX rats may not necessarily signal an energy shortage in the brain, but may reflect a decrease in energy expenditure by central neurons. These data also suggest that differences in cortical levels of glycogen after SD among inbred mouse strains may be due to strain differences in glucocorticoid response to SD.

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0036.A

Enhanced Cortical Synaptic Plasticity in Post-Critical Period Rats After REMS Deprivation

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Introduction: REMS deprivation extends the postnatal critical period (PCP) when an *in vitro* form of cortical synaptic plasticity can be demonstrated. Subsequent studies suggest that suppressing REMS in rats that are beyond the PCP does not evoke this developmentally regulated expression of synaptic plasticity. Here we support these findings, but show that there is an interim period when REMS deprivation affects this form of synaptic plasticity in post-PCP rats. However, this revived plasticity is only able to be evoked for about three weeks beyond the normal PCP.

Methods: REMS deprivation was effected by the multiple-pedestal-over water method, with modifications to accommodate the older animals used in this study. The somewhat larger pedestals (7.0 cm) allowed the animals to obtain variable amount of sleep before the loss of postural control ended the ongoing sleep bout. Postnatal (PN) ages of the rats ranged from PN37 to PN 60 at the start of the treatment, which continued for seven to ten days until the animal was sacrificed, the brain extracted and prepared for in vitro, long-term potentiation (LTP) studies. The recording electrode was positioned in visual cortical layer II-III. The stimulation electrode was positioned either in the middle layer (IV) or at the interface of layer VI and underlying white matter (the WM-interface). After a stable baseline of 20 min, theta burst stimulation (TBS) was delivered through the stimulation electrode. The response was assessed 20 min after TBS and was required to exceed baseline values by 120%. As a control for the viability of the tissue, a failure of WM-interface-stimulated LTP (that is, a failure of the developmentally regulated form of LTP), was accepted as a valid negative datum only if TBS directed at layer IV in the same animal resulted in LTP. For this study, the animals were grouped into two age-groups, a younger group (PN44 to 60 at the time of testing, n=8) and an older group (PN61-68, n=8).

Results: TBS of the WM-interface did not potentiate layer II-III responses in any of the animals in the older group (0 / 8). On the other hand, in the younger group of rats TBS of the WM-interface resulted in LTP in seven of the eight animals. Animals in the older group consistently failed to exhibit LTP after stimulation of the WM-interface with TBS compared to the younger group (Pearson's 2 = 9.14, with continuity correction, p 0.001).

Conclusions: As indicated by ability to induce LTP after TBS is delivered to the WM-interface, developmentally regulated synaptic plasticity can be easily extended by REMS-deprivation in PCP rats. In addition, for about three weeks after the end of the usual PCP for its induction, a short period of REMS-deprivation during this interim phase can cause the molecular changes necessary to once again evoke this type of cortical synaptic plasticity. After this short interim period, however, this particular, developmental form of synaptic plasticity becomes impervious to the influences of the removal of the cortical activity that occurs during REMS. It appears that whereas the usual course of developmental events may lead to a consolidation of this type of synaptic plasticity in visual cortex, the mechanisms that effect this plasticity remain accessible to influences of altered sleep patterns for a short period of time. Insofar as LTP is a model of plastic molecular changes that underlie developmental synaptic rearrangements, and learning and memory, these results suggests that during what is the adolescent period for a rat, REMS continues to affect brain development, memory and learning, for an additional period of weeks.

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0037.A

Orexin-2 Receptor Selective Agonist, [Ala11]orexin-B Promotes Wakefulness In Freely Behaving Rats

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Introduction: Orexins A and B are novel neuropeptides involved in the regulation of feeding and arousal state. Orexin-containing neurons are localized in the lateral hypothalamic area and densely project to the locus coeruleus, ventral tegmental area, dorsal raphe nuclei and tuberomammillary nucleus (TMN). Recent report show that there is direct synaptic connectivity between orexin nerve terminals and histaminergic neurons in the TMN where the orexin-2 receptor (OX2R) is abundantly expressed. Previously, we also reported that icv infusion into the third ventricle of both orexins A and B induced significant arousal effect in the rats. The data indicated that orexin A is more effective in causing a state of arousal than orexin B at the same dose. Orexin A has equal affinity for both the orexin-1 (OX1R) and OX2R but orexin B only shows affinity for the OX2R. Hence, orexins A and B may play important physiological roles in the regulation of sleep-waking cycle through both the OX1R and OX2R receptor sites. In this study, we investigate the effects of

intracerebroventricular (icv) infusion into the third cerebral ventricle of newly developed OX2R selective agonist, [Ala11]orexin-B on the sleep-waking cycle in rats.
Methods: Male Sprague-Dawley rats were chronically implanted with cortical EEG and neck EMG electrodes. A stainless steel cannula for icv infusion was chronically inserted into the third ventricle. EEG and EMG were monitored for three consecutive days, during continuous icv saline infusion at a rate of 10 ml/h. For 5-h diurnal period, [Ala11]orexin-B (1, 10, 40 nmol/50ul saline) replaced the icv infusion of saline.
Results: [Ala11]orexin-B at the dose of 10 nmol markedly increased the amount of wakefulness by 153.7 % ($n=4$, $p<0.05$) whereas orexin B at the same dose caused an increase of 99.8 % ($n=6$, $p<0.01$) over the baseline value. [Ala11]orexin-B caused dose-dependent increase in wakefulness. The enhancement of wakefulness was due to a marked reduction in both non-REM sleep and REM sleep.
Conclusions: Icv infusion into the third ventricle of OX2R selective agonist, [Ala11]orexin-B induced significant arousal effect in the freely behaving rats. The efficacy of [Ala11]orexin-B is comparable to that of orexin B at the same dose. The result indicates that OX2R mediate physiologyical regulation of arousal state in the freely behaving rats. Thus, our results suggest that exogenous administration of orexin B agonist, [Ala11]orexin-B might be useful therapeutically for the treatment of sleep disorders.

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0038.A

A Developmental Investigation of Eye Movements During Paradoxical Sleep as a Biological Marker in a Demyelinating Disease in the Rat

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Introduction: Taiep rats are myelin mutant rats that present with a progressive demyelination of the central nervous system, marked by an accumulation of microtubules in the oligodendrocytes in several areas, including the optic nerve. The resulting symptoms are tremor, ataxia, immobility, epilepsy, and paralysis (taiep). Previous work has shown that eye movement density (EMD) is decreased in taiep rats compared to normals in 12-hour electrophysiological recordings during the 12-hour part of the light cycle. Taiep rats at age 4 and 8 months were compared to age-matched normal rats to determine the following: developmental progression of the amount of EMD during paradoxical sleep (PS) in taiep rats; the relationship of EMD to the light-dark cycle in taiep rats; and assessment of qualitative differences in eye movements between taiep and normal rats.
Methods: Nine male taiep rats and nine male normal rats between the ages of 90-120 days underwent surgical implantation of epidural electrocorticographic (ECoG) and electromyographic (EMG) electrodes from the temporalis muscle, according to standard procedures. In addition, electrodes were inserted bilaterally on the nasal side of the orbital bone to record electro-oculographic (EOG) activity. After 3 adaptation days, each rat underwent 24-hour recordings at both 4 months and 8 months. A 12/12 hour light /dark cycle (lights on at 06:00) was used and room temperature maintained 22-26 degrees. Each record was scored using 22 second epochs for PS episodes, EMD, duration of episode, and artifact. An algorithm-based program was developed to identify and score eye movements and calculate EMD.
Results: There were many salient features to this study to determine EMD as a biological marker. Taiep rats, on average, had shorter PS episodes ($p<.01$) and less total PS time ($p<.01$) than their normal counterparts. Time of day effects were broken into four 6-hour segments starting at 06:00. There was some direction towards older taiep's having increased EMD during the dark cycle than normal rats. EMD was not significant by condition or age, although young taiep rats did have less EMD than young normals ($p=.08$). Qualitative results indicate older normal rats have more eye movements (EM) in a faster frequency range (15-17 Hz) than older taiep rats ($p<.01$). Young normals rats tend to have a faster inter-EM interval (60-80 ms) than younger taiep rats ($p=.08$).
Conclusions: Our findings suggest that measures of EMD during PS can distinguish differences between a demyelinating diseased and a normal group of rats. The decrease in EM frequency, fragmented PS episodes, and time of day effects all suggest differences due to demyelination in the areas of eye movement generation and possibly circadian rhythm synchronization. EMD differences were apparent in the young group, but variability due to the disease may have compromised any real effects. Measuring EMD during PS may be another tool used in detection and progression of demyelinating diseases, and may undercover additional impairments.

0039.A

Congenital Agenesis Of The Corpus Callosum In Mice Is Associated With Altered Regional Sleep EEG Dynamics In Mice

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Introduction: Global changes of low frequency EEG power in NREM sleep are considered to reflect variations of an intensity parameter of sleep. Evidence is accumulating that under increased sleep propensity not only the temporal evolution of the EEG changes, but also its topographic dynamics. A larger rebound of the slow-wave activity band (SWA, EEG power between 0.75 and 4.0 Hz) in NREM sleep has been reported in anterior, i.e. frontal derivations, compared to posterior derivations in humans and rodents after sleep deprivation (SD). The physiological significance of regional differences in the SWA rebound in rodents remains unclear. Congenital agenesis of the corpus callosum in mice provides an opportunity to study regional EEG differences during sleep in conditions of altered intra- and interhemispheric neocortical connectivity.
Methods: Sleep was recorded in male mice with a congenital lack of the corpus callosum and in normal C57BL/6 mice during a 24-h baseline, 6-h SD and subsequent 18-h recovery. Two derivations (parietal and frontal) were recorded from each of the hemispheres. The vigilance states NREM sleep, REM sleep and waking were scored and spectral analysis was performed for 4-s epochs. Coherence between hemispheres was computed for artifact-free 12-s epochs.
Results: Interhemispheric EEG coherence differed significantly between the three vigilance states in both mouse strains. In acallosal mice coherence in all vigilance states was significantly lower than in control mice. The largest strain difference was seen in NREM sleep where coherence values were reduced in acallosal mice compared to wild-type mice for all frequency bins. Also in REM sleep and waking, interhemispheric coherence was lower in acallosal mice than in controls with the exception of two frequency bands (REM sleep, 3.5-5.5 Hz; waking, 2.5-7.0 Hz). During recovery from 6 h SD, when sleep pressure is enhanced, the initial frontal predominance of low EEG frequencies in NREM sleep was lower in acallosal mice than in controls.
Conclusions: The state and frequency specific pattern of interhemispheric EEG synchronization in acallosal mice indicates that the corpus callosum plays an important role in the functional interhemispheric interactions during sleep. An interesting observation was the smaller anterior-posterior power gradient in the sleep EEG within a hemisphere after SD in acallosal mice. This strain difference may be a consequence of the known alteration of intracortical connectivity accompanying congenital callosal agenesis due to the formation of the longitudinal Probst bundles.

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0040.A

Effect Of Bicuculline Perfused In DRN On 5-HT Levels In The DRN And FC

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Introduction: The suppression of dorsal raphe neuron (DRN) serotonergic cell firing has been proposed to be an initiator of REM sleep. GABAergic modulation of the serotonergic neurons may be important in such generation of REM sleep and perfusion of a GABA agonist into DRN increase REM sleep. The present study investigated the GABAergic modulation of the DRN serotonergic cells by perfusing the GABAA antagonist bicuculline into the DRN. It was hypothesised that blockade of the DRN GABAA receptors would enhance serotonergic neuronal activity, and thereby increase DRN and frontal cortex (FC) extracellular 5-HT levels and reduce REM sleep amounts. DRN and FC extracellular 5-HT levels were measured and sleep-wake behaviour was monitored.
Methods: Male Sprague-Dawly rats were implanted stereotaxically with electrodes for EEG and EMG recording and guide cannulas in the dorsal raphe nucleus (DRN) and frontal cortex (FC) for drug perfusion and serotonin recovery. Following adaptation to the recording situation, baseline sleep was recorded (day 0). Probes were inserted through the guide cannula 17 hours before first experiment day (CMA 12/1mm and CMA 12/3mm). On day 1 of the experiment the probes were perfused with aCSF continuously (0,8 ml/min). On day 2 of the experiment the DRN probe was perfused with 3/25/30/50/100 mM bicuculline (0,8 ml/min), while the FC probe was perfused with aCSF both experiment days. EEG and neck EMG recording monitored sleep changes. Simultaneously, on-line detection of extracellular levels of serotonin was performed using microdialysis coupled to high performance liquid chromatography with electrochemical detection. The EEG recording started at 09.00 ± 5 minutes and dialysate sampling at 10.00. Probes were histologically verified to be located in the DRN and FC.
Results: 25/30/50 and 100 mM bicuculline perfused in DRN increased DRN 5-HT in a dose dependant matter. The 5-HT levels in FC were not much affected by the DRN bicuculline perfusion. 3 mM bicuculline perfusion into the DRN did not change extracellular levels of 5-HT in DRN or FC compared to aCSF perfusion. Sleep data are being processed.
Conclusions: 3 mM Bicuculline did not alter 5-HT levels, but higher doses perfused in dorsal raphe nucleus increased DRN serotonin levels dosedependently. The finding suggests that GABA play a role in the regulation of DRN serotonergic activity and thereby, possibly in the regulation of REM sleep.

0041.A

Core Body Temperature and Locomotor Activity in Orexin Knockout Mice

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Introduction: Circadian rhythms, sleep/wake state, and locomotor activity are the major factors influencing core body temperature (CBT) in mammals. To determine the relative roles of these factors, we examined patterns of core body temperature in orexin knockout (orexin-KO) mice in which sleep/wake regulation is fundamentally altered [Cell 1999. 98:437-51].
Methods: We studied male, 3-4 month old, orexin-KO mice and wild type (WT) littermates that had been backcrossed to C57BL/6J for 6-7 generations. Mice were implanted with EEG/EMG electrodes and CBT/locomotor activity (LMA) transmitters and allowed 2 weeks to recover. Spontaneous behavior was recorded in 12:12 LD conditions after 5 days of acclimation. CBT and LMA were analyzed in 5 minute intervals. Sleep/wake behavior was scored in 10 second epochs and expressed as Percent Wake, Percent NREM sleep and Percent REM sleep in 5 minute bins. T-tests and two-way analysis of variance were performed using SAS v6.12 for Windows.
Results: The average amounts of wake and NREM sleep did not differ between groups, but the amount of REM sleep was increased in the orexin-KO mice, especially during the dark period. Orexin-KO mice also had less LMA, particularly at the beginning of the dark episode. Average CBT was slightly higher in orexin-KO mice for the entire 24-hour recording but was much less variable during both light and dark conditions, with a dampening of ultradian variations in CBT. CBT was significantly influenced by group (WT vs orexin-KO), by LD condition, and by their interactions. As a function of locomotor activity, CBT was higher during the dark than during the light in both groups, with no difference between the orexin-KO and WT animals. As a function of percent wake, there were significant differences in CBT by group, by LD condition and by their interactions.
Conclusions: CBT is much less variable in orexin-KO mice than in WT mice during both light and dark conditions. Possibly this is due to differences in metabolic rate, but more likely it is due to the exceptionally short bouts of wake and NREM sleep in orexin-KO mice [Cell 1999. 98:437-51]. With such short bouts, CBT does not fall as far during an episode of sleep nor does it rise as far during an episode of wake. Analysis of CBT during constant darkness should eliminate one source of masking effects on CBT and clarify the circadian effects on CBT in these animals. The unique sleep-wake behavior of these animals provides an opportunity to understand the influence of sleep and wake bout length on CBT.

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0042.A

Hypocretin-1 (Orexin-A) Levels in Cerebrospinal Fluid of Rats After Short-Term Stress Procedures

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Introduction: The hypocretins (orexins) are recently discovered neuropeptides and their normal function is not completely understood. However, a number of studies have suggested a role in energy homeostasis, feeding behavior, promotion or maintenance of wakefulness and locomotor activity. Additionally, prepro-hypocretin mRNA expression has been showed to be modulated by glucocorticoids, suggesting that stress procedures can increase hypocretins neurons activity. Hypocretins' content in cerebrospinal fluid has been an easy and useful indirect measurement of hypocretin neuronal activity. For these reasons, we hypothesized that immobilization and cold exposure could increase Hypocretin-1 (Hcrt-1) in cerebrospinal fluid (CSF) of rats.
Methods: We used 3 months old male Wistar rats maintained under water and food ad libitum, constant temperature (22-24ºC) and 12:12 light:dark cycles (lights on 7:00am). The animals were distributed into control groups (n=24), cold groups (n=18), and immobilization groups (n=20). Each group was subdivided into two groups for CSF collection

at lights turn-on (Zeitgber Time-0, ZT-0) and 8 hours after (Zeitgber Time-8, ZT-8). Control (C) groups were maintained in home-cages during these procedures until CSF taps. Cold exposure was performed in a cold chamber at 4ºC, individually inside a wire-mesh cage, for 50 minutes. Animals in the immobilization groups were placed, individually, inside plastic cylinders, 21 X 6cm (length x diameter) for 50 minutes. CSF taps at ZT-0 were performed in the dark period under red lights. CSF Hcrt-1 levels were measured with commercially available 125I RIA kits. Values were expressed as means±SD. One-Way ANOVA followed by Tukey's test to the case of unequal samples sizes was used to determine significance of differences after procedures. Statistical significance was defined as $p<0.05$.

Results: Since firstly a significant difference emerged (Student-t=8.18, $p<0.001$) in Hcrt-1 levels between control groups, we carry out the analysis among experimental groups according to CSF taps schedule (i.e. within ZT-0 and within ZT-8). Significantly differences by ANOVA (Fs(2,27)s=8.77) were revealed at ZT-0. We find a decrease in Hcrt-1 levels after short-term immobilization (879.30±136.02pg/mL; n=9) compared to control (1098.72±148.22pg/mL; n=12) and cold exposure (1150.02±156.63pg/mL; n=9) groups. There were no differences among groups at ZT-8 (control 568.92±168.25pg/mL, n=12; immobilization 694.35±154.70pg/mL, n=11; cold exposure 742.19±223.32pg/mL, n=9).

Conclusions: In conclusion, short-term immobilization or cold exposure were not sufficient to increase Hcrt-1 levels in CSF at ZT-0 or ZT-8. On the contrary, immobilization decrease Hcrt-1 levels in CSF only at ZT-0, when Hcrt-1 was higher in control group.

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0043.A

GHRH Mediates Somatostatin Actions on Sleep

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Introduction: Growth hormone-releasing hormone (GHRH) stimulates GH secretion in the pituitary and promotes non-REM sleep (NREMS) in the preoptic region-anterior hypothalamus (POAH). Somatostatin, which is an ubiquitous inhibitory neurotransmitter in the CNS, inhibits the activity of GHRHergic neurons via sst2 receptors. Previous experiments show that intracerebroventricular (icv) injections of the somatostatin analog, octreotide (OCT), which acts predominantly on sst2 receptors, elicit prompt inhibition of sleep and GH secretion followed by increases in EEG delta power during NREMS. OCT also elicits immediate angiotensin-like effects: drinking, vasopressin secretion, and rises in blood pressure in rats. Inhibition of angiotensinergic activity blocks the angiotensin-like actions of OCT whereas the sleep effects remain unaltered. The aim of the current experiments was to determine the role of GHRH in octreotide-induced sleep responses.

Methods: a) Hypothalamic contents of GHRH and angiotensin II were measured by means of RIA, 10 min, 1 h, 3 h, and 6 h after icv injection of 0.1 mg OCT in rats (n=13-15). b) The brain sites mediating sleep (recorded during the 12-h light period) and drinking responses (10 min postinjection) to OCT were mapped by means of microinjection of 0.02 mg OCT into various structures (n=43) in rats. c) The sleep responses to systemic OCT (200 mg) were determined in normal C57BL/6 mice (n=11), and in mice with non-functional GHRH receptors (n=12). The vehicle was used for control injections in all the experiments.

Results: a) Icv OCT elicited release of angiotensin II 10 min postinjection (-27.1 ± 3.5% below control). GHRH release was inhibited (+31.5 ± 9.1% above control) in hour 1 when sleep was also suppressed. The accumulated GHRH was released between hour 1 and hour 6 postinjection when delta power during NREMS was enhanced.b) Ten microinjections out of 43 tests elicited drinking. Positive drinking sites were in/around the subfornical organ and the rostral periventricular area. In contrast, sleep suppression (-55-60% in hour 1) occurred after OCT injection in and around the arcuate nucleus where GHRHergic neurons reside, and after microinjection into the POAH where these neurons project. These injections did not elicit drinking.c) OCT injection induced prompt drinking, and significant sleep suppression (hour 1) followed by enhancements in EEG delta power during NREMS in control mice. OCT elicited drinking in mice with non-functional GHRH receptors yet it failed to alter sleep.

Conclusions: Stimulation of sst2 somatostatin receptors suppresses sleep via inhibiting GHRHergic neurons. The periventricular structures mediating angiotensin-like effects of OCT do not overlap with the known localization of the GHRHergic system.

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0044.A

Effect of Sleep Deprivation on Seizures Induced by Cocaine

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Introduction: Medical emergency units are increasingly having to deal with convulsions associated with cocaine abuse, which are seen as a major determinant of cocaine-related lethality in humans. Cocaine is an excitatory drug that inhibits catecholamine reuptake and induces sleep deprivation (SD). In view of the fact that SD modifies dopaminergic receptors producing D2 supersensitivity and also alters the action of drugs, the aim of this study was to determine whether SD and other classical stress modalities alter the convulsive seizures induced by cocaine in male rats.

Methods: 50 rats were divided into five groups submitted to SD, footshock, immobilization and forced swimming, and one control group. At the end of a four day period of stress, they were injected with cocaine and placed in observation cages.

Results: In the SD group, 90% of the animals presented cocaine-induced seizures, against only one in the control group. In the other stress groups, seizure was observed in 50% of the immobilized rats, 30% of the rats given footshock and 10% of those submitted to forced swimming. Those submitted to immobilization, shock and forced swimming did not differ significantly from the control group.

Conclusions: Therefore SD may trigger a marked increase in number of cocaine-induced convulsive seizures, indicating that the absence of sleep per se has a stronger effect than the other stress conditions in relation to modulating the convulsive effect of cocaine. These results should be seen as a warning that cocaine users may suffer overdose if deprived of sleep.

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0045.A

Projections From Sleep-Regulatory Regions of the Preoptic Area to the Perifornical Lateral Hypothalamus

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Introduction: The preoptic area of the hypothalamus is a critical sleep-regulatory brain region. Neurons in the median preoptic nucleus (MnPN) and the ventrolateral preoptic area (vlPOA) express c-Fos protein immunoreactivity (IR) during sleep and exhibit elevated discharge rates during both nonREM and REM sleep compared to waking. Using anterograde tracer, we have previously shown that the MnPN projects to

multiple brain regions implicated in the control of arousal, including the hypocretin-IR neuronal field in the perifornical lateral hypothalamus (PFLH). In the present study, we attempted to confirm the MnPN projection to the PFLH using the retrograde tracer, Fluorogold (FG), and to determine if MnPN-PFLH projection neurons exhibit sleep-related fos-IR.

Methods: During a single surgery, rats were prepared for chronic sleep-wake recordings with cortical EEG and neck EMG electrodes and they received a unilateral pressure microinjection of FG (4% in NaCl; 0.2ul volume) aimed at the PFLH. Following a 10 day recovery period, rats were permitted 2 hours of spontaneous sleep from CT2-CT4 in a recording chamber to which they had been acclimated. On-line scoring of sleep-waking states was performed to determine that rats spent at least 70% of the recording time asleep, to ensure c-Fos expression in MnPN and vlPOA neurons. If this criterion was met, rats were sacrificed at CT4. Two sets of sections (40m in thickness) through the preoptic area and PFLH were collected. One set was processed for fluorescent visualization of FG. The other set was immunostained for both FG and fos protein to permit light microscopic detection of single and double-labeled neurons.

Results: Two rats received small FG injections confined to the PFLH area, in the region of hypocretin neurons. In both cases, retrograde labeling was observed throughout the MnPN. In addition, FG-positive neurons were observed ventral to the anterior commissure, extending laterally to the bed nucleus of the stria teriminalis. Few FG-labeled cells were observed in the vlPOA. Preliminary analysis indicated that >50% of the FG-positive neurons in the MnPN were also positive for fos-IR.

Conclusions: These results confirm our previous findings with anterograde tracer, that the MnPN is a significant source of afferents to the hypocretin neuronal field in the PFLH. They further indicate that sleep-regulatory neurons in the vlPOA do not project to this brain region in significant numbers. Preliminary findings indicate that a majority of MnPN-PFLH projection neurons exhibit sleep-related fos-IR. These results, combined with our recent findings that a majority of MnPN sleep-active neurons are GABAergic, supports the hypothesis that the MnPN is a source of sleep-related inhibitory modulation of the hypocretin neuronal system.

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0046.A

Human Sleep Architecture Shifts Due to Auditory Sensory Input

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Introduction: The animal experimental quasi total lack of sensory input and the bilateral surgical cochlear lesion provoked shifts in the sleep characteristics. The sleep analysis of profound post-lingual deaf human patients -that have been successfully implanted with an intra-cochlear devise- was our target to further support the animals´ postulated effects of the auditory input on sleep.

Methods: Two female patients, 67 and 56 years old, were studied up to now. The intra-cochlear surgical implant was carried out ~2 years before with successful hearing results (Vowel recognition, 78-88%; Consonant recognition, 48-55%; Speech tracking, 47-70/min). Four nights sleep (each patient) were analyzed, being the two first nights recorded with the implant OFF (controls) while during the other two nights the cochlear implant was ON. A complete set of electrodes were used for sleep stage diagnosis. Our Human Sleep Unit consists of a bedroom and toilet being the computer placed in an adjacent room. The off-line sleep analysis was done by three different trained judges. Being aware that sleep stages percentages at the ages of our patients are quite variable, we used each patient data as its own control. This non-invasive experiment was carried out according to International rules, our Medical School local regulations and the patients approval.

Results: The first two control nights with the intra-cochlear implant OFF exhibited, in comparison to normal hearing of similar age person, a decreased stage I, increased stage II, no change in stage III while a diminution of the stage IV and enhanced paradoxical (REM) sleep was present. However, the two nights recorded with the implant ON in comparison with the implant OFF nights presented different sleep scoring shifts: both patients showed a variable amount of stage I, a decrease of stage II without stage III changes. The main result was a net increase of stage IV while paradoxical (REM) sleep decreased, showing a closer scoring to normal values. Subjectively, both patients emphasized the recorded night with the implant ON was more restorative, perhaps associated to a higher scoring of stage IV.

Conclusions: The auditory information is constantly arriving at the CNS, both from the body and environment. Moreover, the auditory unitary analysis and stimulation during sleep in animals showed, correspondingly, no-change and firing shifts without any "silent" unit on passing to sleep and a diverse sleep organization. A profound post-lingual deaf person surely has suffer changes in their central auditory neuronal firing and networks organization -cortical plasticity- that, in turn, would affect many other brain cell assemblies determining changes in sleep. We propose that, after a successful intra-cochlear implant, the hearing recovery would produce networks re-organization that in turn would change sleep architecture.

0047.A

Neurons of the Caudolateral Peribrachial Region Express C-Fos During Quiet Sleep

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Introduction: The preoptic region of the hypothalamus has been recognized as a "key" center of the generation of quiet (NREM) sleep (QS). Utilizing Fos immunoreactivity as a marker of neuronal activity, activation of this hypothalamic area has been found to occur during QS in the rat; however, there are no reports regarding c-fos expression in the brainstem during this behavioral state. In the present study, we found that a circumscribed region in the caudolateral peribrachial area of the cat is selectively activated during QS.

Methods: Eighteen adult male cats were prepared for recording during sleep and wakefulness. The animals were maintained for a period of 60 to 90 minutes preceding euthanasia in the following behavioral states: a) quiet wakefulness (QW, n = 4); b) active wakefulness (AW, n = 4), in which the animals were restrained and stimulated with loud clicks; c) QS (n = 4); or d) AS induced by the microinjection of carbachol into the nucleus pontis oralis (AS-carbachol, n = 6). Thereafter, the animals were sacrificed and immunocytochemistry was carried out for Fos, as well as for Fos and choline acetyltransferase or tyrosine hydroxylase. The number and distribution of single and double immunostained neurons were analyzed.

Results: Animals that were sacrificed at the end of the 60 to 90 minutes period of QS exhibited very few Fos immunoreactive neurons throughout the brainstem, with one exception. In all animals a cluster of Fos-immunoreactive neurons was present in the caudolateral peribrachial region (P 3 to 4, L 4 to 5, and H -2.5 to -4, according to Berman's atlas). The number of Fos immunoreactive neurons in this area during QS (63.6 ± 7.0) was significantly higher compared to QW (7.0 ± 2.3, $P < 0.0001$), AW (9.4 ± 2.4, $P < 0.0001$) or AS-carbachol (11.8 ± 2.5, $P < 0.0001$). The Fos immunoreactive neurons in the peribrachial region were neither cholinergic nor catecholaminergic.

Conclusions: In the present study we describe a group of non-choliner-

gic, non-catecholaminergic neurons in the caudolateral peribrachial region that express c-fos during QS. This is the same region that has been previously implicated in PGO-wave generation; therefore, it is possible that PGO activity during the immediate pre-active sleep period could be responsible for the occurrence of c-fos expression that we observed. However, we consider this explanation unlikely because these neurons did not express c-fos during AS-carbachol, a behavioral state that is characterized by a large number of PGO-waves.The present data open new avenues for the exploration of the brainstem control of QS, as well as interactions between brainstem and forebrain sites that are involved in the generation and/or maintenance of QS and AS.

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0048.A

MCH-Containing Neurons and the Control of Sleep and Wakefulness

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Introduction: We have demonstrated that hypocretinergic neurons in the cat are active during wakefulness, in conjunction with somatomotor activity, as well as during active sleep (AS). Neurons that utilize melanin-concentrating hormone (MCH) as a neurotransmitter are intermingled and are functionally related to hypocretinergic neurons. In the present study we examined MCH immunoreactivity in the cat as well as Fos immunoreactivity in MCH neurons during sleep and wakefulness. In addition, we also examined the effects on sleep and wakefulness when MCH was microinjected into the nucleus pontis oralis (NPO), a critical region in the control of these states. Finally, utilizing cholera toxin subunit-b (CTb) as a retrograde marker, we examined MCH-ergic projections to the pontine reticular formation.
Methods: Sixteen cats were used. In two cats, MCH (0.4-1.5 µg, 0.25 µl) was microinjected unilaterally into the NPO while sleep and wakefulness were monitored. In six cats, CTb was applied to the same pontine site. In addition, all animals were maintained for a period of 60-90 minutes preceding euthanasia in one of the following behavioral states: a) quiet wakefulness (n = 3); b) active wakefulness with motor exploratory activity (n = 3); c) active wakefulness without motor activity, in which the animals were restrained and stimulated with loud clicks (n = 3); d) quiet sleep (n = 4); or e) AS induced by carbachol (n = 3). Thereafter, the animals were sacrificed and double immunocytochemistry was performed for CTb and MCH, Fos and MCH as well as for MCH and hypocretin-2. The number and distribution of immunostained neurons were analyzed.
Results: MCH-containing neurons were found in the hypothalamus and zona incerta; co-localization with hypocretin was not observed. MCH-containing neurons were determined to project to areas of the mesopontine reticular formation such as the locus coeruleus, LDT-PPT, dorsal raphe and NPO. C-fos expression in MCH-containing neurons was not detected in relation to the behavioral states that were examined, which is different from the behavioral-dependent activity of hypocretinergic neurons. Microinjections of MCH into the NPO decreased the latency to AS (6.2 ± 1.4 vs. 24.3 ± 2.6 minutes, $P < 0.001$) and produced a small increase in the time spent in this state (23.6 ± 0.8 vs. 18.7 ± 0.9 minutes, $P < 0.005$).
Conclusions: Although anatomical data suggest that the MCH-ergic system may play a role in the control of sleep and wakefulness, we did not observe Fos immunoreactivity in MCH-containing neurons during these behavioral states. In addition, the effects on sleep obtained by the microinjection of MCH into the NPO were minimal. Therefore, based on these data, it appears that the MCH system is not primarily involved in the generation of either sleep or wakefulness.

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0049.A

The Hypothalamic Hypocretinergic System Modulates Auditory Unit Firing at the Inferior Colliculus

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Introduction: The inferior colliculus (IC) is a mesencephalic obligatory relay in the ascending auditory pathway. This nucleus is involved in the sound frequency and intensity processing as well as in the sound-source localization. Strikingly, the way the IC auditory neurons respond to sound stimulation is severely modified across the waking-sleep cycle. On the other hand, several reports have posited that the hypothalamic hypocretinergic system is involved in the regulation of sleep and wakefulness; disruption of this system results in narcolepsy. The hypocretinergic neurons that are active during wakefulness with motor activity and REM sleep, project to the inferior colliculus amid other regions. In the present report we studied the influence of juxtacellular application of hypocretin-1 to auditory inferior colliculus neurons in vivo. Our hypothesis is that the hypothalamus, through hypocretinergic descending influences, modulates the auditory information processing in the IC.
Methods: Three adult guinea pigs placed in a stereotaxic frame were surgically prepared under urethane anesthesia with small holes in the skull for electrode access, and with polyethylene tubes fixed to the middle ears where earphones were connected. Conventional extracellular unitary activity recording and hypocretin applications were performed with double glass micropipettes. The recording electrode was filled with sodium acetate and sky blue. For pressure microinjections (5 to 50 PSI, 300 ms) of hipocretin-1 (10 µM), we used micropipettes with 10-12 µm diameter tips, separated 50-100 µm from the tip of recording electrode. Sound stimuli consisted of tone-bursts of 50-100 ms, 5 ms rise-fall time, 10 to 20 dB SPL above the unit threshold, at the neurons' characteristic frequency. The recorded neurons were analyzed off-line by interval and peristimulus histograms performed before and after hypocretin applications. Statistical analysis of the responses was carried out using the Mann-Whitney test.
Results: Seven auditory neurons were recorded in the central nucleus of the IC. These neurons responded to contralateral sound stimulation either at the beginning (On response) or throughout the duration of the tone burst (Sustained response), with a latency of 8 to 15 ms. In five neurons, hypocretin applications produced a statistical significant increase in the firing rate of the evoked response up to a 110% of the control value. This increase in the response had a delay of 10 to 20 seconds and lasted approximately 3 minutes, returning to control values afterwards. On the other hand, hypocretin did not modify the temporal configuration of the discharge while the spontaneous firing was scarcely affected.
Conclusions: The present data illustrate that the hypothalamus, through a descending hypocretinergic pathway, facilitates neuronal response to sound in the IC. We suggest that the hypothalamus may regulate the flow of information through the auditory system in relation to emotional drives, or according to different behavioral states.

0050.A

Stimulation of the Nucleus Reticularis Gigantocellularis Suppresses Dorsal Spinocerebellar Tract Neuron Activity and Releases Amino Acid Neurotransmitters in Clarke's Column of the Upper Lumbar Spinal Cord

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Introduction: Preliminary studies from our laboratory indicate that ascending sensory transmission via Clarke's column dorsal spinocerebellar tract (DSCT) neurons during the state of wakefulness or quiet sleep is markedly reduced following stimulation of the medullary nucleus reticularis gigantocellularis (NRGc). Stimulus trains and intensities that produce large amplitude strychnine sensitive IPSPS recorded from lumbar motoneurons (Brain Research, 423: 353-358) are also capable of markedly suppressing ongoing spike activity and antidromically propagated action potentials of DSCT neurons. These effects are partially attenuated by intravenous injection of strychnine. Glycine may partially mediate the NRGc-induced suppression of DSCT neurons during wakefulness. NRGc conditioning also produces short-latency excitation of individual DSCT neurons. In the present study, we explored the effect of the same conditioning stimuli applied to the medullary NRGc on the population response of DSCT neurons as well as on levels of amino acids glycine, GABA and glutamate in Clarke's column.

Methods: Two adult cats were prepared for sleep state recording and identification of Clarke's column dorsal spinocerebellar tract neurons. The location of Clarke's column at L3 was confirmed electrophysiologically by recording characteristic short-latency (2.9-3.2 ms) field potentials evoked by low-intensity stimulation of the anterior cerebellar lobule. Monopolar conditioning stimuli (4 pulses, 0.8 ms pulse width, 2.5ms pulse interval, 40-80 microamps, 1.0 Hz) were applied to NRGc (P8, L1.5, H-6.5) at conditioning–test (CT) intervals of 15-50 ms and the amplitude of cerebellar-evoked field potentials recorded in Clarke's column were compared against unconditioned responses. The recording electrode was then replaced by a dialysis probe (Model A-I-40-02, Eicom, Kyoto, Japan). Behavioral state was continuously monitored and dialysis samples (10 microliters) collected during wakefulness in the absence and presence of NRGc stimulation. Glycine, GABA and glutamate levels in the dialysates were determined by HPLC with fluorescent detection.

Results: Stimulation of the NRGc during wakefulness (peak effect: CT intervals 15-30 ms) markedly suppressed cerebellar-evoked field potentials recorded in Clarke's column. To date, glycine levels were increased during NRGc stimulation by ~23% (n=12 stimulation trials) when compared to unconditioned levels. GABA levels increased by 29% during NRGc stimulation (n=8 stimulation trials) whereas GLU levels increased by 295% (n=11 stimulation trials) compared to unconditioned control levels.

Conclusions: The results of the present study indicate that electrical stimulation of the NRGc suppresses the population response of DSCT neurons and causes a release of glycine and GABA in Clarke's column. The increased levels of glycine and GABA may partially inhibit DSCT spike activity observed herein and in our previous single unit studies. In addition, glutamate levels were also increased and may promote enhanced activity of local inhibitory interneurons and/or exert direct excitatory actions on DSCT neurons. The fact that glycine and GABA levels were elevated during NRGc stimulation, albeit to a lesser degree than that observed without NRGc conditioning during the active sleep state (see abstract by Taepavarapruk, N. et al.), suggests that the NRGc may be one of several brainstem areas responsible for attenuation of ascending sensory transmission through Clarke's column during the state of active sleep.

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0051.A

Light Effects On The Sleep Pattern In Drosophila Melanogaster

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Introduction: Light is an important regulator of circadian rhythms and has direct effects on sleep-waking behavior. The fruit fly Drosophila melanogaster has been used successfully for molecular and genetic dissection of complex behaviors, including circadian rhythms. Recently, the presence of a sleep-like state has been demonstrated in the fruit fly. The goal of this study was to characterize acute effects of light on sleep in flies.

Methods: Flies were cultured at 21 degrees C, 68% humidity, 12:12 light:dark cycle, on yeast, dark corn syrup and agar food. Motor activity of individual flies was continuously recorded using the Drosophila Activity Monitoring System (DAMS; see Biesiadecki et al., this meeting). The wild-type Canton-S strain, 115 isofemale lines collected in the wild between 1994 and 2002, and approximately 2000 mutant lines produced by insertional and EMS-induced mutagenesis were tested. Flies (7-11 day-old) were recorded during 3 baseline days, followed by 24h of various lighting schedules, including a 3h:3h LD schedule, short LD periods of variable lengths, and total darkness. All LD schedules included 12h light and 12h dark.

Results: During a 12:12 LD cycle, all wild type flies exhibited a diurnal rest-activity pattern and males on average slept more than females, primarily because of the presence of a long sleep period during the middle of the 12 h light period (see Holladay et al., this meeting). During short LD cycles, average activity during the subjective day was greater than activity during subjective night, consistent with the expected circadian influences. During subjective night, both male and female flies were more active in the short light than in the short dark periods. During subjective day, short LD cycles had minimal effects of sleep in female flies; when effects were observed, they were similar to those seen at night (i.e., sleep increased in the dark). Male flies showed the opposite pattern during subjective day: sleep amounts increased following lights on and decreased following lights off. Both male and female flies showed increased arousal late in subjective day on all LD schedules as well as in constant darkness. Most mutant strains (>95%) showed patterns similar to wild type strains.

Conclusions: This study shows that in fruit flies, acute effects of light on sleep patterns are more pronounced during subjective night. These results therefore add yet another similarity between fly sleep and mammalian sleep. The response to acute light was highly conserved in hundreds of wild type and mutant strains. The fact that male flies show increased sleep during subjective day in comparison to females, particularly in a 12h:12h LD cycles, may in part be due to a direct effect of light.

0052.A

Hypocretin/Orexin (H/O) Elevates [Ca2+]si s in Locus Ceruleus (LC) Neurons via Activation of OXs1s and OXs2s Receptors

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Introduction: H/O synthesizing neurons of the lateral hypothalamus

play a central role in thenormal control of behavioral state and the disorder narcolepsy. They have widespread central projections, with the LC, a structure linked to arousal and attention, receiving among the heaviest projections in the CNS. Two H/O receptors have been identified, each having distinct but often overlapping distributions. In the LC, *in situ* hybridization studies suggest expression of OXs1sRs but not OXs2sRs (Marcus et al., J Comp Neurol 435:6, 2001). Accordingly, H/O-A, which exhibits equal affinity for both receptors, is reported to be more effective at exciting LC neurons than H/O-B, which has higher affinity for OXs2sR. As part of our ongoing investigations into the actions of H/O on sleep-regulating neurons, we examined whether H/O increases [Ca2+]si s in LC cells. Moreover, to determine the receptors involved, we monitored [Ca2+]si s from cells obtained from wildtype mice (C57BL/6) and from mice lacking each H/O receptor (OXs1sR -/- or OXs2sR -/-).

Methods: Mouse brainstem slices were loaded with Ca2+-indicator by incubation in fura-2 AM (3 m). [Ca2+]si s was monitored by optically imaging fluorescence changes from LC cells (380 nm excitation).

Results: In wildtype mice, H/O (Orexin-A, 300 nM) induced reversible increases in [Ca2+]si s in 57% of LC cells. Somatic responses had 3 profiles: 1) a slow rise to a smooth plateau; 2) "spiky" transients arising from a stable baseline, and 3) a combination of the two others. All these Ca2+-transients were independent of voltage-dependent Na+ channels, SERCA-pump activation and the sodium/calcium exchanger but were abolished by lowering extracellular Ca2+, indicating they all required calcium influx. As in wild-type cells, 57% of OXs2sR -/- cells responded to H/O with similar patterns that were dependent on extracellular Ca2+. Surprisingly, 13% of OXs1sR -/- LC cells also responded similarly.

Conclusions: This study demonstrates that H/O elevates [Ca2+]sis over multiple time courses by activating Ca2+ influx pathway(s) in LC cells. Since stimulation of OXs1sRs alone (OXs2sR-/-) evoked similar response profiles in an equivalent fraction of cells to that observed in wild-type LC, OXs1sRs are sufficient to mediate these responses in all LC cells capable of such responses. The surprising finding that stimulation of OXs2sR alone evoked similar response profiles in 13% of OXs1sR-/- LC cells supports the presence of functional OXs2sRs within this nucleus. One possibility is that OXs2sRs are present on a subpopulation of LC cells that also express OXs1sRs. Such an outcome would raise the possibility that H/O transmission to a subpopulation of LC neurons could be selectively regulated by differential modulation of H/O receptor subtypes.

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0053.A

Sleep Homeostasis in the Fruit Fly

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Introduction: Sleep in Drosophila Melanogaster shares many features of mammalian sleep (Hendricks et al., 2000; Shaw et al., 2000; Nitz et al., 2002). Among these is homeostatic regulation, as indicated by an increase in sleep duration after 6-12h of sleep deprivation (SD). In mammals, SD is followed not only by an increase in sleep duration, but also by an increase in sleep intensity, which can be measured by an increase in sleep continuity as well as in slow wave activity. Moreover, SD in humans impairs performance in vigilance tasks. The goal of this study was to determine whether SD in flies 1) increases sleep continuity and 2) affects performance in a vigilance task.

Methods: Motor activity of individual female Canton-S flies was recorded at 1 min intervals using the infrared Drosophila Activity Monitoring System (DAMS) during 3 baseline days, 6, 12, 24h SD (6 experiments per SD duration; n = ~100 flies/experiment, end of SD at light onset), and 2 days of recovery (REC1 and REC2). Sleep was defined as any period of uninterrupted behavioral quiescence lasting > 5 min. Sleep continuity was measured using the S-score, which increases during uninterrupted sleep and decreases otherwise. In the vigilance task, a complex stimulus was applied on alternating sides of the glass tubes housing the flies in the DAMS. The stimulus triggered an escape response forcing the flies to cross the beam in the middle of the glass tube. This response was measured as a decrease in the latency to beam crossing after the stimulus.

Results: For the first 6h of REC1 after SD, flies slept significantly more minutes than during baseline (mean±SE: SD6: +52.3±3.3; SD12: +81.7±3.7; SD24: +84.7±2.6; $p<0.0001$). For the remaining of REC1-2, sleep duration was not increased. Sleep continuity, as measured by the S-score, also increased significantly for the first 6h of REC1 (baseline: 35.1±1.4; SD6: 79.6±2.5; SD12: 80.8±3.9; SD24: 139.4±2.8; $p<0.0001$). The S-score remained higher during the dark period of REC1 after 24hSD (baseline = 448.3±8.3; 24hSD = 606.7±3.5; $p<0.05$). During baseline, the mean beam crossing latency after the stimulus was, for active flies, 11.6±1.3 sec, compared to 27.0±2.3 sec with no stimulus (paired t-test, $p=0.05$). After 24h SD, beam crossing latency after the stimulus increased (19.3±4.6 sec) and did not differ significantly from the mean latency without the stimulus (23.4±1.5 sec; $p>0.3$).

Conclusions: In flies, as in mammals, the rebound of sleep after SD depends on the duration of SD. Moreover, sleep after SD is less fragmented in flies as it is in mammals. Finally, SD reduces vigilance measures in flies as it does in humans.

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0054.A

State-Dependent Control Of Lumbar Motoneurons By The Lateral Hypothalamus

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Introduction: Stimulation of the nucleus pontis oralis (NPO) during wakefulness induces a powerful postsynaptic excitatory drive onto motoneurons. On the other hand, during active (REM) sleep, the identical stimulus to this nucleus promotes postsynaptic inhibition in motoneurons of the brainstem and spinal cord. This phenomenon, termed reticular response-reversal, indicates that a neuronal network within the NPO acts bimodally to exert state-dependent motor drives. Hypocretinergic neurons, which are exclusively located in the hypothalamus, project to the NPO. Hypocretinergic neurons also send projections to the ventral horn in the spinal cord where they terminate in apposition to lumbar motoneurons. Based on these data, we sought to determine if lumbar motoneurons respond to electrical stimulation of the hypothalamic region where hypocretin-containing cells are located and whether their response, if present, varies in a state-dependent manner.

Methods: Experiments were performed on three adult, acutely-prepared cats under a-chloralose anesthesia. Strut electrodes were used for bipolar electrical stimulation of the lateral hypothalamic area where hypocretinergic neurons are located in the cat (A 10, L 1.5, H -2, according to Berman's atlas; 10 ms trains of 4 pulses, 500-1000 mA, 0.8 ms). Stimulation of the hypothalamus and simultaneous intracellular recording from lumbar motoneurons were performed prior to and during the active sleep-like state that followed the injection of carbachol into the NPO (AS-carbachol).

Results: Electrical stimulation of the lateral hypothalamus elicited, during control conditions, i.e., prior to AS-carbachol, an EPSP with a peak latency of approximately 15 ms. In contrast, during AS-carbachol, electrical stimulation of the lateral hypothalamus resulted in a reduction in amplitude of the EPSP and the generation of a large-amplitude IPSP with a peak latency of approximately 50 ms.

Conclusions: The present data indicate that the excitation of neurons in the lateral hypothalamus promotes motor excitation prior to AS-carbachol and motor inhibition during AS-carbachol. This bimodal, state-dependent response induced in motoneurons is similar to the phenomenon of reticular response-reversal which occurs following stimulation of the NPO prior to and during AS-carbachol in a-chloralose anesthetized cats as well as during naturally-occurring states of wakefulness and active sleep. We suggest that the response-reversal that occurs following hypothalamic stimulation is mediated by the NPO; circuitry within the NPO directs this activity via excitatory or inhibitory descending motor pathways, depending on the animal's behavioral state.

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0055.A

Natural Variation in the Sleep Phenotype in Drosophila Melanogaster

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Introduction: Sleep in flies is associated with increased arousal thresholds, changes in brain electrical activity, changes in gene expression, and it is homeostatically regulated, as it is in mammals (Hendricks et al., 2000; Shaw et al., 2000; Nitz et al., 2002). Fly sleep occurs mostly at night, but male flies also have a "siesta" during the day. As in mammals, sleep deprivation (SD) is followed not only by an increased amount of sleep, but also by increased sleep continuity (Biesiadecki et al., this meeting). A full characterization of the sleep phenotype in Drosophila melanogaster has been performed so far in just one wild type strain, the Canton-S strain, which has been maintained in the laboratory for several decades. Here we investigate sleep and sleep homeostasis in >100 lines derived from single female flies (isofemale lines) collected in the wild between 1994 and 2002.
Methods: Flies were cultured at 21oC, 68% humidity, 12:12 light:dark cycle, on yeast, dark corn syrup and agar food. Forty-three isofemale lines were collected in 1994 in North Carolina (gift of Dr TFC Mackay), 70 lines were collected in May 2002 in Mexico (Indiana Stock Center), and 2 lines were collected in August 2002 in Wisconsin. Motor activity of individual flies (7-11 day-old, n = 10-16 /line) was continuously recorded using the Drosophila Activity Monitoring System (DAMS; Biesiadecki et al., this meeting) during 3 baseline days, 24 hours of SD by gentle shaking (ending at light onset), and 1-2 days of recovery after SD. Sleep continuity was measured using the S-score (Biesiadecki et al., this meeting).
Results: Like Canton-S flies, all wild type strains tested slept mainly during the night. Males slept more than females because of a "siesta" in the middle of the light phase (min of sleep/24 hours, mean ±SE: females 655±122; males 796±153). In all lines, sleep amount and continuity increased after SD. Comparing short and long sleeper lines (<500 min, n=12 lines, vs >750 min, n=24 lines, data for females) we found that, while losing a similar amount of sleep during SD (78.1±7.6% vs 76.9±3.2%), short sleepers recovered a higher percentage of sleep (60.7±14.4% vs 17.6±4.2%; $p<0.001$). The relative increase in S-score after SD was also larger in short than in long sleeper lines (894.9±174.4% vs 243.3±7.0%; $p<0.0001$). Similar results were obtained when comparing males of the same long vs short sleeper lines.
Conclusions: The sleep phenotype in fruit flies is extremely well preserved across >100 wild type strains. Flies are diurnal; males sleep more than females; SD is followed not only by a sleep rebound but also by increased sleep continuity. For both genders, recovered sleep is more abundant and more continuous in short sleeper lines than in long sleepers.

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0056.A

Hypocretin Regulation in a Primate Model of Human Wake Regulation

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Introduction: Hypocretin is a newly discovered neuropeptide, the loss of which results in the sleep disorder narcolepsy. Hypocretin neurons are located in the lateral hypothalamus and send dense, excitatory projections to all monoaminergic cell groups. As hypocretin is only consistently detected in brain tissue or CSF, examination of its physiologic regulation in humans is limited. Current animal models of hypocretin physiology (e.g., murine, canine, feline, rat) are wholly unsatisfactory as proxies for human physiology. These animals have polyphasic wake (multiple, short duration episodes spread throughout the day), unlike humans who typically consolidate wake into a single, daily, 16 h episode. Hypocretin has been hypothesized to be integral to wake-consolidation behavior and may thus have a different regulation in humans and polyphasic species. To address this question, we have begun to examine hypocretin physiology in a diurnal (day-active), wake-consolidating mammal, the squirrel monkey (Saimiri sciureus).
Methods: Using a group of 30 female monkeys (housed in six groups of five monkeys), we examined the daily variation in cisternal CSF hypocretin concentration. Monkeys were each sampled at two time points, twelve hours and two weeks apart, such that one group was sampled every two hours across the 24h day. The light:dark cycle was 12:12 with lights on at 0700. We also examined cisternal hypocretin concentrations in a separate group of 5 male and 5 female monkeys that had their wake extended by 4 hours. To assess the influence of stress on hypocretin measures, we analyzed CSF cortisol concentrations from the same samples. Hypocretin-1 and cortisol were analyzed by RIA.
Results: Hypocretin-1 concentrations exhibited a strong time of day effect, with lowest concentrations occurring around typical wake time (coincident with lights-on). After a few hours of wakefulness, concentrations began to rise linearly, reaching a plateau during the early evening. Elevated concentrations were maintained until just after the monkeys went to sleep, with concentrations falling throughout the night. The daily mean (± SD) was 298 pg/mL ± 7.64 pg/mL with an oscillation amplitude of 66.7 pg/mL ± 10.3 pg/mL (31% oscillation). The peak occurred at 1811 ± 26 minutes, two hours before the typical sleep onset of 2010. Extending wake by four hours induced a small (13.43 % ± 2.372 %), but significant ($p < 0.0005$) increase in hypocretin that was not related to the change in cortisol. The change in hypocretin during the wake extension appeared to be sexually dimorphic as males had a consistently greater change than the females.
Conclusions: Given the daily pattern of hypocretin and the effects of wake extension on hypocretin, our data are in agreement with the theory that hypocretin is regulated by both a circadian and a homeostatic component in a sleep consolidating mammal. The relative contribution of each of these components requires further study. Other components, such as activity and feeding, and how they relate to the regulation of hypocretin in a wake-consolidating mammal will also need to be addressed in future studies.

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0057.A

Changes In Extracellular Glutamate Levels In The Medial Prefrontal Cortex Of The Rat During Sleep And Wakefulness

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Introduction: Functional neuroimaging studies have demonstrated a state-dependent change in glucose metabolism in the prefrontal cortex in humans, in which glucose metabolism is higher during wakefulness and REM sleep than during slow wave sleep (Buchsbaum et al., Life Science 1989 45:1349-1356). Some studies have also reported higher metabolic rates in the anterior medial prefrontal and other limbic prefrontal areas during REM compared to wakefulness. The neurochemical underpinnings of these state-related changes are unknown. Work performed by Magistretti's group indicates that increased glucose utilization is related to local increase in glutamate (Magistretti et al., Philos Trans R Soc Lond B Biol Sci, 1999 354:1155-1163). In the present study, we sought to determine whether extracellular glutamate levels in the medial prefrontal cortex of the rat change during the different states of sleep and wakefulness.

Methods: Experiments were performed in four Sprague-Dawley rats. One minute microdialysate samples were obtained from the medial prefrontal cortex at a rate of 2ul/min. Glutamate was measured off-line with high performance liquid chromatography with electrochemical detection. Samples were classified according to the state of the sleep-wake cycle the rat was displaying at the time of collection (with correction for dead time). Statistical analysis was performed using one-way analysis of variance (ANOVA) to compare dialysate glutamate concentrations measured during wakefulness, non-REM, and REM. Fisher LSD test was used for post-hoc comparisons. Glutamate values in each sample were converted into percent of each animal's wakefulness mean value.

Results: Extracellular glutamate levels changed according to the state of the animal. When compared to levels obtained during wakefulness, glutamate levels were 83.2 ±4.5 (mean±SEM) % during non-REM sleep, and 115.8±22.6 % during REM. The difference between the three groups was statistically significant ($F_{2,108}=3.86$). Post-hoc analysis showed that levels of glutamate were significantly higher during wakefulness and REM sleep than during non-REM sleep. Differences between wakefulness and REM were non-significant.

Conclusions: In agreement with the functional neuroimaging literature, glutamate levels in medial prefrontal cortex were higher during wakefulness and REM sleep. Although levels were highest during REM sleep, the difference between REM and wakefulness was not statistically significant. Because glutamate is an excitatory neurotransmitter, these results are also in agreement with the concept that both wakefulness and REM are "active" states, whereas non-REM sleep implies a more "restful" state. Also, these results suggest that non-REM sleep is characterized not only by an increased inhibition over cortical neurons as other authors have pointed out, but also by a decrease in excitatory transmission.

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0058.A

A Time Series Model Of The Probability Of Transition Into A REM Sleep Episode

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Introduction: The probability of a transition into a REM sleep episode is related to the recent history of REM sleep occurrence, as suggested by the relationship between the length of a given REM episode an the length of the following interval, i.e., short-term REM sleep homeostasis. The sequence of alternating episodes of REM sleep and intervals without REM sleep can be described as a time series. An appropriate way to model the dynamics of REM recurrence is to estimate the probability of transition into REM at a given time as a function of the distribution of REM sleep epochs in a preceding time window.

Methods: Continuous recording of 16 rats for 3 days were reduced into time series where 15-second epochs were assigned to REM sleep, NREM sleep or wakefulness, and then further reduced to two states: REM sleep episode or interval. For the present analysis, only data from hours 2-11 after lights-on were considered. A maximum likelihood approach was used to estimate the transition probabilities by fitting a feed-forward neural net model to the data. The model consisted of 60 binary inputs corresponding to the presence or absence of REM sleep in each epoch within the preceding 15-minute time window, a first layer that extracts 6 trainable moving averages, a hidden layer of 20 units with logistic activation and a single unit output layer with logistic activation. The training target was coded in the same way as the input. A cross-entropy error function was applied, allowing the results to be interpreted as a probability value.

Results: The resulting probability is an index of the stability of the state as a function of the recent history. Entering an interval, a stabilization process is evidenced by an increase in the probability of remaining in the interval state. This process is modulated by previous history, e.g., the longer the preceding episode, the faster the increment in stability and the higher its maximum level. A refractory effect is also evidenced by a plateau at that maximum level. The duration of these effects under different conditions can be estimated by a simple evaluation of the trained non-linear stochastic model.

Conclusions: A time series model approach allows for a quantitative analysis of REM sleep dynamics, expressed as the stability of the interval state as a function of recent history of REM occurrence. The functional map that is obtained offers a more detailed description of temporal properties of the homeostatic process and provides a reference framework heuristically useful for hypothesis concerning its neural substrate.

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0059.A

Sleep-Wake Related Discharge Properties of Basal Forebrain Neurons Recorded and Labeled by the Juxtacellular Technique

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Introduction: The basal forebrain (BF) appears to play a polyvalent role in the modulation of cortical activity and sleep-wake states, facilitating cortical activation with wake (W) and/or paradoxical sleep (PS) on the one hand and promoting cortical slow activity and slow wave sleep (SWS) on the other. Using juxtacellular recording and labeling of units in anesthetized animals, we previously discerned that different BF cell groups could fulfill different roles in cortical modulation (Manns, Alonso and Jones, JN, 2000). In order to study the discharge properties and roles of identified BF neurons in natural sleep-wake states, we hereby recorded and labeled units using the juxtacellular technique in unanaesthetized, head-restrained rats.

Methods: Long-Evans rats (200-250g) were operated under ketamine/xylazine/acepromazine (65/5/1 mg/kg, i.p.) anaesthesia for

implantation of EEG-EMG electrodes and of a U-frame for subsequent fixation of the head to the stereotaxic instrument. Single units were recorded using glass micropipettes filled with 0.5 M NaCl containing Neurobiotin, and 1-4 recorded cells were labeled per animal by the juxtacellular technique. Neurobiotin-filled cells were visualized using Cy2-conjugated streptavidin.

Results: Across W-SWS-PS states, the average discharge rate varied significantly ($p<0.001$) for all BF units and greatly (by >100%) for the majority of units. Groups of cells could be distinguished according to their different rate and pattern of discharge across sleep-wake states: 1. 'W/PS-active bursting' that discharged in rhythmic bursts in association with theta activity during W and PS and virtually ceased firing during SWS. 2. 'W/PS-active tonic' that discharged in a tonic manner during W and PS and virtually ceased firing during SWS. 3. 'SWS-active bursting' that discharged in bursts during SWS in association with cortical slow activity and rarely fired during W or PS. 4. 'SWS-PS-active' that discharged in an irregular manner at higher rates during SWS and PS than during W. 5. 'PS-active' that discharged in an irregular manner during PS and rarely fired during W or SWS. 6. 'W-SWS-PS active' that discharged at a rapid rate with minimal though significant variation (<100 %) across states and with the highest rate during W or PS. Neurobiotin-labeled units from these different groups were co-distributed within the substantia innominata and magnocellular preoptic nucleus.

Conclusions: Given the large variations in their discharge patterns and/or rates across sleep-wake states, BF neurons have the potential to strongly modulate the activity of cortical or subcortical targets in a state-selective manner. The multiple BF cell groups could thus regulate cortical and peripheral activity while promoting different sleep-wake states, some promoting cortical activation along with W and/or PS and others cortical slow wave activity along with SWS.

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0060.A

Modulation Of Short-Term REM-Sleep Homeostasis By The Episode-Interval Relationship Within The Preceding Cycle And By Previous Incidence of REM-Sleep

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Introduction: Short-term REM-sleep homeostasis is evidenced by the relationship between length of a REM episode and length of the following interval, with longer episodes being followed by longer intervals. The episode-interval relationship within a cycle can be hypothesized to be influenced by the previous episode-interval cycle. (E.g., the interval should be longer than expected for the current episode if in the previous cycle a long episode was followed by a short interval). The episode-interval relationship should also be modulated by the previous occurrence of REM-sleep, allowing for an assessment of the time course of that effect.

Methods: REM-sleep episodes and intervals were determined from state scoring in 15-second epochs of continuous recordings from 15 rats for 3 consecutive days. Only data from hours 4:00 to 12:00 after lights-on were considered. Episodes and intervals were classified as short or long using thresholds of 1.0 and 6.0 minutes, respectively. How the fraction of long intervals in the current cycle was affected by combinations of current-cycle episode, preceding-cycle interval and preceding-cycle episode could be evaluated by chi-square tests. The amount of REM-sleep in minute 1 to 10 before the start of the episode of each cycle was computed. Robust regressions were performed of duration of current interval on REM-sleep incidence in each minute.

Results: The overall fraction of cycles with long intervals was .38. That fraction was .60 in cycles with long episodes vs. .25 in cycles with short episodes ($p<0.001$), evidencing short-term REM-sleep homeostasis. Episodes and intervals of the preceding cycle did not have by themselves a significant influence on this fraction: .36 if preceding interval had been long vs. .39 if short; .40 if episode of preceding cycle had been long vs. .37 if short. Nevertheless, the difference among the four episode-interval combinations of the preceding cycle was significant ($p=0.001$), the fraction of long intervals being much higher, .47, for the preceding combination long-episode/short-interval. Differences were more drastic when only cases with short episode in the current cycle were considered (E.g., .39 for long-episode/short-interval vs. .19 for short-episode/short-interval). Robust regressions of interval duration on REM-sleep incidence in previous minutes were significant at .001 level for minutes -1 to -4, at .02 level for minute -5, and non significant for minute -6 backwards.

Conclusions: The episode-interval relationship of the preceding cycle influences short-term homeostasis in the current cycle. A preceding long-episode/short-interval combination lengthens the interval of the current cycle. The influence of REM-sleep from previous cycles on length of current interval can be demonstrated limited to minutes -1 to -5 before the start of the current cycle.

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0061.A

C-Fos Expression in Neurons of the Posterior Hypothalamus, Including those Containing Orexin (Orx) or Melanin Concentrating Hormone (MCH), following Sleep Deprivation or Recovery

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Introduction: The posterior hypothalamus plays an important role in promoting waking. Within that region, Orx-containing neurons are known to be particularly critical since their loss results in narcolepsy. They also play an important role in energy balance potentially stimulating metabolism through the sympathetic nervous system and/or hypothalamo-pituitary-adrenal axis. Other neurons in the region contain MCH, the influence of which is yet unknown upon sleep-wake states. MCH, however, appears to play a different, potentially opposite, role from orexin in energy balance, apparently decreasing metabolism. The Orx and MCH neurons could accordingly play different roles in the promotion of wake vs. sleep. To examine this possibility, we examined whether c-Fos, as an indicator of neuronal activity, is differentially expressed in Orx and MCH neurons in response to sleep deprivation vs. recovery and thus as a function of wake vs. sleep.

Methods: Male Wistar rats (200-250 g.) were housed individually in cages where they were treated operationally for: 1) total sleep deprivation (SD, by gentle touching) for 3 hours, 2) total sleep deprivation for 3 hours followed by sleep recovery (SR) for 3 hours, or 3) natural sleep and waking as sleep control (SC) for 3 hours. At the end of the 3 hour experimental period at ~300 pm, they were immediately sacrificed under pentobarbital anaesthesia (100 mg/kg, i.p.). Brains were processed for dual immunohistochemical staining of c-Fos, using black, DAB-Ni as chromogen, and Orx or MCH, using pink, alpha-naphthol pyronin B, as chromogen. Single c-Fos, single MCH or Orx and double c-Fos MCH or Orx immunopositive (+) cells were mapped and counted using a computer image analysis system equipped for stereological analysis.

Results: Preliminary results reveal that c-Fos+ cells are prominent in the posterior hypothalamus following sleep deprivation and are greater in number in SD than in SR animals. Double-labelled c-Fos+/Orx+ cells were also more numerous in SD than in SR animals. On the other hand, double-labelled c-Fos+/MCH+ cells were less numerous in SD than in SR animals.

Conclusions: As indicated by c-Fos expression, the population of neurons in the posterior hypothalamus are more active in association with

waking than sleep as reflected here in animals having total sleep deprivation vs. recovery. This population includes neurons containing Orx that is known to be important for maintenance of waking and to have an excitatory action on many other neurons comprising arousal systems. On the other hand, neurons containing MCH may play a different role, possibly opposite to that of Orx neurons, and promote sleep or physiological processes conducive to sleep.

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0062.A

Orexin-A Enhances Serotonin Release In The Dorsal Raphe But Not The Median Raphe Of Freely Behaving Rats

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Introduction: The role of serotonergic neurons of the dorsal (DRN) and median raphe (MRN) nuclei in the regulation of behavioral state is well known. It is also known that orexinergic neurons project to both DRN and MRN. Recently, in vitro electrophysiological studies have revealed that orexins excite the serotonergic neurons of the DRN. We hypothesize that orexins might increase serotonin (5-HT) release and enhance wakefulness. To test this prediction, we infused orexin-A and -B into DRN and MRN, in vivo, in freely behaving rats, and 1) measured extracellular 5-HT level and 2) recorded behavioral states.
Methods: Under standard surgical procedures, male Sprague Dawley rats (350-450 g) were implanted with microdialysis guide cannula, targeted toward DRN or MRN for later insertion of microdialysis probe. 1) 5-HT measurement: Samples were manually collected every 20 min and analyzed within 20 min by HPLC. 2) Behavioral state recordings: In separate experiments, infusion of orexins in DRN or MRN was carried out for 3 hours during the lights-on (inactive) period and behavioral states were electrographically recorded and compared to control days without orexin infusion.
Results: 5-HT measurement in the DRN: Initial dose dependent studies suggested that infusion of orexin-A into the DRN produced a dose-dependent increase in DRN 5-HT ($p<0.05$). The maximum increase was ~160% above baseline at 100 uM. In contrast, infusion of orexin-B (100 uM) into the DRN produced ~50% increase in 5-HT in the DRN ($p<0.05$). All the increases in 5-HT returned to the baseline after the termination of orexin infusion.5-HT measurement in the MRN: Infusion of orexin-A (100 uM) in the MRN did not cause any effect on extracellular 5-HT. However, infusion of orexin-B in MRN produced a significant increase (~50%) in extracellular 5-HT ($p<0.05$). Effect of orexins on behavioral states: Preliminary studies with infusion of orexin-A (10 uM) in the DRN increased wakefulness and suppressed both nonREM and REM sleep. Further work is in progress.
Conclusions: Orexin-A produced a large dose-dependent increase in 5-HT release in DRN, but had no effect in MRN. orexin-B enhanced 5-HT release in both DRN (although less than orexin-A) and MRN. Orexins enhance wakefulness, and an increase in 5-HT release may be an important mechanism.

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0063.A

Correlates of Sleep Pressure During Long-Term Sleep Deprivation in the Rat

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Introduction: Electrophysiological markers of sleep homeostasis, notably EEG slow-wave activity (SWA), are well established in many species. Quantitative models of the dynamics of sleep pressure have been developed (Process S; Borbely 1982; Daan et al., 1984; Franken et al., 1991). Candidate molecular markers of sleep pressure have recently been identified based on gene expression screening after short- and long-term sleep deprivation (SD; Cirelli and Tononi 2002) using the disk-over-water method (DOW; Rechtschaffen et al., 1983, 1989). The relationship between electrophysiological and molecular markers of sleep pressure has not yet been established.
Methods: After 24-h baseline recordings, rats were subjected to total SD using the DOW for 4-14 days (n=15). At the end of SD animals were decapitated and their brains were used for molecular analyses. The EEG (occipital derivation) and EMG were recorded continuously throughout the experiment. Sleep stages were scored visually based on 4-s epochs. Power spectra of consecutive 4-s epochs (FFT routine, Hanning window) were calculated for the EEG. In 4 animals, simulations of Process S during the whole recording were performed with parameters optimized on the time course of SWA during baseline.
Results: The amount of NREM sleep occurring during SD varied between 7.0 and 22.5% of recording time (n=15). In all 4 animals in which simulations of Process S were performed, we obtained a close fit between data and simulation during the baseline. The optimized time constants parametrizing the exponential increase of process S was slower (Ti=16.0±2.1h) than that parametrizing its decrease (Td=2.9±0.3h). In three animals, the level of Process S reached a fluctuating plateau after 1-2 days (average value 169.4%; 100%=baseline average, NREM sleep=16.7% of recording time). In one animal, Process S continued to increase during the 4-day SD, and reached 227.2% of baseline. In this animal SD was more effective than in the previous 3 rats (NREM sleep=10.1% of recording time).
Conclusions: Using short scoring epochs (4-s), we found that rats subjected to long term SD with DOW obtain significantly more sleep than previously reported using 30-s epochs (NREM sleep=15.4±1.0% with 4-s epochs vs 8.6±1.1% with 30-s epochs, n=12). Consistent with previous results, the time constants of Process S were such that Ti was much larger than Td. Simulating Process S during SD suggests that sleep pressure may stabilize after 1-2 days if animals obtain >10% sleep, but continues to grow otherwise. This result is predicted by Ti/Td. The fast decrease of Process S also predicts a rapid decline of sleep pressure within the first hours of recovery sleep. Further work will establish whether the level of Process S in individual animals correlates with the level of molecular markers of sleep homeostasis.

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0064.A

Activity of Somatosensory Neurons of the Inferior Olive Across Sleep-Wake (S-W) Cycle

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Introduction: Somatosensory neurons of the rostral dorsal accessory olive (SSRDAO neurons) are sensitive to light mechanical cutaneous stimulation and cease their discharge during movement in active waking (AW). The pontine oral reticular nucleus (PnO) is involved in suppression of motor output and modulation of somatosensory inputs during waking and rapid eye movement (REM) sleep and might modulate the activity of SSRDAO neurons in these behavioral states. The current study was undertaken to determine the discharge patterns of SSRDAO neurons, which receive inputs from PnO sites suppressing motor activity, across S-W cycle.

Methods: Experiments were done using 4 male Wistar rats weighting 300-350 gm. Rats were surgically prepared for chronic extracellular recording in the inferior olive and electrographic assessment of S-W states. Bipolar stimulating electrodes (stainless steel, 100 mm) were inserted in the lateral hypothalamus (LH) and medial part of the PnO to induce and inhibit motor activity in animals. SSRDAO neurons were identified by touch to hairs of the back, head, and mechanical stimulation of the vibrissae. Unit firing rates were analyzed by paired t tests.
Results: A total of 31 SSRDAO neurons sensitive to tactile stimulation were recorded in the rostral dorsal accessory olive. Twenty-two of these neurons were excited by single pulse electrical stimulation (150-300 mA, 0.2 ms) of PnO inhibitory sites with a latency ranging from 1.1 ms to 6.0 ms with a mean 2.0±0.2 ms (n=22). These cells had an average spike duration of 1.96±0.03 ms and showed regular firing rate (26.3±3.2 Hz, n=22, min=14, max=69) during quiet waking (QW). Electrical stimulation (100-250 mA, 0.2 ms, 30 Hz) of the LH evoked exploratory locomotor behavior and produced a depression of activity in SSRDAO neurons (80.5±1.3% reduction, min=69, max=89, df=21, $p<0.0001$), which correlated with bursts of EMG recorded from neck muscles. In contrast, similar PnO stimulation suppressed motor activity of animals and increased the firing rate of SSRDAO neurons by an average of 156±12% (min=84, max=312, df=21, $p<0.0001$) compare with QW. Analysis of unit activity during nonREM sleep revealed that SSRDAO neurons kept firing rate at a similar rate to that seen in QW (df=21, $p>0.4$). In tonic REM sleep, these cells increased firing rate by an average 95.4±8.5% (min=43, max=178, df=21, $p<0.0001$) compare with QW. During phasic REM sleep events, firing rate of SSRDAO neurons was decreased by an average of 78±2% (min=61, max=94, df=21, $p<0.0001$) compared with tonic REM sleep.
Conclusions: These results suggest that inhibitory influences of phasic motor systems on SSRDAO neurons are triggered during REM sleep. Moreover, the decrease of SSRDAO neuron firing rates during phasic REM sleep events may be linked to the additional elevation of tactile thresholds during these periods as compared to that of tonic REM sleep.

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0065.A

GABAergic Mechanisms In The Control Of Median Raphe 5-HT Neurons: Effect On Hippocampal Theta Rhythm

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Introduction: Theta rhythm in the hippocampus is prominent during REM sleep due in large part to cessation of 5-HT neuronal firing in the median raphe nucleus (MR). 5-HT input is also involved in the control of theta under urethane anesthesia. The activity of 5-HT neurons is strongly modulated by different transmitter systems including GABA. Intra-MR administration of either GABAA [1] or GABAB agonists [2] elicited lasting hippocampal theta at short latencies. The effect of baclofen was antagonized by selective GABAB receptor antagonists but these antagonists, when injected alone, did not affect the hippocampal electroencephalogram (EEG). In this study the role of tonic GABAergic input to 5-HT neurons in the control of hippocampal theta was tested by blockade of GABAA receptors in the MR.
Methods: The experiments were conducted in 33 rats anesthetized with urethane. Hippocampal EEG was recorded and the dynamics of theta and non-theta patterns of activity was monitored and compared in 1 hr controls and during and after injection of bicuculline methiodide (BMI) using reverse microdialysis. The microdialysis probe (0.24 mm diameter, 3 mm membrane length) was inserted into the MR tilted by 24 deg so the membrane extended over the entire rostro-caudal extent of the MR, in midline saggital plane. BMI was dissolved in artificial cerebrospinal fluid (ACSF) in concentrations of 0.05mM (n=4), 0.1mM (n=5), 0.2mM (n=8), 0.5mM (n=7), and 1.0mM (n=11) and perfused for 1-2.5 hours (rate: 80ul/h).
Results: Microdialysis administration of BMI in doses 0.05 and 0.1mM had no effect on hippocampal EEG, i.e. the activity irregularly shifted back and forth between theta rhythm and large amplitude irregular waves. After increasing the dose to 0.2 mM, theta was completely eliminated and did not reappear until 15-30 min after the perfusion was switched to ACSF. In high concentrations (1.0mM) BMI had an opposite effect. After a short period of inhibition, theta rhythm recurred and continued until after switching back to ACSF. The character of the rhythm was different from control; theta oscillations appeared fragmented i.e. they were regularly interrupted by short (<0.5s) segments of low amplitude, high frequency bouts, every 3-7s.
Conclusions: 1. Inhibition of theta by GABAA receptor blockade revealed a GABAergic tone to MR normally controlling 5-HT output to hippocampus, as activation of 5-HT neurons suppresses theta. 2. We hypothesize that lasting theta rhythm after high doses of BMI was due to disinhibition of local GABAergic neurons which could act on GABAB receptors selectively localized on 5-HT neurons [2].References: [1] Kinney GG, Kocsis B and Vertes RP, Injections of muscimol into the median raphe nucleus produce hippocampal theta rhythm in the urethane anesthetized rat. Psychopharmacology 1995; 120:244-248.[2] Varga V, Sik A, Freund TF and Kocsis B, GABAB receptors in the median raphe nucleus: distribution and role in the serotonergic control of hippocampal activity. Neuroscience 2002; 109:119-132.

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0066.A

Hypocretinergic Modulation of the Reticular Control of Lumbar Motoneurons During Carbachol-induced Atonia

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Introduction: The nucleus pontis oralis (NPO) and gigantocellularis (NRGc) play a crucial role in the state-dependent control of motor activity. For example, stimulation of the NPO and NRGc results in the excitation of motoneurons during wakefulness, whereas glycinergic motor inhibition occurs following delivery of the identical stimulus to the same reticular nuclei during active sleep. This phenomenon, termed reticular response-reversal, entails the initiation by the NPO, not only of motor excitation during wakefulness, but also of a diametrically opposite motor drive, inhibition, during active sleep. Because the hypocretinergic system projects to the NPO, NRGc and spinal cord motoneurons, we sought to determine the effects of this peptide on the state-dependent, synaptic drives of NPO and NRGc origin that control motoneuron activity.
Methods: Experiments were performed on four adult, acutely-prepared cats under a-chloralose anesthesia. Intracellular recordings from lumbar motoneurons were obtained prior to and during the active sleep-like state induced by the injection of carbachol into the NPO (AS-carbachol). Hypocretin-1 was pressure-ejected juxtacellularly (100 mM, at 2-40 PSI for 5-30 s) in conjunction with electrical stimulation of the NPO or NRGc (10 ms trains of 4 pulses, 20-100 mA, 0.8 ms).
Results: In all experiments, motoneurons depolarized following the juxtacellular application of hypocretin-1. Stimulation of the NPO and NRGc elicited, prior to AS-carbachol, a predominant excitatory drive consisting of a large-amplitude EPSP. This NPO- and NRGc-induced response decreased in amplitude following the application of hypocretin-1. In contrast, during AS-carbachol, stimulation of the NPO and NRGc resulted in a reduction of the EPSP and the generation of a large-amplitude IPSP, which is known to be mediated by glycine. Following hypocretin-1 application, the amplitude of the IPSP was enhanced in conjunction with motoneuron depolarization. Interestingly, this IPSP

maintained its large amplitude even when the resting potential was maintained at a level of polarization identical to that which was present in the motoneuron prior to hypocretin-1 application.
Conclusions: In conclusion, hypocretin is capable of modulating NPO and NRGc-induced synaptic potentials during control conditions and AS-carbachol. The decrease in the amplitude of the NPO- and NRGc-induced EPSP that followed hypocretin application during control conditions is likely due to depolarization and an increase in the input conductance of motoneurons. On the other hand, because the hypocretin-induced enhancement of the AS-carbachol specific, glycine-mediated IPSP was maintained at control levels of resting potential, we suggest that hypocretin activates one or more voltage-independent ionic conductances in lumbar motoneurons, which results in the strengthening of their inhibition during AS-carbachol. Therefore, the activation of the hypocretinergic system is expected to enhance, at segmental levels, the NPO and NRGc-induced motoneuron inhibition during active sleep. The data also demonstrate a role for hypocretin, at the level of the spinal cord, in the phenomenon of reticular response-reversal.

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0067.A

Co-localization of g-aminobutyric Acid and Acetylcholine in the Somas of Neurons in the Latero-dorsal and Pedunculo-pontine Tegmental Nuclei in the Cat

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Introduction: Cholinergic and g-aminobutyric acid (GABA) mechanisms in the dorsolateral pontomesencephalic tegmentum have been implicated in the control of active sleep. We have previously reported that GABA immunoreactivity is present in cholinergic terminals in the latero-dorsal and pedunculo-pontine tegmental nuclei (LDT/PPT). In order to test the hypothesis that acetylcholine and GABA are co-localized in LDT/PPT neurons, we employed double-labeling, immunofluorescence methods for determining the coexistence of these neurotransmitters in somatic neuronal profiles in the LDT/PPT of the cat.
Methods: Double immunofluorescent techniques were employed using tyramide signal amplification (Renaissance TSA-Direct, NEN, Boston, MA) and lissamine rhodamine B sulfonyl chloride (LRSC). Either biotinylated donkey anti-rabbit (for rabbit anti-GABA) or anti-guinea pig (for guinea pig-anti-GABA) IgG was applied for one hour at room temperature. Sections were then washed and the second primary goat ChAT antibody was applied overnight. Sections were viewed and photomicrographs were taken using a Nikon fluorescent microscope equipped with a spot camera. Selected sections were also viewed through a Leica TCS confocal microscope in order to confirm the location of GABA and ChAT immunoreactivity within individual cells in the LDT/PPT.
Results: GABA immunoreactivity appeared green (fluorescein-tyramide); ChAT immunoreactivity was red (LRSC). GABA immunoreactivity was observed in somas and in neuronal processes. Most GABA-immunolabeled neurons were small (10-20 mm), although some medium to large sized cells (20-40 mm) were also present. ChAT immunoreactivity occurred mainly in cell bodies and proximal dendrites. On numerous occasions, ChAT and GABA immunoractivities were observed in the same cell. GABA was co-localized with ChAT in cells that were considered to be typically cholinergic on the basis of their size and shape (20-30 mm in diameter, fusiform or multipolar in shape. Approximately 50% of the ChAT-immunolabeled neurons were also GABA immunoreactive.
Conclusions: We conclude that GABA and acetylcholine are co-localized in the cell bodies of neurons in the LDT and PPT nuclei. This finding provides an anatomical basis for the putative synaptic interactions between GABAergic and cholinergic neuronal systems in the LDT and PPT in the control of sleep and waking states.

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0068.A

Do the Processor Neurons in the Rat Brain Show the L/F-Noise-Like Dynamics During Paradoxical Sleep?

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Introduction: We have investigated spontaneous neuronal activity in the various brain regions during sleep in the cat, including the premotor, visual, and somatosensory cortices; ventrobasal, lateral geniculate, and reticular nuclei of the thalamus; hippocampus; mesencephalic reticular formation; and cerebellum. The neuronal activity in all of these regions (we call them processor systems) commonly had the 1/f-noise-like spectrum during paradoxical sleep (PS) in the frequency range below 1 Hz. We have hypothesized that the neurons in the processor systems generally show the 1/f-noise-like dynamics in their activity during PS. In this study, we recorded the spontaneous neuronal activity in the ventroposterior thalamic nuclei (VP) in the rat during sleep-wakefulness cycles and tested whether this phenomenon may be generalized among mammals or not.
Methods: Experiments were performed on 2 unanesthetized, head-restrained rats. The animals were operated under pentobarbital anesthesia for recording single neuronal activity in the VP with cortical EEG and neck EMG. After a week of recovery period, sleep-deprivation was performed for 12 hours prior to the recording session. Single unit activity was recorded extracellularly using glass pipette microelectrodes simultaneously with EEG and EMG. After the experiment, the recording sites were marked by iontophoretically ejected Pontamine Sky Blue and histologically confirmed. Analysis was performed on the records during episodes of PS, slow wave sleep (SWS) and wakefulness (W) lasted for more than 128 sec. Power spectrum was estimated from successive spike counts of unit activity by FFT.
Results: Thirty-two data segments lasting 128 sec during PS, 18 during SWS, and 6 during W were obtained from 29 VP neurons. The neuronal activity during SWS had significantly lower firing rate (3.2 ± 1.7 spikes/sec) than that during W (11.6 ± 9.1 spikes/sec) or PS (14.8 ± 5.1 spikes/sec) and relatively constant firing pattern without marked fluctuations. In contrast, during PS, the mean firing rate resembled that during W, and slow, large fluctuations in activity were observed. Power spectra estimated from these activities were 1/f-noise-like during PS in the low-frequency range (0.04-1.0 Hz) and white-noise-like during SWS. In long-sustained records, spectra across 2 or 3 episodes demonstrated similar shape and similar slope of the regression line of the spectrum. During W, the neuronal activity had small short-term variations but no long-term fluctuations in their firing rate, and thereby it yielded a white-noise-like spectrum in the low frequency range of 0.04-1.0 Hz.
Conclusions: Our working hypothesis that the processor neurons show the 1/f-noise-like dynamics in their spontaneous activity during PS was supported also in the rat VP. It suggests that this 1/f-noise-like dynamics may be a general characteristic so much as to be able to define the state of PS at the neuronal level. White-noise-like dynamics during W suggests that the processor system in this state may be basically under the global stabilization and stand ready to adequately respond to external inputs.

0069.A

Neurotransmitters To Maintain Tonic Firing Of The Serotonergic Neurons In The Dorsal Raphe During Wakefulness In Rats

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Introduction: It is well known that the serotonergic neurons in the dorsal raphe have an important role in the regulation of sleep and waking. They are tonically active during waking (W), decrease their firing during slow wave sleep (SWS) and cease firing during paradoxical sleep (PS). It has been shown that monoaminergic, glutamatergic and orexinergic influences are excitatory on these neurons. The present experiment was done to examine, under unanesthetized natural sleep-waking condition, which neural systems were involved to keep the tonic firing of the serotonergic neurons during W.
Methods: The head of unanesthetized rats was fixed painlessly to a stereotaxic instruments by a plastic plate anchored to the skull. Single neuronal activity was recorded through a glass pipette electrode and each drug was applied iontophoretically or by pressure through one of a seven barreled glass pipette glued to the recording electrode. Serotonergic neurons in the dorsal raphe were discriminated from others by broad action potential (positive component > 0.8 msec) and regular, tonic firing during waking.
Results: Spontaneous firing of the 5HT neurons in DR were excited by glutamate (n=8) and orexin A or B (5 of 6 neurons). Excitation by glutamate was observed at every states of sleep-waking cycles including W, SWS an PS, while excitation by orexins was observed only during SWS or PS when the firing rate was low. Noradrenaline caused inhibition in 5 of 6 neurons when applied during W or SWS. An alpha-1 receptor agonist (phenylephrine or methoxamine) increased the firing rate during SWS or PS up to the level during W in 11 of 16 neurons, while it had no effect when applied during W (n=8). Histamine had almost no effect at every stages (n=10).
Conclusions: In rats, the major source to maintain tonic firing of 5HT neurons during W would be glutamatergic and orexinergic neurons. Noradrenaline would also have a role to maintain the firing during W, however it might has also inhibitory influences in some cases during W.

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0070.A

Sleep and Stress Response in Female Knock-out Mice that do not Express the Serotonin Transporter

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Introduction: Serotonin (5-HT) is involved in both sleep regulation and stress response. Stress-elicited activation of the hypothalamo-pituitary-adrenocorticotropic (HPA) axis triggers a delayed REM sleep rebound as well as adaptive changes at serotonergic receptors. In addition, the response of HPA axis to an acute stress is more pronounced in females than in males, and selective serotonin reuptake inhibitors (SSRI), the most widely used antidepressants, are often more efficient in women than in men. In order to investigate the involvement of the serotonergic system in the sleep response to acute stress, we have used female mice that do not express the 5-HT transporter (5-HTT-/-). In such animals, this genetic deletion results in a tonic increase in 5-HT levels in the extracellular space, leading in turn to the desensitization of 5-HT1A and 5-HT1B receptors.
Methods: Under general anaesthesia, female mice of the 5-HTT-/- and wild-type (5-HTT+/+) CD1 strains were implanted with electrodes for polygraphic sleep monitoring. After recovery and habituation to the recording conditions (12h light-dark cycle, light-on at 7:00, food and water ad libitum), polygraphic recordings of the spontaneous sleep-wakefulness cycle were performed during 96h (baseline), then during 24h after an immobilization stress challenge (mice were tightly wrapped in a plastic grid from 17:30 to 19:00) performed during the dioestrus phase. Control values were obtained from prior recordings performed after a sham immobilization challenge in each animal, under the same conditions. In parallel, seric corticosterone levels were measured in other animals at various times after the immobilization and sham procedures.
Results: Under baseline conditions, 5-HTT-/- mutants exhibited both larger amounts of REM sleep and a higher frequency of theta rhythm compared to 5-HTT+/+ mice (mean $\pm$ SEM, REM/24h: 146 $\pm$ 2, n=9, vs 97 $\pm$ 4 min, n=7, $p<0.001$; peak of theta: 7.8 $\pm$ 0.1 vs 7.3 $\pm$ 0.1 Hz, $p<0.0001$). No differences between the two strains were observed with regard to the other states of vigilance.After the immobilization stress, 5-HTT+/+ mice (n=5) exhibited a REM sleep rebound which occured after a 12h-delay, i.e., on the following day (REM/12h: 62.6 $\pm$ 4.0 vs 49.6 $\pm$ 5.5 for the sham controls, $p<0.05$). In contrast, 5-HTT-/- mice (n=5) exhibited similar amounts of REM sleep during the whole 24h-recording session after the immobilization and the sham procedures.In both strains, corticosterone levels were enhanced immediately after the stress (~2.5-fold for 5-HTT+/+ and ~2-fold for 5-HTT-/- mice). Then, 14h after the stress, corticosterone levels had returned to baseline levels in 5-HTT +/+ mice, but were still elevated (~1.6-fold) in 5-HTT-/- mutants.
Conclusions: Female mice that do not express the 5-HT transporter exhibit enhanced amounts of REM sleep. This phenomenon might be explained by the desensitization of post-synaptic 5-HT1A and 5-HT1B receptors, because these receptors exert a negative control on REM sleep. The deficiency of REM sleep rebound after acute stress in 5-HTT-/- mutants might reflect, in addition to 5-HT receptors impairment, disturbances of the HPA axis, as shown notably by the persistent elevation of corticosterone levels after the stress session.

0071.A

Inhibition of Serotonin Synthesis During Development Restores Normal REM Sleep Levels in 5-HT Transporter Knock-out Mice

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Introduction: Mutant mice lacking the gene encoding the serotonin transporter (5-HTT-/-) exhibit larger amounts of REM sleep than their wild-type counterparts (5-HTT+/+). This phenomenon is probably due to permanent desensitization of central 5-HT1A and 5-HT1B receptors in response to tonic increase in extracellular 5-HT levels resulting from absence of 5-HT reuptake in the mutants. Our hypothesis was that such adaptative changes in 5-HT receptors are initiated mostly during the developmental period. Thus, we designed an experimental protocol aimed at reducing extracellular 5-HT levels by inhibiting 5-HT synthesis during development in 5-HTT-/- mice. Sleep-wakefulness patterns were then examined in these animals at adult age.
Methods: Chronic treatment: 5-HTT-/- pups were treated daily with the 5-HT synthesis inhibitor pCPA (100 mg/kg i.p.) or saline from the 5th to the 19th posnatal day. A reference group of 5-HTT+/+ mice received saline (0.1ml, i.p.) during the same developmental period.Surgery and polygraphic recording: Experiments were performed in 2-3 month-old male mice. Under general anaesthesia (mix of 20 mg/kg xylazine –100 mg/kg ketamine), animals were implanted with the classical set of electrodes for polygraphic sleep monitoring. After 10 days of recovery and habituation to the experimental conditions (12h light-dark cycle, light on from 7:00 to 19:00), their spontaneous sleep-wakefulness cycle was

recorded during 48h, and the amounts of each state of vigilance were averaged for each animal during a single 24h-period.
Results: 5-HTT-/- mutants treated with saline exhibited an enhancement in both the amounts of REM sleep and the frequency of theta rhythm, compared to 5-HTT+/+ mice (mean±SEM, REM/24h: 137±3, n=5, vs 107±6 min, n=4, $p<0.005$; peak of theta: 8.0±0.1 vs 7.2±0.1 Hz, $p<0.0001$). After pCPA treatment, these values were decreased in 5-HTT-/- mice (REM/24h: 115±6, n=5; peak of theta: 7.2±0.1 Hz, $p<0.005$ and $p<0.0001$, respectively, compared to saline-treated 5-HTT-/- controls), notably during the dark period. No differences between strains or treatments were observed with regard to the other states of vigilance. Thus, 5-HTT-/- mutants treated with pCPA exhibited the same sleep phenotype as 5-HTT+/+ mice. Preliminary data indicated that this phenomenon persisted in one-year old mice.
Conclusions: The present data suggest that the REM sleep enhancement characteristic of 5-HTT-/- mutant mice is caused by high extracellular levels of 5-HT in the central nervous system at early stages of postnatal development. They show that it is possible to permanently reverse the 5-HTT-/- sleep and EEG phenotypes by inhibiting 5-HT synthesis during a limited developmental period.

0072.A

Estrogen Supplement Restores Impaired Sleep Patterns In Old Female Rats

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Introduction: At menopause estrogen levels of a woman decline dramatically, triggering several health discomforts. Hormone replacement therapy (HRT) is a medical treatment that combined with a progestin artificially increases the levels of estrogen. It is popularly prescribed in Western countries, but less so in Japan. Although women often develop insomnia during the perimenopausal period, whether HRT improves their sleep problems is not fully known. This study, therefore, examined in an animal model the effects of estrogen (Es2s) treatment on sleep and cholinergic activity in the brain.
Methods: Aged female Sprague-Dawley rats (20 E4 mo, 632 ± 24.7 g bw, n=18) were anesthetized with pentobarbital sodium and implanted with EEG and EMG electrodes. During recovery from surgery, the rats were acclimated to subcutaneous (sc) injections. After acclimation to daily injections, all the rats received 0.1 ml of sesame oil (vehicle for Es2s) sc on day 0 then either 20 mg of Es2s (17b-estradiol benzoate) or vehicle sc for a following week. Injections were performed at 17.30 h, and polygraphic recordings were monitored between 20.00 E7.00 h (light period: 08.00 E0.00 h) for 8 days including day 0 as a baseline control. Another group of female rats (22 E5 mo, 691 ± 33.4 g bw, n=8) given Es2s was sacrificed on day 8, and their brains were removed. Choline acetyltransferase (ChAT) activity was determined in Ch1-6 neurons and specific cerebral regions including the basal forebrain, hippocampus, and frontal-occipital cortex. Data were analyzed statistically by ANOVA with post-hoc comparisons.
Results: Compared with young females in diestrus, old females spent less time in non-REM sleep during the light period but more time in REM sleep during the dark period ($P<0.05$). These phenomena contributed to make little difference in daytime and nighttime sleep, indicating that the nocturnal variation of sleep-wake activity in rats became blunted when they aged. However, Es2s treatment even with single dose tended to improve the disrupted sleep pattern in old female rats. By the time the continuous Es2s treatment finished after a week (day 7), the duration of daytime non-REM sleep increased by 16.3 %, whereas the nighttime REM sleep decreased to 73.8 %. ChAT activity in old females was lower in most examined regions than that in young controls, and its significant differences were found in the medial septal area, laterodorsal tegmental nucleus, basal forebrain, and hippocampus ($P<0.05$). Repeated Es2s treatment tended to increase ChAT activity in those regions, but not as high as that in young females.
Conclusions: The results demonstrate that old female rats show an impaired sleep-wake distribution, which could be in part due to a decrease in cholinergic presynaptic activity. Since Es2s treatment was effective on restoring their sleep patterns and cholinergic system, Es2s supplement can be a possible therapeutic choice for postmenopausal disorders of sleep and consciousness.

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0073.A

Non-monotonic Changes Of Sleep EEG Dynamics In Rat Barrel Cortex Associated With Long-term Sensory Deprivations

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Introduction: Sensory deprivation is known to alter the neural organizations involved for processing the deprived neural information even after maturation. However, long-term effects of the sensory deprivation have not yet been well-understood. In order to investigate the long-term effects on the post-mature neural organizations and their relation to sleep functions, cortical EEG dynamics during sleep in adult rats are measured during up to a month, while somatosensory inputs are constantly deprived by cutting whiskers unilaterally.
Methods: Used animals were six adult male Sprague-Dawley rats (2 Months). EEG electrodes were implanted bilaterally on dura over the barrel cortices and a reference electrode was placed over the cerebellum. First, for the control under LD12:12 cycle, polygraphic signals were being recorded for 4hr from the beginning of the light period in two successive days before the whisker cut. Then, after all whiskers on right side were cut at the every beginning of the light period, 4hr-polygraphic recording started. Scoring of sleep stages was done every 10s by visual inspection. Here, non-rapid eye movement sleep (NREM) was categorized into two stages, light and deep NREMs, based on a percentage of slow wave appearance in each scoring epoch, i.e., NREM with 50% or more percentage is called “deep” and below 50% “light”. Spectral powers of d- and band EEG were estimated by FFT for every 16s intervals and averaged through an epoch. d-power during the deep NREM, and d-powers during the light NREM, and the power during rapid eye movement sleep (REM) were subject to comparison between the intact and the deprived cortical barrel areas, which was quantified by the ratio of the power in the deprived area to the intact.
Results: In five rats of six, both d- and band spectral powers of EEG in the sensorially-deprived barrel cortex decreased in comparison with the intact from 2nd day to 10th day. This tendency was pronounced in d-band powers during the light and deep NREMs, which was shared by all the five rats. Subsequently, the ratio tended to increase from 10th day to 25th day. The ratio after 25th day was observed to restore or exceed the control value.
Conclusions: Both d- and band spectral powers of EEG in the sensorially-deprived barrel cortex initially decreased in comparison with the intact, and then alternately their ratios to the intact increased. The resulting changes in EEG dynamics are expected to be caused by neural reorganizations associated with the long-term sensory deprivation. Mechanisms underlying their non-monotonic long-term change deserve studying further.

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0074.A

An Individual Fingerprint of Human NREM Sleep: The Antero-posterior Topography of the Middle EEG Frequencies

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Introduction: Recent topographic analyses of sigma EEG activity during NREM sleep pointed to the existence of two distinct sleep spindle (SS) types: "slow" spindles at ~12 Hz more pronounced over the frontal sites, and "fast" SS at ~14 Hz more pronounced over centro-parietal sites; the former declining and the latter increasing over consecutive sleep episodes. Functional dissociations have also been reported, as a function of age and maturation, homeostatic and circadian factors, menstrual cycle phase, pregnancy and pharmacological agents. These results have been interpreted according to two functionally separated spindle generators.On the other hand, lower and higher frequencies of SS have been attributed to a single mechanism, namely, the duration of hyperpolarization-rebound sequence in thalamocortical neurons; and cortical areas on which "slow" SS have been detected are related to those thalamic nuclei in which relay cells display long hyperpolarizations.In fact, most studies showing the two cortically-independent SS bulk the bounds of sigma band from the traditional 12-14 Hz range, including frequency bins traditionally considered within the alpha band. Secondly, there are great inter-individual differences, and topographical analyses on between-subject averaged data could confound individual (different) cortical topographical distributions with the existence of different topographically-specific SS. Finally, spindle frequency could change as a function of the same variables differently affecting the two types of SS. Topographical EEG analysis in single subjects could allow to disentangle the question.
Methods: Data from sleep recordings (Fz-A1, Cz-A1, Pz-A1, Oz-A1) of 10 normal males served as database. The subjects participated in a SWS deprivation study (six consecutive nights). Power values were calculated across a 8.00-15.50 Hz range in a 0.25-Hz resolution for NREM episodes of each subject. Absolute power was transformed into z scores.
Results: Four subjects had one spectral peak in the range of SS frequencies on all derivations (12.25-13.25 Hz); three others had two spectral peaks on different derivations, with one peak higher on Fz (10.25-11.25 Hz) and another peak higher on Cz-Pz (13.50-13.75 Hz); the last three subjects had two spectral peaks discernible only on Fz (respectively at 10.00-10.50 and 12.50-13.00 Hz).
Conclusions: Individual data show one kind of SS, ranging within the 12.25-13.75 Hz, and in some subjects alpha activity peaking on more anterior brain sites. However, the most impressive result is the high spectral invariancy of individual antero-posterior topography in the 8.00-15.50 Hz frequency range, notwithstanding wide changes in sleep architecture across the six nights (one adaptation, two baselines, two nights without SWS, one recovery). This invariancy of EEG topography may be related to brain anatomy, and studies comparing monozygotic and dizygotic twins will allow to demonstrate this hypothesis.

0075.A

Intermittent Hypoxia: Redox Changes in Serotonergic Control of Hypoglossal Motoneurons

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Introduction: Sleep state-dependent withdrawal of serotonin (5-HT) at upper airway dilator motoneurons contributes to sleep-dependent suppression of dilator muscle activity in obstructive sleep apnea. These studies tested the hypothesis that chronic intermittent hypoxia results in oxidative injury to upper airway motoneurons, thereby diminishing serotonergic motoneuronal excitation.
Methods: A series of acute microinjections was performed in adult rats exposed to either intermittent hypoxia (FIO2 nadir 9%; RDI=40) or sham intermittent hypoxia (FIO2 nadir 19%; RDI=40) for 3 weeks. The effects of serotonin agonists and antagonists on hypoglossal whole nerve activity were measured across dose-response curves. A third group of rats received a superoxide dismutase mimetic (tempol) throughout intermittent hypoxia. Isoprostanes, 5-HT binding and protein kinase C activity were measured in hypoglossal nuclei for all three groups.
Results: Although baseline hypoglossal nerve activity and the IC50 responses for methysergide were unchanged for the groups, the responsiveness of hypoglossal motor neurons to 5-HT was significantly reduced under conditions of IH3wk. The LogEC50 for hypoglossal 5-HT was 2.6±.04uM (IH3wk) and 1.7±.09 uM(SH3wk), $p<0.01$ and the Emax for hypoglossal 5-HT was reduced 172±16% (IH3wk) versus 245±38% (SH3wk), $p<0.01$. 4-hydroxyl-2,2,6,6-tetramethylpiperidin-1-oxyl administered (tempol) in drinking water throughout exposure to IH3wk (T-IH3wk) normalized the 5-HT ECmax, 215±12%,$p<0.05$ and reduced the logEC50 to 2.1±0.3, $p=.05$. IH3wk did not alter post-synaptic 5-HT receptor transcription (mRNA copy numbers for single hypoglossal motoneuron 5-HT2A and 2C, N.S.), and relative [3H] DOI binding within the hypoglossal nucleus was unchanged. Isoprostane (d4-8,12-iso-iPF2a-VI) levels were increased 2-fold with IH3wk, $p<0.05$, but not under conditions, T-IH3wk. Protein kinase C activity within the hypoglossal nucleus was unchanged with intermittent-hypoxia.
Conclusions: The results presented here several important implications for the effects of sleep-disordered breathing on neural function. The data demonstrate that chronic intermittent hypoxia reduces the responsiveness of hypoglossal motor neurons to 5-HT. Thus, the severity of intermittent hypoxia in persons with obstructive sleep apnea may have significant effects on responsiveness of upper airway motor neurons to serotonergic drugs. Second, the present study showed a large (two-fold) increase in isoprostanes in the dorsal medulla, suggesting that intermittent hypoxia, as in our protocol, may result in significant lipid peroxidation in medulla. With peroxynitrite production implicated in the pathogenesis of several neurodegenerative processes, it will become important to determine if intermittent hypoxia, as in obstructive sleep apnea, can accelerate the progression of neurodegenerative disorders. Finally, the intermittent hypoxia-induced alteration in 5-HT responsiveness, associated with increased lipid peroxidationand without a change in 5-HT receptor density, raises the possibility that the responsiveness of other neurotransmitters, particularly glutamate, may be affected by intermittent hypoxia.

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0076.A

Chronic Intermittent Hypoxia Results in Prolonged Alterations in Sleep Architecture and Sleepiness

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Introduction: Although many persons with obstructive sleep apnea notice a marked improvement in alertness shortly after beginning effective CPAP therapy for obstructive sleep apnea, lingering daytime somnolence and fatigue are not uncommon. We hypothesized that irreversible oxidative injury from obstructive sleep apnea might result in long term or permanent injury to monoaminergic arousal systems and other forebrain neurons important in wakefulness control.
Methods: Adult male C57BL/6J mice were exposed to either intermittent hypoxia (FIO2 nadir 9%, RDI = 40/hr) or sham intermittent hypoxia (FIO2 nadir 19%, RDI = 40/hr) for 9 of the 12 hours of the light period for 4 consecutive weeks. Mice were then anesthetized with ketamine/xylazine and implanted with 4 electroencephalographic electrodes and two dorsal nuchal muscular electrodes for recording behav-

ioral state using our previously described methods. Mice were allowed to recover for 7 days following electrode implantation in their home cages with littermates. One week post-operatively, the mice were anesthetized lightly with isofluorane; electrode recording cables were connected to implants, and mice were placed in individual recording chambers and allowed to acclimate for 5-7 days before behavioral recordings. We designed a murine multiple sleep latency test involving four nap opportunities for 20 minutes spaced every 30 minutes from 2-4 pm. We validated that 7 hr sleep deprivation significantly reduces the murine MSLT in 4 strains of inbred mice (DBA, C57, C3H, AJ). Baseline sleep recordings were obtained then 2 weeks after terminaton of intermittent hypoxia or sham hypoxia. Following 48hr baseline sleep recordings a MSLT was performed as above. Mice recovered for one day. 7 hr sleep deprivation was performed the next morning from 7 am until 2pm using intermittent ambient air blown into the recording cages whenever an individual mouse showed slowing or increased EEG amplitude on monitors. At 2pm, the post-sleep deprivation MSLT commenced. Recovery sleep was recorded from 4 pm until the following morning.

Results: Baseline total sleep time in B6 mice exposed to intermittent hypoxia was increased by two hours, 849±30 min/24 hour, compared with 646±56 min in mice exposed to sham hypoxia, $p<0.01$. The increase was present for both the light and dark periods. The most dramatic finding was an increased in REM sleep time from 51 ±6 min/24 hr in sham hypoxia mice to 88±6 min/24 hr in mice exposed to intermittent hypoxia, $p<0.01$. The increase following intermittent hypoxia was significant for both the light and dark periods. The baseline multiple sleep latency times were not significantly different for the two groups at baseline (sham, 12±2 min and CIH , 10± 2 min) and both groups showed substantial reductions in the MSLT following 7 hr sleep loss in the beginning of the light period (sham, 6±1 and CIH, 2±1, p's<0.05). The striking difference between groups was a much greater reduction in MSLT time after sleep loss in the mice exposed to intermittent hypoxia.

Conclusions: Four weeks of intermittent hypoxia results in alterations in sleep architecture and light period wakefulness lasting at least 2 weeks after termination of exposure to intermittent hypoxia. The findings of increased total sleep time, with a larger increase in REM sleep time than NREM sleep time would be consistent with alterations in the monoaminergic arousal systems. Monoaminergic neurons are at increased vulnerability to oxidative stress, and thus, it is possible that intermittent hypoxia results in irreversible oxidative injury to the monoaminergic neurons and this, in turn, results in the refractory sleepiness and fatigue following optimal therapy for sleep apnea. Studies to measure forebrain monoamines in these mice are underway.

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0077.A

Caffeine Induces c-Fos Expression In Arousal-Related Aminergic Neuronal Groups In Rat

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Introduction: Caffeine is the most commonly used psychostimulant in the world. However, neuronal mechanisms mediating its stimulatory effect are not fully understood. We recently reported, using c-Fos as a marker for neuronal activation, that psychostimulant doses of caffeine induce activation of hypocretin/orexin-containing neurons which play an important role in arousal. Here we examined whether other components of the arousal system, specifically aminergic neuronal groups, are also activated by caffeine, by using dual immunostaining for c-Fos and aminergic transmitter markers.

Methods: Adult male Wistar rats were injected with 10, 30 or 75 mg/kg, i.p. caffeine, or saline. Ninety minutes after injection, rats were deeply anesthetized and perfused for double-label immunohistochemistry for c-Fos and neurotransmitters or related enzymes, including: histidine decarboxylase to visualize histaminergic neurons in the tuberomammillary nucleus (TMN); tyrosine hydroxylase to visualize noradrenergic neurons in the locus coeruleus (LC), and dopaminergic neurons in the ventral tegmental area, substantia nigra pars compacta and midbrain central grey; and serotonin to visualize serotoninergic neurons in the dorsal raphe nucleus (DRN).

Results: Compared to saline, caffeine at 10 and 30 mg/kg increased locomotion, whereas at the higher dose (75 mg/kg) it induced immobility. Saline controls exhibited only small numbers of c-Fos positive cells in all regions examined. The magnitude of increase in c-Fos expression differed among neuronal groups and doses. In general, the most robust expression occurred in LC noradrenergic neurons. Two low doses of caffeine increased the numbers of noradrenergic and histaminergic neurons immunoreactive for c-Fos by 450% and 30%, respectively. Serotoninergic neurons in the DRN showed no changes in Fos immunoreactivity. The highest dose of caffeine increased c-Fos immunoreactivity by 1000% in noradrenergic and serotoninergic neurons, and by 80% in histaminergic neurons. Caffeine at any dose used failed to induce c-Fos immunoreactivity in dopaminergic neurons in the ventral tegmental area, substantia nigra pars compacta and central grey. In comparison with our previous study, the increase in Fos expression in orexin-containing neurons was less than in noradrenergic neurons but greater than in histaminergic neurons.

Conclusions: These results indicate that caffeine induces c-Fos expression differentially among aminergic arousal-related cell groups. Low locomotor-stimulant doses increase Fos immunoreactivity in LC noradrenergic neurons and TMN histaminergic neurons, as well as orexin-containing neurons, but not in DRN serotoninergic neurons. A higher, locomotor-depressant dose induces c-Fos expression in all of these neurons. Dopaminergic neurons in ventral tegmental area, substantia nigra pars compacta and midbrain central grey did not respond to caffeine with changes in c-Fos expression. These aminergic neurons and orexin-containing neurons that are activated at low caffeine doses might play a role in mediating behavioral activation induced by caffeine. Studies of c-Fos expression in cholinergic arousal-related cell groups after caffeine are in progress.

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0078.A

The Role of Nitric Oxide in Regulation of Sleep Need

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Introduction: It is has been found that accumulation of adenosine in the basal forebrain can be a key mechanism mediating effects of prolonged wakefulness. Recently we established that local energy depletion in the basal forebrain, induced by infusion of 2,4-dinitrophenol, mimicked the effects of sleep deprivation leading to site-specific accumulation of extracellular adenosine and increasing subsequent sleep. Nitric oxide (NO), an intercellular signalling molecule, has been reported to inhibit the energy production and stimulate extracellular adenosine accumulation in rat forebrain neurons in culture. We suggest that release of NO in the basal forebrain during prolonged wakefulness could be a possible mechanism underlyng adenosine accumulation and increase in sleep need. In order to test this hypothesis we studied the effects of local infusions of a NO synthesis inhibitor (L-NAME) and a NO donor (DETA NONOate) on sleep.

Methods: Under anesthesia 8 male rats were implanted with electrodes for recording of EEG and EMG and guide cannulae. Microdialysis probes were aimed to the basal forebrain (n=4) or adjacent non-cholinergic areas (n=4) as a control. Experimental schedule for each rat was as follows: sleep deprivation for 3h preceded by 1h baseline and followed

by 2h of recovery sleep; sleep deprivation for 3h combined with L-NAME (0.6mM) infusion; infusions of L-NAME and DETA NONOate (1mM) for 3h during normal sleep-wake cycle preceded by 3h baseline. The EEG was recorded for 24h and scored for wakefulness, non-REM and REM sleep. Period of maximal increase in sleep (5pm-2am) was chosen for final quantitative analysis. After the experiments the locations of the probe tips were verified histologically. Statistical significance was assessed using one way ANOVA followed by Dunnet's post-hoc test.
Results: Sleep deprivation induced an increase in sleep by 50.6 ± 8.8% (one-way ANOVA $F(3)=14.084$, $p<0.001$, post-hoc Dunnet's test $Q=4.532$, $p<0.05$). Infusion of L-NAME into the basal forebrain during sleep deprivation completely suppressed the effect of prolonged wakefulness, but infusion of L-NAME outside the basal forebrain during prolonged wakefulness was ineffective: sleep was significantly elevated by 47.3 ± 7.9% (one-way ANOVA $F(3)=14.084$, $p<0.001$, post-hoc Dunnet's test $Q=3.656$, $p<0.05$). L-NAME infusion during normal sleep-wake cycle into the basal forebrain or outside did not influence sleep. Infusion of DETA NONOate during normal sleep-wake cycle into the basal forebrain mimicked the effects of prolonged wakefulness and increased sleep by 50 ± 7.7% (one-way ANOVA $F(2)=31.908$, $p<0.001$, post-hoc Dunnet's test $Q=6.531$, $p>0.05$). Changes in sleep after infusion of DETA NONOate into the non-cholinergic area (-5.5 ± 5.3%) were insignificant.
Conclusions: NO may be one of the key intercellular signalling molecules involved in regulation of sleep need.

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0079.A

Serotonin Modulation Reveals Two Types of GABAergic Sleep Promoting Neurons In The Ventrolateral Preoptic Nucleus (VLPO)
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Introduction: Recent studies supported the crucial role of the ventrolateral preoptic nucleus (VLPO) in the sleep onset and maintenance. The VLPO contains GABAergic neurons sending inhibitory projections to major systems of arousal and being active during sleep according to previous functional cFos staining studies. Using intracellular recordings and single cell RT-PCR experiments in rat VLPO slices, we previously identified a large contingent of GABAergic, triangular-shape cells that displayed a prominent low threshold spike (LTS) and were strongly inhibited by noradrenaline and acetylcholine, two major transmitters of arousal. These LTS cells must correspond to sleep-promoting neurons, recorded in vivo within this area, and postulated to inhibit the systems of arousal to which they project. The aim of the present study was to investigate the neuromodulation of the sleep promoting neurons by serotonin, a neurotransmitter crucial for sleep regulation.
Methods: Basal forebrain slices containing the VLPO were obtained from 15-20 days old rats (OFA) according to standard procedures. Individual 300 or 400 mm thick slices were transferred to a thermoregulated (32°C) chamber, under either a dissecting microscope for sharp intracellular recordings or a Zeiss Axioscop with an infrared camera for juxtacellular and patch-clamp recordings of identified cells. Slices were maintained immersed and continuously superfused at 3-5 ml/min with oxygenated ACSF. Slices containing one biocytin-filled neuron were revealed by using the classical DAB histochemical technique.
Results: Juxtacellular recordings demonstrated that serotonin (100 mM, 15 sec), bath-applied on noradrenaline-inhibited cells (10 mM, 10 sec), induced either excitation with an increased of the firing rate (53% of the cells) or inhibition of the spontaneous activity (47%). These data suggested the presence of two types of LTS-cells within the VLPO. Patch-clamp recordings with electrodes containing Biocytin combined with single cell multiplex RT-PCR confirmed that both types of cells were triangular in shape, located within the VLPO and expressed GAD65 and/or GAD67 mRNA (n=30), further supporting their GABAergic nature. Additional molecular data indicated that LTS-cells excited by serotonin only expressed 5HT2c and 5HT5a receptor mRNA. On the other hand, the inhibition by serotonin of the second type of LTS-cells was mediated by 5-HT1A receptors, since similar inhibition was obtained with the specific agonist, 8-OH-DPAT (1 mM, 20 sec).
Conclusions: While further molecular combined with pharmacological studies are still necessary, we hypothesize that serotonin has a complex action in the VLPO simultaneously maintaining wakefulness through its inhibitory action and preparing sleep by its excitatory action.

0080.A

Motor Cortex Excitability Upon Awakening From REM and NREM Sleep: A Study by Means of Transcranial Magnetic Stimulation
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Introduction: There is increasing evidence that human sleep may be considered as a local process with use-dependent characteristics. For instance, the spectral analysis of sleep EEG showed that NREM sleep is characterized by a fronto-occipital power gradient. Coherently, a larger reduction of frontal regional cerebral blood flow as compared to other cortical areas has been described during sleep. The aim of this study was to assess the motor cortex excitability by applying, for the first time, Transcranial Magnetic Stimulation (TMS) immediately upon awakening from NREM and REM sleep, and recording the corresponding motor evoked potentials (MEPs).
Methods: Ten subjects slept for 4 consecutive nights in the laboratory. During the first night (adaptation), motor thresholds (MTs) had been assessed during pre-sleep wakefulness (before lights off), as well as upon awakening from stage 2 and REM sleep. The stimulator was a Magstim 200 Mono Pulse with a figure-of-eight coil with external wing diameter of 9 cm (peak magnetic field: 2.0 T). The MEPs were recorded from the *Abductor Digiti Minimi* muscles, in both hands. The individual MTs were defined as the lower intensity able to produce at least 3 MEPs with 100 mV of amplitude (peak-to-peak) in 6 consecutive stimulations.
Results: A repeated measure ANOVA State (Wake, REM, Stage 2) by Hemisphere (Left, Right) showed a significant main effect for State ($F=13.75$; $p=0.0003$), with an increasing linear trend of MTs from wake to Stage 2, with REM sleep showing intermediate values ($F=23.63$; $p=0.001$). While during wake and stage 2 MTs were identical, during REM sleep they were higher over the right hemisphere ($p=0.04$).
Conclusions: The increase of MTs upon awakening from stage 2 confirms by an independent method that NREM sleep is characterized by lower levels of brain excitability as compared to REM sleep, whose MTs values are closer to wakefulness levels. During REM sleep, however, the right motor cortex is characterized by a lower excitability than the left one, as indicated by the higher MT over the right hemisphere.

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0081.A

Sleep Pattern in Rats with Spinal Cord Injury
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Introduction: Is known that in literature the sleep pattern in subjects with sedentary spinal cord injury (SCI) reveals a longer period of sleep

when compared with SCI athletes. The purpose of this study was to evaluate the pattern of sleep in rats after a SCI.
Methods: Nineteen Wistar male rats were submitted to two periods of recording of their sleep pattern. After baseline recording (24 h), all groups were submitted to SCI and SHAM procedure and their sleep was monitored over seven days. The parameters evaluated were Total Sleep Time (%TST), Total Wake Time (%TWT), Total Slow Wave Sleep (%SWS), Total Paradoxical Sleep (%TPS), Latency Sleep (LAT) and Number of Arousal (NA).
Results: The results show that the rats with SCI revealed a tendency of a reduction of sleep efficiency during the light period. In the dark period the rats revealed a increase of sleep efficiency when compared with the group SHAM and their baseline. This increase of sleep could be due to a decrease of the %TWT (baseline to 3rd and 5th days and SHAM- 3rd, 4th, 5th and 6th days, $p<0.05$ – ANOVA, Tukey test) and an increase of the %SWS (baseline to 5th day and SHAM- 3rd, 4th, 5th and 6th days, $p<0.05$ – ANOVA, Tukey test), returning to the baseline values after 5 days of recording. No differences were observed about the number of arousal and sleep latency.
Conclusions: The results show an increase of sleep efficiency during the dark period of the rats with SCI. The increase the sleep of the SCI group during the dark period may be justified by the fact of these animals had shown reduced locomotion activity after SCI, returning to the baselines values after adapt to new behavior pattern.

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0082.A

Orexinergic Modulation of Preoptic Anterior Hypothalamic Neurons During Waking and Sleep in Unrestrained Rats

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Introduction: Extensive evidence suggests that the hypothalamic neuropeptides, orexins (hypocretins) are involved in several physiological functions including sleep-wake regulation. The preoptic anterior hypothalamic area (POAH) contains dense orexin neuronal terminals and receptor mRNAs. Local microinjection of orexin-A into POAH produces arousal, but the neuronal types mediating such effects are not known. We recorded extracellular activity of POAH neurons across sleep-wake cycle and used adjacent microdialysis to examine influences of orexin-A on their sleep- and wake-related discharge in unrestrained rats.
Methods: Three Sprague-Dawley rats were surgically implanted with (a) EEG and EMG electrodes for chronic recording of sleep-wake states, (b) five pairs of microwires into POAH for recording extracellular neuronal activity, and (c) a guide cannula positioned ~0.5 mm lateral to the microwires for delivery of orexin-A adjacent to the recorded neurons with a microdialysis probe. The sleep-wake discharge of POAH neurons was continuously recorded (a) across 3-5 sleep-waking episodes during artificial cerebrospinal fluid perfusion (baseline), (b) during perfusion of orexin-A for 10 min, and (c) during washout period. A > 25% change in nonREM sleep/wake was used as a criterion to classify neurons into wake-related, sleep-related, or state-indifferent types.
Results: The effects of orexin-A were studied on 18 POAH neurons (3 for 5mM, 11 for 10mM, and 2 for 25mM). In presence of orexin-A, POAH neurons as a group exhibited significantly increased discharge (mean $\pm$ SEM) during waking (1.71 ± 0.45 vs. 2.17 ± 0.63; $Z = -2.066$, $p = 0.03$) and slightly but insignificantly elevated discharge during nonREM sleep (1.92 ± 0.43 vs. 2.21 ± 0.51; $Z = -0.37$, $p = 0.7$). Of 18 neurons, 9 were sleep-related, 7 were wake-related and 2 were state-indifferent neurons. Orexin-A increased the discharge of wake-related neurons during both waking (2.92 ± 1.01 vs. 3.76 ± 1.47) and nonREM sleep (0.88 ± 0.30 vs. 2.77 ± 1.27). Five of 7 wake-related neurons exhibited increased discharge during both waking and nonREM sleep. Orexin-A produced marginal effect on the discharge of sleep-related neurons during waking (0.92 ± 0.20 vs. 1.10 ± 0.23) but decreased their discharge during nonREM sleep (4.34 ± 1.27 vs. 1.97 ± 0.34). Six of 9 sleep-related neurons exhibited decreased discharge during nonREM sleep whereas 3/9 exhibited increased discharge during both waking and nonREM sleep. In presence of orexin-A, 2/2 state-indifferent neurons exhibited increased discharge during both waking and nonREM sleep.
Conclusions: These preliminary results suggest that in naturally awake and sleeping animals, orexin-A exerts differential effects on POAH wake-related and sleep-related neurons. The results show that orexin-A predominantly activates wake-related and inhibits sleep-related neurons and support a wake-promoting role of orexin-A in the POAH.

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0083.A

The Effects Of The Intra-Medial Preoptic Nucleus (MPO) Microinjection Of A NO Donor And A NO Synthase Inhibitor On Sleep In Rats

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Introduction: The stimulation and inhibition of NO-ergic mechanisms in the brain have complex effects on sleep. Intracerebroventricular (icv) injection of L-NAME, a NO synthase (NOS) inhibitor suppresses both NREMS and REMS in rats and rabbits. Icv injection of SIN-1 and SNAP, two NO donors, enhance NREMS in rats. Microinjection studies revealed that some of the target sites for the effects of NO-related drugs reside in various brain stem structures such as the raphe nuclei and the pedunculopontine area. Our recent findings suggest that the anterior diencephalic region also contains structures that may also be involved in the sleep effects of NO donors and NOS inhibitors. By using bilateral microinjection technique, we tested the possible role of the suprachiasmatic nucleus (Ribeiro and Kapás, APSS 2003) and the MPO in mediating the effects of NO donors and NOS inhibitors on sleep. MPO appeared to be one of the a likely targets, since it is rich in NOS positive neurons and fibers, the nucleus is key to various behavioral effects of NO and experimental manipulation of the region that includes the MPO is known to affect sleep.
Methods: Rats were implanted with electroencephalographic (EEG) electrodes, a brain thermistor and bilateral guide cannulae for intra-MPO microinjections. The target site for the injection was 1.40 mm posterior and 0.4 mm lateral to bregma and 8.40 mm ventral from the surface of the skull. EEG and brain temperature were recorded on a first baseline day when the animals were only handled, on a second baseline day when saline was injected bilaterally, on a test day when the NO donor NOC-18 (1 ug, n = 4) or the NOS inhibitor L-NAME (10 ug, n = 4) was injected bilaterally in volumes of 50 nl. On the next, recovery, day, saline was injected again. All injections were performed during the last 30 minutes of the light phase. Recordings started at dark onset and lasted for 23 h after each treatment.
Results: Bilateral intra-MPO injection of 50 nl pyrogen-free saline elicited significant changes in sleep as compared to the handling baseline when the animals were not injected. In the first 4 h after the injection, NREMS and REMS were increased by 60% and 130%, respectively. We found a similar effect after intra-SCN injection of saline (Ribeiro and Kapás, APSS 2003). Neither L-NAME nor NOC-18 elicited significant changes in NREMS or REMS as compared to the effects of saline.
Conclusions: It is unlikely that the MPO plays a critical role in the sleep-related actions of NO donors and NOS inhibitors when they are injected at dark onset. Since the effects of L-NAME depend on the timing of the injection, it cannot be excluded that the MPO may contribute

to the wake-promoting effects of L-NAME when it is injected during the light phase of the day.

0084.A

Pyrilamine, an H1 Receptor Antagonist, Alters Arousal to Multimodal Stimuli

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Introduction: The histaminergic system is well-known to participate in the regulation of wakefulness. In addition, histamine affects many other aspects of arousal. The purpose of the following experiment was to quantify the role of H1 receptors in global arousal and, conversely, to explore a novel assay to measure global arousal. In addition, we started to explore the influence of genetic sex on histamine's regulation of arousal. To this aim, we have begun to measure the effect of pyrilamine (PYR) on the behavior of mice in a multimodal assay of arousal, which measures sensory alertness, voluntary running wheel activity, and fear responsiveness.
Methods: Thirty-two Swiss-Webster mice, castrated males and ovariectomized females, received subcutaneous injections of either vehicle, 15 mg/kg, 35 mg/kg, or 55 mg/kg of PYR. Thirty minutes following the injection, changes in sensory responsiveness (as measured by changes in home cage activity), running wheel activity, and non-conditioned fear (elevated plus maze behavior) or conditioned fear (contextual fear-conditioning paradigm) were measured.
Results: Results showed that the highest dose of PYR tended to decrease horizontal activity (HA), vertical activity (VA), and exploration of the homecage (TD) in response to an array of sensory stimuli. PYR had its greatest impact on the arousal response to a tactile stimulus (TD:F=5.16, p=0.04). Similarly, the highest dose of PYR also tended to decrease running wheel activity compared to vehicle-treated mice (F=3.6, p=0.09). Interestingly, while PYR decreased sensory responsiveness and running wheel activity, even the highest dose of PYR did not induce sleep on a behavioral level. Among a large number of assays in which reactions to PYR were similar between males and females, sex differences were suggested in the effect of 35 mg/kg of PYR on running wheel activity and sensory responsiveness. At 15 mg/kg of PYR, mice exhibited a significant decrease in the number of open arm entries (F=6.77, p=0.02), a significant increase in time spent in the closed arms of the maze (F=6.04, p=0.03), and a significant decrease in rearing (F=9.46, p=0.01). No difference was detected between PYR-treated mice and vehicle-treated mice in a contextual fear-conditioning paradigm.
Conclusions: These results demonstrate that histamine is important for the regulation of behavioral arousal in many different contexts. Furthermore, the effect of PYR is not purely a sedative one, indicating a complex role of histamine in arousal regulation.

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0085.A

Dialysis Delivery Of The GABAsAs Antagonist Bicuculline To The Medial Pontine Reticular Formation Of Conscious Cat Increases Acetylcholine Release

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Introduction: Microinjection of the GABAsAs antagonist bicuculline into cat pontine reticular formation increases the amount of time spent in rapid eye movement (REM) sleep and shortens REM latency (J Neurophysiol 82: 2015, 1999). The mechanisms underlying the bicuculline-induced REM sleep enhancement are not understood. REM sleep is significantly increased by pontine microinjection of cholinomimetics (Sleep 22:835, 1999), and REM sleep is characterized by increased acetylcholine (ACh) release within the medial pontine reticular formation (mPRF) (J Neurosci 17:774, 1997). The foregoing data raise the question of whether bicuculline enhances REM sleep by increasing ACh release. This study is testing the hypothesis that dialysis administration of the GABAsAs antagonist bicuculline into the mPRF of conscious cat causes increased ACh release in the mPRF.
Methods: Cats (N=3) are implanted with standard electrodes for polygraphic identification of sleep/wake states. For each experiment, a microdialysis probe is aimed stereotaxically for the mPRF and perfused with Ringer's solution (3 ul/min). Control dialysis samples (30 ul) are collected during unambiguous states of wakefulness, non-REM (NREM) sleep, and REM sleep. The probe then is perfused with one of four concentrations of bicuculline (0.1, 0.3, 1, or 3 mM) dissolved in Ringer's and ACh is simultaneously quantified (pmol/10 min) using high performance liquid chromatography with electrochemical detection. Histological confirmation of dialysis probe placement is pending.
Results: Bicuculline caused a concentration dependent increase in ACh release (ANOVA: F=33.4; df=4, 67; p<0.0001). This finding demonstrates that GABAsAs receptors modulate ACh release in the mPRF of unanesthetized cat. The highest concentration of bicuculline (3 mM) significantly increased ACh release (Dunnett's test, p<0.01) and produced a REM sleep-like state. Lower concentrations of bicuculline (0.1 and 0.3 mM) did not increase ACh release and animals remained awake. Enhancement of REM sleep by intrapontine drug administration is known to be dependent upon site of drug administration within the pons. Determining the degree to which these concentration dependent effects of bicuculline covary with pontine site of bicuculline delivery also will be important.
Conclusions: These data demonstrate that dialysis delivery of bicuculline to the pontine reticular formation increases ACh release and increases REM sleep. The results provide preliminary support for the hypothesis that blockade of pontine GABAergic neurotransmission enhances REM sleep, in part, by causing an increase in pontine ACh release.

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0086.A

Brain Levels of Orexin B are Decreased in Junior Rats Neonatally Treated with REM Sleep Suppressant of Clomipramine

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Introduction: Orexin (hypocretin) producing cells in the hypothalamus are wake promoting neurons with widespread axonal connection throughout the brain. Orexin A and orexin B synthesized in orexin neurons promote wakefulness and suppress REM sleep. Neonatal rat has 70% or higher of REM sleep and 30% or less of wakefulness in the first week of life (Jouvet-Mounier et al, Dev Psychol 1970; 2:216-239). The wake/REM sleep (W/R) ratio in neonatal rats is (30%/70%=0.43) and increases progressively as rat matured (47.8%/14.1%=3.39 on P27, calculated from Vogel et al, Physiol Behav 2000; 68:453-61). The paralleling change of REM sleep decrease and wake increase indicates that maturation of orexinergic neurons may play a crucial role in the W/R ratio change and that the disinhibited REM sleep found in adult rats neonatally treated with clomipramine (CLI) may be a sign of defective wakefulness (Mirmiran M, et al, Brain Res 1981; 204: 129-46). This suggests my hypothesis that adult CLI rats have defective development of orexinergic neurons. The following study examined the orexin B levels in multiple brain regions in adult CLI rats.
Methods: Thirteen Long Evans hooded neonatal rats were injected with CLI 20 mg/kg (n=7) or equivolume saline (SAL, n=6), sc, twice daily

from postnatal 8 to 21 days. At PN 30, rats were sacrificed by decapitation. Brains were removed, frozen on dry ice and dissected into 14 regions. Peptide extraction was carried out by boiling in 0.5M acetic acid for 15 minutes. Orexin B was measured using commercially available 125I RIA kits (Phoenix Pharmaceuticals, Belmont, CA). Twenty five µl of peptide solution was mixed with 75µl of RIA buffer and directly applied to the RIA. The detection limits of the assay were 100 pg/ml. All comparative samples were measured in a single assay and the intra-assay variation was <5 %. Differences in brain region immunoreactive peptide levels were compared using ANOVA followed by post-hoc LSD.

Results: Orexin B levels were highest in the hypothalamus, septum, thalamus, amygdala and medulla oblongata compared to other brain regions. Compared to saline, significantly lower orexin B levels were observed in the frontal cortex (p=0.004), thalamus (p=0.04), septum (p=0.02) and midbrain (p=0.008) regions of CLI treated rats. Lower levels were also observed in the amygdala, but this did not reach statistical significance (p=0.07). Interestingly, immunoreactive hypocretin 2 levels were higher in the pons, medulla and cerebellum from CLI treated rats compared to saline. No significant difference in any other brain or hypothalamic region was noted.

Conclusions: Neonatal REM sleep deprivation by CLI resulted in the reduced orexin B levels in multiple brain regions. This occurs some seven half lives after the last dose of CLI supporting a role for REM sleep in the determination of orexin system in the developing brain.

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0087.A

Localization Of The Gabaergic And Non-Gabaergic Neurons Projecting To The Sublaterodorsal Nucleus And Potentially Gating Paradoxical Sleep Onset

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Introduction: We recently showed in rats that iontophoretic application of bicuculline or gabazine (two GABAa antagonists) and kainic acid (a glutamate agonist) but not of carbachol (a cholinergic agonist) specifically in the sublaterodorsal nucleus (SLD) induced with a very short latency a paradoxical sleep-like state characterized by muscular atonia, EEG activation and theta activity. Based on these results, we hypothesized that PS-executive neurons (PS-on) localized in the SLD are tonically inhibited during waking and slow wave sleep by GABAergic neurons. To determine the origin of the GABA and non-GABAergic inputs to the SLD, we combined the retrograde tracing with cholera toxin b subunit (CTb) with glutamate decarboxylase (GAD) immunohistochemistry.

Methods: Male Sprague-Dawley rats (280–320g, n=9) received an iontophoretic CTb injection in the SLD (15 min, 7sec on/off, 1µA) according to stereotaxic coordinates and extracellular recordings. The SLD was found 500µm ventral to the rostral locus coeruleus nucleus or mesencephalic trigeminal nucleus. After 7 days recovery, the animals were perfused by 500 ml of a fixative composed of 4% paraformaldehyde, 5% sucrose and 0.2% picric acid in 0.1M PB. For the double-staining experiments, coronal free-floating sections were firstly treated for GAD immunohistochemistry with a rabbit primary antiserum (1:8000 in 0.1% KPBS without Triton X-100, 3 days), revealed with the classical ABC and DAB histochemical technique. These same GAD-stained sections were then submitted to the CTb detection with a goat primary antiserum (1:20000 in PBS with Triton X-100, 4 days), revealed with the ABC and BDHC technique. To precisely determine the location and estimate the number of CTb+ and GAD+/CTb+ stained neurons, both cell types were bilaterally plotted and counted in three SLD CTb-injected rats on sections from the basal forebrain to the medulla oblongata.

Results: The presence of a substantial number of singly GAD-immunoreactive neurons was first found in the SLD. Following CTb injections restricted to the SLD, we found that around 20-25% of the numerous retrogradely labeled cells localized in the lateral hypothalamic area and the mesencephalic and pontine reticular nuclei were GAD-immunoreactive. A large number of GAD-negative retrogradely labeled cells was also seen in the central amygdala, the ventral and lateral bed nucleus of the stria terminalis, and the lateral and ventrolateral periaqueductal gray.

Conclusions: From these anatomical results, we propose that the activation of the PS-executive neurons from the SLD is due to the removal of a tonic inhibition from GABAergic neurons localized within the SLD and in the mesencephalic and pontine reticular nuclei. From our and previous results, we further suggest that the cessation of activity of these GABAergic neurons at the onset of PS could be due to the removal of an excitatory input from neurons localized in the ventrolateral periaqueductal gray and just ventral to it.

0088.A

Adrenergic Signaling is Critical for Regulation of Wakefulness, REM Sleep, and Sleep Homeostasis

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Introduction: Although many studies have suggested that adrenergic signaling is important for sleep/wake regulation, previous pharmacologic and lesion approaches have generated conflicting results. To examine the roles of norepinephrine (NE) and epinephrine more specifically, we studied sleep in gene-targeted mice lacking dopamine beta-hydroxylase (DBH), the enzyme that converts dopamine to NE. In these mice, NE and epinephrine are absent.

Methods: EEG/EMG recordings were performed in DBH (-/-) and littermate controls. Baseline sleep was recorded for 48 hours under a 12-hour light/dark cycle. Mice were then subjected to 6 hours total sleep deprivation beginning with lights-on. Sleep was scored in 10 second epochs, and EEG spectra were analyzed using a fast fourier transform.

Results: DBH (-/-) mice slept ~2 hours more per day than controls. Despite the increased amount of sleep, DBH (-/-) mice had half the normal level of REM sleep (~1 hour less). In general, differences were present across the 24 hour cycle, although some effects were observed to be dependent on the time of day. The decrease in waking in the DBH (-/-) mice was due to a decrease in the duration of waking bouts, in spite of an increase in the number of waking bouts. For REM sleep, the DBH (-/-) mice had fewer REM bouts and they were of shorter duration. Spectral analysis indicated that there was a decrease in theta power during REM sleep and an increase in delta power during NREM sleep in the DBH (-/-) mice. Following sleep deprivation, control mice had increased NREM and REM sleep accompanied by increased NREM sleep delta power. DBH (-/-) mice did not exhibit these homeostatic changes.

Conclusions: Our results indicate that adrenergic signaling maintains arousal by inhibiting the transition from waking to NREM sleep. In addition, adrenergic signaling is important for the initiation and maintenance of REM sleep. Adrenergic neurons of the locus coeruleus are quiescent during REM sleep; therefore, a lack of adrenergic signaling has been proposed to be responsible in part for the activation of REM sleep. However, because DBH (-/-) mice have less REM sleep, we hypothesize that either the dynamic decrease in adrenergic activity leading up to REM sleep, or low but significant levels of adrenergic signaling, helps to promote the initiation and maintenance of REM sleep. Finally, our results support the idea that adrenergic signaling is important for sleep homeostasis.

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0089.A

Quantitative Analysis of Cholinergic Afferents to the Ventrolateral Preoptic Area: Role in Waking Mechanisms

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Introduction: The ventrolateral preoptic nucleus (VLPO) plays a key role in sleep generation and is likely inhibited by structures that promote wakefulness. Since acetylcholine inhibits GABAergic VLPO neurons in vitro, we hypothesize that cholinergic innervation of the VLPO may promote wakefulness. Indeed, our prior data demonstrate that iontophoretic application of carbachol into the VLPO of head-restrained rats powerfully induces wakefulness relative to saline, and application of cholera toxin B-subunit (CT-b) into these sites retrogradely labeled neurons in the mesopontine tegmentum staining positive for choline acetyltransferase (ChAT). In spite of these data, a recent publication failed to identify VLPO cholinergic afferents. We therefore performed a quantitative analysis from our original data of VLPO cholinergic afferents with direct comparison to afferents from other wake-promoting structures.
Methods: Carbachol or normal saline was iontophoretically administered for 15 minutes into the VLPO from a multibarrel pipette assembly in 6 awake, head-restrained, rats while recording sleep-wake states. CT-b was iontophoretically injected from an adjacent barrel at the end of the experiment. Cholinergic afferents to the VLPO were identified using CT-b and ChAT double immunohistochemistry. A quantitative analysis of CT-b+ and ChAT+ positive neurons was performed in 4 rats and quantitatively compared to CT-b+ neurons identified in the tuberomammilary (TM) nucleus, dorsal raphe (DR), and locus coeruleus (LC).
Results: Iontophoretic carbachol administration into the VLPO increased wakefulness 162% relative to saline control ($p<0.001$). Successful CT-b injection sites were located in the VLPO (n=2), dorsal LPOA (n=1) or between the VLPO and the horizontal limb of the diagonal band (n=1). We found that the mesopontine tegmentum was the only source of cholinergic input to the VLPO and surrounding area. Approximately two double labeled cells (CT-b+ and ChAT+) were identified on each slice in the mesopontine tegmentum of all animals. The majority of these cells were found in the LDT, with a minority in the pedunculoponitine tegmental nucleus (PPT), but none in the lateral parabrachial nucleus. Of all CT-b+ cells in the LDT/PPT, less than 19% double stain for ChAT. However, total cholinergic input from the LDT/PPT was actually superior to the CT-b+ cells identified in either the TM or LC. Only the DR contained more CT-b+ cells.
Conclusions: Physiological data demonstrate that acetylcholine inhibits VLPO GABAergic neurons in vitro, and our data demonstrate that carbachol administration into the VLPO or adjacent LPOA powerfully promotes wakefulness. Although prior published data failed to identify cholinergic afferents to the VLPO, our anatomical data demonstrate that the LDT/PPT is the only source of cholinergic input to the VLPO. Indeed, cholinergic afferents are quantitatively similar to afferents from other known waking structures. Together, these data suggest that the mesopontine tegmentum may promote wakefulness by releasing acetylcholine into the VLPO.

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0090.A

Differential Kinetics Of Hypocretin-1 And -2 In The CSF After Intracerebroventricular (ICV) Administration

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Introduction: The half-life of hypocretins in the blood is short, and only a small fraction of hypocretins penetrates the brain after systemic administration. Therefore, intracerebroventricular (ICV) administration has been widely used to assess central effects of hypocretins. With this technique, different potencies for hypocretin-1 and -2 in sleep-wake regulation, feeding and other behaviors have been reported. These differences could be partially explained by the difference in the selectivity of both peptides toward hypocretin receptors 1 (Hcrtr1) and 2 (Hcrtr2) as well as differential distributions of the two receptors in the brain and the permeability of hypocretins to particular brain sites from the ventricles. However, little attention has been paid to the kinetics of hypocretins. We therefore investigated the kinetics of the hypocretins in the CSF after ICV administration in rats.
Methods: A 26 gauge stainless steel guide cannula was chronically implanted into the lateral ventricle of adult male Wistar rat (n=8). Hypocretin-1 (n=4) or -2 (n=4) at 10nmol was injected into the lateral ventricle through the cannula at ZT2 (ZT0=time of lights-on). Cisternal CSF taps were repeated 2hr (ZT4) and 4hr (ZT6) after the ICV injection. One week later, ICV injections for hypocretin-1 and -2 were repeated with a cross-over design, and the CSF taps were performed with the same time schedule. A week after the second ICV administration, CSF taps were performed at ZT2 in order to collect basal hypocretin levels. Hypocretin-like immunoreactivity levels in the CSF were evaluated by radioimmunoassay kits (Phoenix Pharmaceuticals). In addition, biological activity of hypocretins in the same CSF was quantified with Ca2+ mobilization assays in HEK-293 cells expressing rat Hcrtr2 using a FLIPR384 fluorimetric imaging plate reader system.
Results: Basal hypocretin-1 and -2 levels (at ZT2) in the CSF were 0.27±0.02 (947±69 pg/ml) and 0.11±0.03 nM (329±86 pg/ml), respectively. Hypocretin-2 levels were significantly lower than those of hypocretin-1 ($p<0.01$). ICV hypocretin-1 increased the hypocretin-1 level in the CSF by 800-fold from the baseline ($p<0.01$) with the elevation lasting over 4 hours. In contrast, after ICV hypocretin-2, no significant rise in hypocretin-2 levels in the CSF was found. In the Ca2+ mobilization assay, the baseline CSF collected at ZT2 induced Ca2+ influx in rat Hcrtr2 expressing cell line, but much greater responses were observed from the CSF samples after hypocretin administration. There were significant correlations between changes in hypocretin levels (sum of the hypocretin-1 and -2 levels) and biological activities obtained from Ca2+ mobilization study in the CSF before and after ICV injection of hypocretin-1 or -2. Interestingly, ICV hypocretin-1 injection did not modify endogenous CSF hypocretin-2 levels, nor hypocretin-2 injection did modify endogenous hypocretin-1 levels, suggesting that ICV injections of hypocretins are not likely to exhibit any negative- or positive-feedback on the hypocretin system.
Conclusions: Hypocertin-1 is more stable than hypocretin-2 in the CSF. When ICV injection is used, the difference in kinetics of the two hypocretins should be taken into consideration for interpreting the observed in vivo effects. The physiological roles of the different kinetics of the two hypocretins are not known, but hypocretin-2 may preferentially mediate shorter-lasting effects.

0091.A

Age-Related Decline in the Level of Histamine Receptor mRNAs in Mouse Brain

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Introduction: Sleep in the elderly is characterized by frequent awakenings, decreased deep slow-wave sleep (Stages 3 and 4), and concomitant decreased slow wave frequencies in the electroencephalogram (EEG). In addition, daytime alertness is reduced, indicating a decline in the regulation of wakefulness. Many of these changes in sleep architecture also occur in aged laboratory rodents. We hypothesize that these age-related changes in sleep are related to underlying changes in neurotransmitters

involved in the regulation of sleep and wakefulness. In the present study we examined the neurotransmitter histamine (HA), which is known to involved in the maintenance and/or generation of wakefulness. Age-related changes in mRNA for the HA synthetic enzyme histidine decarboxylase (HDC) and three HA receptors (H1R, H2R, H3R) were determined in eight brain regions from young (3 mo), middle-aged (12 and 18 mo) and old (24 mo) male C57BL/6 mice.

Methods: A total of 24 mice (six animals/group) were sacrificed between 1100-1400h and eight brain regions were dissected: cortex, thalamus, hypothalamus, basal forebrain, hippocampus, cerebellum, pons, and medulla. HDC mRNA levels were measured in the hypothalamus whereas HA receptor mRNAs were measured in all eight brain areas. mRNA levels were quantified using a real-time fluorescence detection method as previously reported1. The "target" cDNA of interest (HDC, H1R, H2R, H3R) and a reference cDNA (glyceraldehyde-3-phosphate dehydrogenase, g3pdh) were simultaneously PCR-amplified using oligonucleotide probes with a 5'fluorescent reporter dye (6FAM for the target genes and VIC for g3pdh) and a 3'quencher dye (TAMRA). Amplification curves were generated by fluorescence detection, and levels of HDC and HA receptor mRNA were determined by normalizing to reference values. The resultant ratios were then subjected to MANOVA followed by ANOVA and, where indicated, the Tukey/Kramer post-hoc test.

Results: We found that HDC mRNA levels did not change with age, however, significant differences were found in H1R, H2R, H3R mRNA levels across several brain regions. The largest changes were observed in H1R mRNA, which were significantly lower (27-38%) in cortex, hypothalamus, and medulla of 24-month-old mice relative to 3-month-old animals; age-related variation was also found in the hippocampus. Age-related changes in H2R mRNA were more restricted, with a 28% decrease seen in the pons in the 24-month-old age group relative to the 12-month-old group. In the cerebellum, however, a significant increase in H2R mRNA levels was seen in both 18- and 24-month-old groups relative to the 3- or 12-month-old group. Age-related changes in H3R mRNA were found only in the medulla, where mRNA levels were significantly reduced in both the 18- and 24-month age groups relative to the 3-month group, with the greatest difference between the 3- and 24-month groups (32%).

Conclusions: The HA system is known to be a involved in the generation and/or maintenance of wakefulness and also as a modulator of sleep-wakefulness rhythms, and the age-related changes in HA receptor mRNA may be related to the decreased alertness seen in aging. In addition, since the HA system is known to be influenced by hypocretin (Hcrt) neurotransmission (Huang et al., 2001, Proc Natl Acad Sci USA 98(17): 9965-70) and since we have previously shown that Hcrt receptors decline in aging (Terao et al., 2002, Neurosci Lett 332(3): 109-14), age-related changes in both systems may compound in their effect on alertness, sleep continuity, and diurnal rhythms of sleep and wakefulness in the aged.

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0092.A

Simulating Cortical TMS During Sleep and Wakefulness

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Introduction: Many studies have addressed the effects of sleep on the transmission of information from the sensory periphery to the cerebral cortex through the thalamic gate. However, the effects of sleep on the transmission of information within the cerebral cortex are largely unknown. A promising approach to addressing this issue experimentally is to by-pass the thalamic gate using transcranial magnetic stimulation (TMS) in combination with brain imaging techniques. In preparation for such experimental studies, it is important to elucidate the cellular and circuit events that take place in the cerebral cortex after a TMS pulse. We have developed a detailed, large-scale model of the visual thalamocortical system that can reproduce firing patterns and responses to stimuli during waking as well as generate sleep rhythms such as slow oscillations. We use the model to simulate cortical TMS during wakefulness and the different phases of sleep slow oscillations, in order to i) better characterize the effects produced by TMS and ii) predict how sleep alters information transmission within the cerebral cortex.

Methods: The model contains 65,000 neurons subdivided into three-layered cortical areas and the corresponding thalamic/reticular sectors, ~6,000,000 connections, different kinds of transmitter receptors (AMPA, NMDA, GABAsAs, GABAsBs) and includes synaptic depression, neuromodulation and intrinsic conductances. We simulated the effects of TMS by transiently applying a depolarizing current (duration 250 ms) to model neurons within each cortical layer. The three-dimensional intensity distribution of the simulated current was set as a power function of the approximate anatomical distance between the stimulating coil and each simulated cortical layer. Both single and paired pulses were applied during wakefulness and during the depolarizing and hyperpolarizing phases of the slow oscillation of sleep. The response of the model to TMS during different states was analyzed at multiple levels, from intracellular potentials and currents to integrated population events and local field potentials.

Results: In the waking mode, simulated TMS produced both direct and indirect (trans-synaptic) activation in all 3 cortical layers. In accordance with experimental results, excitatory corticofugal neurons in the infragranular layer displayed repetitive trans-synaptic discharges occurring 3 and 5 ms after each single TMS pulse. Dual-pulse paradigms revealed both facilitatory and disfacilitatory changes in excitability. During sleep, in the hyperpolarized phase of the slow oscillation, stronger stimuli (~200% of the waking intensity) were required to produce direct firing of cortical neurons. Trans-synaptic activation of all 3 layers required a further increase of TMS intensity (~300%).

Conclusions: We have developed and validated the first biophysically realistic simulations of TMS in a large-scale model of the thalamocortical system. The model provides a unique tool to explore and characterize the impact of TMS cortical dynamics from the level of single channels to that of neuronal populations. Simulation results predict that corticocortical information transmission is reduced during the hyperpolarized phases of the slow oscillation of NREM sleep.

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0093.A

GABAsAs Receptor Subunit mRNAs are Differentially Regulated in the Hypothalamic Perifornical Region in Association with Sleep Loss and Circadian Time

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Introduction: Antagonism of hypothalamic perifornical (PF) GABAsAs receptors suppresses sleep and activates motor and autonomic outputs, whereas their stimulation promotes sleep. The biophysical and pharmacological properties of GABAsAs receptors are determined by their subunit composition (a receptor comprises five of at least 21 known subunits), and both the composition and level of expression of GABAsAs receptors may change rapidly. We hypothesized that the expression of hypothalamic GABAsAs receptors varies with the pressure for sleep, thereby regulating sleep-wake behavior homeostatically and/or with circadian rhythm.

Methods: Three groups of 5-6 Sprague-Dawley rats were used; one group was sacrificed at 8-9 am, another at 3-4 pm, and the third also at 3-4 pm but following gentle sleep deprivation (8 am-3 pm). Under isofluorane anesthesia, the brains were extracted, 400 μm hypothalamic

slices (AP -2.1 to -3.0) obtained, and two 400 µm micropunches cut, one from just dorsal to the fornix and another from the dorsomedial/paraventricular (DM/PVN) region. RNA was extracted from each punch, reverse-transcribed, and cDNA aliquots subjected to externally calibrated, real-time PCRs with primers for tubulin, selected GABAsAs receptor subunits and prepro-orexin. For each tissue punch, we determined the number of copies of the target cDNA per 100 copies of tubulin.
Results: None of the GABAsAs receptor subunits was expressed in a regionally-specific manner, whereas the prepro-orexin mRNA level was 21 times higher in the PF than in DM/PVN region ($p<0.03$); in the PF region, it decreased 2.6 fold between 8-9 am and 3-4 pm ($p<0.04$). In both regions, the levels of mRNA for a1, a2 and b2 subunits were significantly higher at 3-4 pm than at 8-9 am. The increase was largest for the b2 subunit in the PF region (from 0.8±0.2 (SE) to 103±34 copies per 100 copies of tubulin; $p<0.01$). For the a1 and a2 subunits, the increase was 4-19 fold. None of these three mRNAs was significantly affected by sleep deprivation. In contrast, for b1 and b3 subunits, the difference between 8-9 am and 3-4 pm was not significant but their mRNA levels increased significantly in the PF region in sleep-deprived rats, when compared to rats housed in the same environment and allowed to sleep. Following sleep deprivation, b1 mRNA increased from 33±5 to 81±19 ($p<0.05$) and b3 mRNA from 194±38 to 370±70 ($p<0.05$). a3 mRNA exhibited no changes.
Conclusions: The levels of a1, a2 and b2 mRNA are lower at the time of sleep onset than at 3-4 pm, with no changes following sleep deprivation; these subunits may contribute to sleep maintenance. The b1 and b3 subunits, whose mRNA levels in the PF region are relatively high at the time of normal sleep onset and increase with sleep deprivation, may play an important role in the homeostatic regulation of sleep.

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0094.A

Nuchal Atonia and Hippocampal Theta Characterize the Sleep of Rats as Young as Two Days of Age

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Introduction: Strict adherence to the conventional defining features of REM sleep poses a problem when one examines sleep patterns across species and even at different ages within a species. For example, in newborn rats, many of the components that are used to define REM sleep in adults appear to be absent, and it had been thought that the only behavioral indicator of sleep is myoclonic twitching (MT). Consequently, many have preferred to refer to this form of infant sleep, which is componentially less complex than REM sleep in adults, as active sleep (AS). Furthermore, it is widely believed that such REM sleep components as rapid eye movements, cortical desynchrony, and muscle atonia, gradually coalesce throughout development in a unified behavioral state. In the present experiments, the relationship between MT and two conventional components of REM sleep — muscle atonia and hippocampal theta activity — was examined in infant rats between 2 and 8 days of age. We show for the first time that both nuchal atonia and hippocampal theta are expressed in neonatal rats.s.
Methods: Experiment 1. EMG was recorded from the nuchal muscle of infant rats inside a temperature-controlled (35.25 Celcius) chamber. A camera was situated above the chamber lid for recording of sleep/wake behaviors. All signals and video were stored to digital videotape for later analysis. The behavior was scored for MT (indicative of the sleeping state) or coordinated movements (CM; indicative of the waking state).Experiment 2. The same method as in Exp. 1. was used. In addition two .002 inch stainless steel electrodes were implanted in the CA1 field and a silver indifferent electrode was implanted in the cerebral cortex. Electrophysiological and behavioral data were recorded for 60 min. All signals were digitized at 6,250 samples/s using a data acquisition system while behavior was scored for MT and CM.
Results: Muscle atonia and MT was found to be tightly coupled. MT did not occur unless the animal was atonic and ceased immediately as muscle tone was restored. Furthermore, embedded in the state of MT and atonia, sporadic episodes of hippocampal theta were frequently recorded in infant rats as young as 2 days of age.
Conclusions: These experiments demonstrate that REM sleep components are expressed at ages younger than previously assumed and are consistent with the view that AS and REM sleep are developmentally continuous behavioral states.

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0095.A

Suppression of the H-current in Septohippocampal GABAergic Neurons Disrupts the Hippocampal Theta Rhythm

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Introduction: Theta oscillations in the hippocampus are present both during wakefulness and REM sleep and are associated with learning and memory tasks. The integrity of the hippocampal theta rhythm depends on the integrity of the septohippocampal pathway that originates in the Medial Septum/Diagonal Band of Broca (MSDB) and conveys both cholinergic and GABAergic fibers to the hippocampus. Recent studies have indicated a key role for the septohippocampal GABAergic pathway in sustaining hippocampal theta rhythm and associated functions. A key characteristic of the septohippocampal GABAergic but not cholinergic neurons is the presence of an H current; this current has been shown to underlie pacemaking in several CNS neurons. We speculated that if the H-current contributes to pacemaking in septohippocampal GABAergic neurons, then a blockade of this current would lead to decreased impulse flow in the septohippocampal GABAergic pathway and possibly, a suppression of the hippocampal theta rhythm. This hypothesis was tested using in vitro and in vivo studies as described below.
Methods: The cellular effects of blocking the H-current in septohippocampal GABAergic neurons were studied in an in vitro brain slice preparation of the rat medial septum/diagonal band of Broca using extracellular, intracellular and whole-cell recording techniques. The retrograde tracer, rhodamine beads, were infused into the hippocampus and brain slices prepared 2 days later. The labeled septohippocampal neurons were visualized using fluorescence microscopy and recorded from. The GABAergic neurons were differentiatef from the septohippocampal cholinergic neurons by their electrophysiological signature and their excitatory response to muscarine. Hippocampal theta rhythm was recorded in vivo in behaving rats.
Results: The effect of the selective H-current blocker, ZD7288, on the firing rate of septohippocampal GABAergic neurons was first determined using extracellular recordings as this non-invasive method allows an unperturbed evaluation of the effects of a drug on cell firing. ZD 7288 reduced the firing rate in 65% of septohippocampal GABAergic neurons (GABAergic SHNs; control – 4.3 ± 1.1 Hz; ZD7288 – 0.67 ± 0.4 Hz; $p=0.004$), suggesting that the H-current contributes to the resting membrane properties of these neurons. Whole-cell recordings were performed to determine the absolute magnitude of the effect of ZD7288, and also to determine the properties of the H-current. ZD7288 produced a profound hyperpolarization (range: 1-7 mV; mean: 5.6 ± 0.9 mV; $p< 0.001$; $n=11$) that was accompanied by a 118 to 642% increase in appar-

ent input resistance (mean increase: 268.7 ± 49.2%; P<0.001; n=11). External Cs but not Ba blocked the H-current. The H-current persisted in the presence of TTX, suggesting that it is constitutively active in these neurons.In behaving rats, infusions of ZD7288 but not saline blocked the hippocampal theta rhythm, shifting the FFT power to lower frequencies, suggesting that the H-current in septal neurons is critical for maintenance of the hippocampal theta rhythm. As expected, carbachol infusions into the MSDB potentiated the hippocampal theta rhythm.
Conclusions: The chief finding of this study is that the H-current contributes to the spontaneous firing activity of septohippocampal GABAergic neurons, such that a blockade of this current inhibits a vast majority of these neurons and leads to a suppression of the hippocampal theta rhythm in vivo. These findings further confirm the importance of the septohippocampal GABAergic neurons in sustaining the hippocampal theta rhythm.

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0096.A

The Distribution Of Hypocretin (Orexin), Hypocretin Receptor-1, And Melanin Concentrating Hormone Immunoreactivity (IR) In The Zebrafish Brain

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Introduction: Hypocretin-1 and -2 (HCRT) have recently been implicated in regulating sleep, and as primary targets in the sleep disorder narcolepsy. In the mammalian brain, hypocretinergic neurons are located in the perifornical hypothalamus and project to histaminergic and monoaminergic systems throughout the brain. Melanin Concentrating Hormone (MCH) is a small peptide originally discovered in fish. Recent evidence from rats suggests MCH neurons and HCRT neurons have reciprocal connections. In mammals MCH-IR neurons are co-distributed with HCRT neurons in the posterior hypothalamus. As an adjunct to developing a mutagenesis screen for HCRT-related mutations in zebrafish, this study was performed to examine the distribution of HCRT and MCH in the zebrafish brain and to identify putative areas of interaction between the two systems.
Methods: Adult male zebrafish (*Danio rerio*, n=42) were euthanized by ice-water immersion and decapitated. The heads were immersion fixed in 4% paraformaldehyde, 0.1% glutaraldehyde in 0.1M tris buffer (TB, pH 7.4) overnight, rinsed in TB, and the brains dissected from the skulls and placed in 30% sucrose in TB overnight. Brains were then embedded in gelatin blocks for easier handling. Blocks were cut on a freezing microtome in the coronal (16 micron thick) or horizontal (14 micron) planes. Series were labeled with antibodies to HCRT-1, HCRT Receptor-1 (HCRTR1), MCH, or double-labeled for MCH/HCRT1R. All incubations were in 10% normal serum, 0.1% Triton X-100 (TX), 0.1M TB, containing the appropriate antibodies (except for a no-primary control). Either fluorescent dye conjugates or the avidin-biotin-peroxidase (ABC) protocol was used for visualization, with diaminobenzidine (DAB) or nickel-enhanced DAB as the chromogen. Double-labeling was done sequentially on the same series. Sections were mounted on gelatin-coated slides, dehydrated, and cleared for light microscopic examination.
Results: HCRT-IR somata were restricted to the midline hypothalamic ventricular areas, primarily the periventricular nucleus of the posterior tuberculum (TPp) and posterior tuberal nucleus (PTN). Cell morphology was mixed, with some cells being medium-large (~20 micron diameter) and ovoid, and some cells being small (~10 micron diameter) and circular. Laterally-projecting fibers extended from the somata of both types. HCRTR1-IR somata were found in the dorsal periventricular hypothalamus (Hd) and lateral aspect of the Hv adjacent to the floor of the brain. These neurons projected densely into the caudal periventricular hypothalamus (Hc) and the Hv, again projecting around but not into the ATN. MCH-IR somata were co-distributed with the HCRT1R-IR somata in the ventrolateral hypothalamus and sent projections to the Hv and Hc as well.
Conclusions: The zebrafish HCRT and MCH systems are distributed distinctly from that of mammals, but cross-talk between the two systems is still likely based on HCRT1R and terminal distribution.

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0097.A

Sleep Disturbances in Rats Exposed to Acute Intermittent Hypoxia

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Introduction: Obstructive sleep apnea (OSA) syndrome is characterized by repeated upper airway obstruction during sleep, which leads to episodes of hypoxia and arousals. Intermittent hypoxia (IH) in animals has been used to mimic the pattern of hypoxia in OSA. Transient sleep disturbance has been reported in rats exposed to IH (Gozal et al., J. Neurosci. 21:2442, 2001). We examined the effects of two days exposure to IH on sleep-wake amounts, EEG delta power and patterns of c-fos protein immunoreactivity in the preoptic area of rats.
Methods: Adult male rats were surgically prepared for chronic cortical EEG and EMG recordings. Following recovery from surgery rats were adapted to a recording/hypoxia chamber for 3 days under normoxic conditions. On day 4, 5 rats were exposed to eucapinc IH (10% O2, 5% CO2, balance nitrogen; 5 min on, 5 min off) for 12 hours during the lights-on portion of the light/dark cycle. Control rats were exposed to normoxia during the 12 hour lights-on period. All rats were exposed to normoxia during the 12 hour dark period. On day 5, rats were again exposed to IH at lights-on (08:00) and permitted spontaneous sleep during the next 4 hours. At 12:00, IH rats were given a lethal dose of pentobarbital followed by cardiac perfusion. Control rats were sacrificed at the same time of day, but were exposed to normoxia throughout. Sections through the median preoptic nucleus (MnPN) and ventrolateral preoptic area (vlPOA) were immunostained for c-fos protein and for glutamic acid decarboxylase, a marker of GABAergic neurons.
Results: In agreement with the findings of Gozal et al., sleep amounts on Day 1 of IH were significantly reduced (15-25% of total sleep time) compared to control levels (50-70%). By Day 2 of IH exposure, sleep amounts approached normal limits (40-50%), but sleep was more fragmented in IH rats compared to controls. EEG delta power during non-REM sleep was significantly reduced in IH-exposed rats compared to normoxic rats. Sleep abnormalities in IH rats were associated with a >50% reduction in the number of MnPN and vlPOA GABAergic neurons expressing c-fos protein immunoreactivity during sleep.
Conclusions: These findings demonstrate that while IH-induced reductions in total sleep time are transient, deficits in sleep continuity and sleep depth, as reflected in EEG delta power, may be more persistent. They further suggest that sleep disturbance evoked by IH may be mediated, in part, via reduced activation of sleep-regulatory GABAergic neurons in the preoptic area of the hypothalamus.

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0098.A

Double Immunofluorescence Study of the Colocalization of Vesicular Glutamate Transporters 1/2/3 and Vesicular Acetylcholine Transporter in the Rat Basal Forebrain and Mesopontine Tegmental Projection Systems

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Introduction: Cholinergic neurons in the basal forebrain (BF) and the mesopontine tegmentum (MT; pedunculopontine and laterodorsal tegmental nuclei) are thought to play important roles in behavioral state control. Both BF and MT cholinergic neurons activate the cortex directly or indirectly during wakefulness, and MT cholinergic neurons are also involved in REM sleep. Although these BF and MT cholinergic neurons are expected to release acetylcholine, there is evidence for colocalization of neuropeptides, and glutamate has been suggested to be colocalized as a transmitter with some of these cholinergic neurons. As part of a study to investigate glutamate colocalization in CNS cholinergic neurons, we investigated the BF and MT projection systems by using antibodies to vesicular glutamate transporters (VGluT)-1/2/3, three recently identified transporters responsible for glutamate uptake into synaptic vesicles.
Methods: Double immunofluorescence (Cy2/3 or Alexa 488/555) and confocal microscopy were used to examine coimmunoreactivity for vesicular acetylcholine transporter (VAChT) and VGluT1/2/3 in the cell bodies of BF and MT cholinergic neurons, and their terminals in selected target areas.
Results: In the BF, scattered neurons in the horizontal limb of the diagonal band, ventral pallidum, substantia innominata, and globus pallidus were immunoreactive (ir) for both VAChT and VGluT3. Neurons double-labeled for VAChT and VGluT3 were also found in the islands of Calleja, olfactory tubercle, nucleus accumbens core and shell, and caudate-putamen. No such double-labeled neurons were observed within the MT or the medial habenula. The VGluT1/2 antibodies used did not label cell bodies, and not surprisingly, no cell bodies double-labeled for VGluT1/2 and VAChT were observed in the BF or MT. Among the target areas of the BF cholinergic projections, no colocalization of VGluT1/2/3 and VAChT immunoreactivities was observed in selected cortical regions including the piriform and entorhinal cortices. Within the BF, VAChT-ir terminals were not VGluT1/2/3-ir. The reticular nucleus of the thalamus, which receives dual cholinergic projections from the BF and MT, was devoid of coimmunofluorescence for VAChT and VGluT1/2/3. In some of the above areas with cholinergic innervation, VGluT1/2/3-ir and VAChT-ir terminals were segregated in distinct patterns, whereas in others they were intermixed.
Conclusions: These results indicate that VGluT3 is present in a small population of cholinergic BF projection neurons, as well as in many cholinergic interneurons in ventral forebrain areas, but not in cholinergic projection neurons in the MT or medial habenula. Evidence for colocalization of VGluT3 in cholinergic terminals in target areas of BF cholinergic projections has so far been negative, possibly due to sparsity of such terminals. The possible absence of VGluT1/2 in BF and MT cholinergic projection systems requires further investigation. The presence of VGluT3 in a subpopulation of BF cholinergic neurons suggests that terminals of some BF cholinergic neurons might release both acetylcholine and glutamate.

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0099.A

Cortical Responsiveness Across the Waking-Sleep Cycle

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Introduction: Behavioral states of vigilance are accompanied by important changes in cortical synaptic excitability related to fluctuations in activity of cholinergic and monoaminergic systems that impact on neocortical neurons. Recent intracellular recordings of cortical neurons in naturally awake and sleeping cats showed that, although the discharge pattern is affected, the mean firing rates of cortical neurons are only slightly changed across the waking-sleep cycle. This observation suggests that information is processed in cortical networks during all behavioral states, but changes in signal transmission are due to modifications in network properties that depend on the state of vigilance.
Methods: We investigated the state-dependent changes in cortical responsiveness in non-anesthetized, non-paralyzed, head-restrained cats. Cats were implanted under deep anesthesia with electrodes for recording of electromyogram, electro-oculogram and electroencephalograms and for stimulation of thalamic nuclei, contralateral cortex and ipsilateral cortex. In addition, one or two recording chambers were implanted for intracellular and multiunit recordings. The cortical responsiveness across the waking-sleep cycle was assessed using field potential, multiunit and intracellular recordings.
Results: We found that the amplitude of action potentials (APs) showed a tendency to decrease during wakefulness (W) and paradoxical sleep (PS) as compared to slow-wave sleep (SWS), probably due to partial inactivation of sodium channels at more depolarized levels of membrane potential. The duration of APs was unchanged across the waking-sleep cycle. The intrinsic excitability was estimated by intracellular application of long-lasting depolarizing pulses. The number of action potentials (APs) evoked by these stimuli was slightly, but not significantly, decreased during SWS, as compared to W or PS. However, short current pulses mimicking excitatory postsynaptic potentials (EPSPs) were significantly less effective in eliciting AP during SWS as compared to W and PS. On the other hand, we found marked changes in synaptic responses of cortical neurons evoked by electrical stimulation of thalamus, contralateral or ipsilateral cortex. Evoked responses in cortical neurons usually consisted of a sequence of EPSPs followed by a long-lasting hyperpolarizing potential. Thalamically evoked EPSPs increased their amplitude during W and PS as compared to SWS, whereas the amplitude of cortically evoked EPSPs was the highest during SWS. The late hyperpolarizing potential was composed of mixture of inhibitory postsynaptic potential (IPSP) and disfacilitation and showed similar changes regardless to stimulated pathway. An important prolongation of the hyperpolarizing potential was observed during SWS as compared to W or PS.
Conclusions: Our results show that behavioral states are associated with specific changes in cortical responsiveness that depend on afferent pathway. These modifications should be important for the way cortical network processes information across behavioral states and for the function of each state.

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0100.A

Hypocretins Excite Septohippocampal Neurons via the Hypocretin type 2 Receptors: Implication for Arousal via a Mechanism of Hippocampal Disinhibition

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Introduction: The hypocretins (Hcrts) are a newly described set of hypothalamic peptides that bind to two different G-protein-coupled receptors, the Hcrt-receptor 1 (Hcrt-R1) and the Hcrt-receptor 2 (Hcrt-R2). The Hcrts have been implicated in normal sleep-wakefulness and in disorders of sleep such as narcolepsy. Human narcoleptics have an 85-100% reduction in the number of Hcrt neurons and Hcrt-null mutant mice exhibit a phenotype strikingly similar to human narcolepsy patients

as well as to canarc-1 mutant narcoleptic dogs. Hcrt-containing neurons, that are located exclusively in the lateral hypothalamic area, provide innervation to most brain structures associated with sleep-wake regulation, which includes a dense innervation of the Medial Septum/Diagonal Band of Broca (MSDB); the MSDB also shows intense axonal degeneration in canine narcoleptics. The MSDB, via its cholinergic and GABAergic projections to the hippocampus, controls the hippocampal theta rhythm that occurs during exploratory behavior and REM sleep. Neurons of the MSDB express the Hcrt receptor 2, the subtype that is mutated in canine narcoleptics.

Methods: The cellular effects of Hcrt on septohippocampal neurons were studied in an in vitro brain slice preparation of the rat MSDB using extracellular, intracellular and whole-cell recording techniques. The retrograde tracer, rhodamine beads, were infused into the hippocampus and brain slices prepared 2 days later. The labeled septohippocampal neurons were visualized using fluorescence microscopy and septohippocampal GABAergic neurons were differentiated from the septohippocampal cholinergic neurons by their electrophysiological signature and their excitatory response to muscarine. Septohippocampal cholinergic neurons were independently identified using a custom-synthesized retrograde tracer, Cy3-192IgG, which is a conjugate of the fluorochrome Cy3 and192 IgG; 192 IgG is an antibody against the p75 receptor. Since the p75 receptor is expressed only by the septohippocampal cholinergic neurons in the MSDB, this marker exclusively labels the septohippocampal cholinergic neurons. Double immunolabeling studies were performed using light and electron microscopy. Antibodies against the calcium-binding protein, parvalbumin, were used to mark septohippocampal GABAergic neurons as this protein is not expressed by any other neuronal populations in the MSDB. Antibodies against the enzyme, choline acetytransferase were used to label the cholinergic neurons.

Results: Using recordings from retrogradely–labeled neurons, we have found that Hcrt2 produces a reversible, reproducible, concentration-dependent and a direct post-synaptic excitation of septohippocampal GABAergic-type neurons with an EC50 of 207 nM. This effect is sodium-dependent but not potassium or chloride-dependent and is attenuated by blockers of the Na+-Ca+ exchanger. Hcrt2 also increases impulse-dependent but not -independent release of GABA within the MSDB. Double-immunolabeling studies confirmed the presence of Hcrt receptor 2 immunoreactivity in septohippocampal GABAergic neurons as well as the presence of Hcrt fibers adjacent to these neurons. Since the septohippocampal GABAergic neurons selectively innervate hippocampal GABAergic interneurons, a Hcrt-excitation of GABAergic neurons would disinhibit hippocampal pyramidal cells, facilitating the generation of the hippocampal theta rhythm.A vast majority of septohippocampal cholinergic neurons (80%) were also excited by Hcrt via a direct post-synaptic action. Double-immunolabeling studies using light and electron-microscopy, revealed the presence of synaptic boutons around septohippocampal cholinergic neurons. Since, the septohippocampal cholinergic neurons innervate hippocampal pyramidal cells, Hcrt actions on cholinergic neurons will cause a direct excitation of hippocampal pyramidal cells.

Conclusions: Hypocretin excitation of septohippocampal GABAergic and cholinergic neurons, would by engaging direct excitatory as well as disinhibitory mechanisms in the hippocampus, promote generation of the hippocampal theta rhythm and associated behaviors. Thus, even though the hippocampus, by itself, is sparsely innervated by Hcrt fibers, it would be profoundly influenced by Hcrts that are released onto the septohippocampal neurons of the MSDB. Moreover, the involvement of Hcrt receptor 2 in these actions may have implications for narcolepsy.

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0101.A

Effect of Lipopolysaccharide on Locomotor Activity and A1 Adenosine Receptor Binding in the Mouse Brain

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Introduction: Lipopolysaccharide (LPS) alters vigilance states in animals and people and induces expression of the transcription factor nuclear factor (NF-kB). NF-kB is a putative positive regulator of the A1 adenosine receptor (A1AR) gene. Both NF-kB and adenosine are implicated in the regulation of sleep. To evaluate this relationship, we assessed core temperature, locomotor activity and A1AR binding properties in mice treated with LPS.

Methods: B6129PF2/J mice were surgically implanted with intraperitoneal transmitters to monitor activity and core temperature. After recovery from surgery, mice were monitored for 24 hours before and after the intraperitoneal administration of either pyrogen free saline (0.2 ml; n=6) or LPS (80ug/0.2ml; n=7), beginning at light onset. Data collection and analysis was carried out using DQ3 software. Mice were sacrificed at light onset 24h after LPS administration, and A1AR binding was measured in cerebral cortex, brain stem, hypothalamus and hippocampus. Briefly, frozen brain regions were thawed, homogenized in 50mM Tris-HCl containing 10 mM MgCl2 and 1 mM EDTA and protease inhibitors, and subjected to centrifugation to obtain the membrane fraction. The radioligand binding assay was performed using 125I-N6-(4-aminobenzyl)-9-[5-(methylcarbonyl)-ß-D-ribofuranosyl] adenine (AB-MECA) (a selective AR agonist). The radioligand [3H]–1,3-dipropyl-8-cyclopentylxanthine ([3H]-DPCPX) (a selective A1AR antagonist) was used to perform saturation binding analysis.

Results: A marked suppression of core temperature and locomotor activity occurred in LPS-treated mice during the 12-24 hour period after treatment. Similar changes were not observed in the saline treated mice. The 125IAB-MECA radioligand binding assay revealed no significant differences in A1AR receptor binding in LPS treated vs. saline treated mice in any of the four brain regions examined. Saturation binding analysis for A1AR in the cortical membranes using increasing concentrations of the antagonist radioligand [3H] DPCPX revealed no change in the number or affinity of the A1AR in the cortex of LPS treated mice as compared to the saline treated mice. This analysis revealed Bmax and Kd values of 420 ± 45 fmol/mg protein and 1.09 ± 0.33 nM, respectively, in LPS treated mice, and values of 487 ± 45 fmol/mg protein and 1.95 ± 1.11 nM in saline treated mice.

Conclusions: Mice treated with LPS demonstrated hypothermia and suppression of locomotor activity, consistent with the development of increased sleep. A1AR in cortical membranes collected from these mice showed no change in number or affinity. These findings are consistent with a lack of involvement of the A1AR in mediating LPS-induced changes in somnolence.

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0102.A

Modulation of Genioglossus Muscle Activity Across Natural Sleep-Wake States by Serotonergic Mechanisms at the Hypoglossal Motor Nucleus

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Introduction: Decreased genioglossus (GG) muscle activity in sleep, especially rapid-eye-movement (REM) sleep can predispose to airway narrowing and obstructive sleep apnea. GG muscle is innervated by the hypoglossal motor nucleus, which in turn receives a tonic excitatory

drive from medullary raphe neurons via release of serotonin (5-hydroxytryptamine, 5-HT) (Kubin et al., Neurosci Lett, 139: 243-248, 1992). Some 5-HT raphe neurons show increased activity with C02 stimulation in-vitro and in-vivo, with these neurons also showing progressive decreases in activity from wakefulness to non-REM and REM sleep. Accordingly, this study tests the hypothesis that 5-HT receptor antagonism at the hypoglossal motor nucleus will decrease GG activity during room air and CO2-stimulated breathing across states of wakefulness and natural sleep.

Methods: Ten rats were implanted with electroencephalogram and neck muscle electrodes to record sleep-wake states, and GG and diaphragm wires for respiratory muscle recordings. Microdialysis probes were implanted into the hypoglossal motor nucleus for perfusion of artificial-cerebrospinal-fluid (ACSF) or 100uM mianserin (broad spectrum 5-HT receptor antagonist) during room air and CO2-stimulated breathing (~7.5% inspired CO2). The chosen dose of mianserin effectively decreases hypoglossal motor output to GG muscle in anesthetized rats. GG activity was expressed as a percentage of maximum activity recorded in each rat. GG activity was continuously quantified in 5 sec epochs as phasic respiratory-related activity, tonic activity (i.e., basal activity in expiration) and peak activity. Sites of microdialysis were verified by post-mortem histology.

Results: CO2 stimulation increased respiratory-related GG activity in non-REM sleep ($p = 0.002$, 2-way ANOVA with repeated measures) but not in wakefulness or REM sleep ($p > 0.500$) where the levels of GG activity were more variable due to ongoing behaviors in wakefulness and sporadic muscle twitches in REM sleep. Nevertheless, 5-HT receptor antagonism at the hypoglossal motor nucleus had significant effects on tonic GG activity in wakefulness ($p = 0.009$). However, contrary to the expectations stated in the hypothesis, tonic GG activity was actually increased rather than decreased by mianserin compared to ACSF ($20.1 \pm 2.0\%$ vs. $14.9 \pm 1.2\%$, $p<0.05$, post-hoc Student-Newman-Keuls). Likewise, in non-REM sleep tonic GG was also increased by mianserin compared to ACSF ($3.1 \pm 0.6\%$ vs. $1.7 \pm 0.3\%$) but this was of marginal statistical significance ($p = 0.074$) likely due to the lower basal GG activities present in non-REM sleep.

Conclusions: The results show that 5-HT receptor antagonism at the hypoglossal motor nucleus increased rather than decreased tonic GG activity in awake and freely behaving rats. Since GG activity is decreased by mianserin in decerebrate or anesthetized animals, these results in a behaving preparation suggest that the balance of excitatory and inhibitory 5-HT influences on hypoglossal motor output is tilted away from excitation perhaps through modulation of inhibitory presynaptic receptors.

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0103.A

Expression Of Choline Acetyltransferase And Its Colocalization With Hypocretin In The Hypothalamus Of The Cat and Guinea Pig

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Introduction: Hypocretins (Hcrt, i.e., Hcrt-1 and Hcrt-2) are neuropeptides that have been suggested to be involved in a variety of brain functions related to motor activity, wakefulness and food consumption, among others. Immunohistochemical and in situ hybridization studies have shown that neurons containing Hcrt are located exclusively in the lateral and dorsomedial hypothalamus. On the other hand, neurons in these same hypothalamic regions also contain choline acetyltransferase (ChAT). Since acetylcholine is critical in the regulation of motor activity as well as sleep and wakefulness, it was of interest to investigate the relationship between hypocretinergic and cholinergic neurons in the hypothalamus and their projections to the brainstem. Accordingly, the present experiment was undertaken to examine whether ChAT and Hcrt were colocalized in the hypothalamus and brainstem of the cat and guinea pig.

Methods: Three cats and four adult guinea pigs were employed in the present study. The animals were deeply anesthetized with sodium pentobarbital (35 mg/kg, i.v.) and perfused transcardially with a fixative containing 4% paraformaldehyde, 15% saturated picric acid and 0.25% glutaraldehyde in 0.1 M phosphate buffer (PBS) (pH 7.4). The brain was then removed and postfixed overnight at 4°C; frozen sections (15 µm in thickness) were then cut with a cryostat. Immunohistochemical staining with DAB color reactions was used to determine the occurrence of ChAT and/or Hcrt in neurons in the hypothalamus. Colocalization of ChAT and Hcrt within the individual neurons and their fibers was investigated by using double immunofluorescence techniques. The antisera used in these experiments were rabbit against ChAT (Chemicon, CA; diluted 1:2000) and goat anti-hcrt-1 (Diagnostic Systems Laboratories, Inc. Texas, diluted 1:1500).

Results: Both ChAT-immunoreactive and Hcrt-immunoreactive neurons were present in the lateral and dorsomedial hypothalamus. The majority of the hypocretinergic neurons were located dorsal and lateral to the fornix; the ChAT-positive neurons were scattered principally in an area surrounding the fornix. Double immunofluorescent staining revealed three types of neurons in these regions: 1) neurons stained by the ChAT antibody; 2) neurons stained by the Hcrt antibody; and 3) neurons stained by both ChAT and Hcrt antibodies. Similar staining of fibers was observed in the brainstem, i.e., there were the fibers stained by ChAT antibody, Hcrt antibody and by both antibodies.

Conclusions: Both cholinergic and hypocretinergic neurons are located in the lateral and dorsomedial hypothalamus of the cat and guinea pig. The present data demonstrate that ChAT and Hcrt are colocalized in neuronal soma in these hypothalamic areas as well as in hypocretinergic projections to the brainstem, indicating that hypocretinergic neurons also utilize acetylcholine as a neurotransmitter.

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0104.A

Cortistatin, a Sleep Modulatory Peptide, Increases Pain Threshold

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Introduction: Cortistatin is a neuropeptide related to somatostatin that induces sleep. It may be affecting other neurotransmission systems such as: Acetylcholine GABA, and Noradrenaline. The perception of pain is a complex process regulated partially by these systems. Therefore, cortistatin may also be involved in the regulation of this process. In this context, we pursue to determine the potential role of cortistatin in pain perception.

Methods: In order to reach this goal we evaluated cortistatin's effect on the hot plate task in rats. Some other neuropeptides, also involved on sleep regulation, were tested too. The groups we used were: Saline, CST, SST, ORX, CLIP and CART. All neuropeptides were intracerebroventricularly injected (0.3nmol/5ml). 30 and 240 min after of the administration all rats were tested in the hot plate task. The time the rat took to start licking its hind paw or jump out the hot plate chamber was recorded.

Results: Ours results indicate that cortistatin increases pain threshold significatly.

Conclusions: These results indicate that cortistatin may be involved in

the regulation in pain perception as much as it is in sleep regulation.

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0105.A

Variability of Somatosensory Responses During Sleep Oscillation: Thalamic and Cortical Components

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Introduction: Thalamus is the main gateway of cerebral cortex. During sleep the information arising from the external world does not properly reach neocortex and possibly is not properly processed at cortical level. The goal of the present study was to elucidate cellular mechanisms of response variability within somatosensory system of cats during sleep-like slow oscillation.
Methods: Acute experiments involving simultaneous multiple multiunit and intracellular recordings were done on cats anesthetized with ketamine-xylaxine. An array of tungsten microelectrodes to record field potentials and multiunit activities was inserted in the somatosensory cortex with an angle of 40° in the vicinity (< 0.5 mm) of one to four recording intracellular micropipettes. In order to study phase-dependent responsiveness of somatosensory system to incoming synaptic volleys we placed bipolar surface stimulating electrodes on the skin over forelimb median nerve.
Results: Peripheral forelimb stimulation elicited field potential and cellular responses in both neocortex and thalamus during all components of slow-sleep oscillation. However, depending on the phase of slow oscillation the responses revealed different latencies and shapes. Each electrical stimulus of forelimb elicited 5-10 identifiable EPSPs in thalamocortical neurons and the total duration of responses lasted for ~30 ms. The latency of first EPSP varied a little (range 7.4-7.7 ms, mean 7.55±0.17 ms). At depolarized levels of membrane potential the first or second EPSP triggered the first spike of thalamocortical neuron transmitting signals toward cerebral cortex. At hyperpolarized levels of the membrane potential, which correspond to depth-positive EEG component the first 3-5 EPSPs were summating and they elicited a low-threshold calcium spike covered with fast sodium spikes. The latency of the first spike then varied significantly (range 8.6-12.4 ms, mean 9.7±1.8 ms). Accordingly, the latency of first negative maximum of cortical field potential was shorter during depolarizing phases of the slow oscillation and was by 6-8 ms longer during hyperpolarizing (depth-positive) phases of the slow oscillation. Fifty eight percent of cortical neurons had tendency to fire during early components of evoked potential occurring during the depolarizing phases of slow oscillation. On the other hand the forelimb stimulation rarely elicited spikes of cortical neurons during EEG depth-positive waves, thus making unlikely intracortical dialog during this phase of the slow oscillation. The standard deviation of the EPSP latencies in simultaneously recorded groups of neurons (n=4) was small (2 to 4 ms) during active network states and increased (6 to 8 ms) during depth positive EEG waves.
Conclusions: We conclude that thalamocortical neurons are able to fire upon arrival of peripheral stimuli during all phases of slow oscillation, but responses during active and silent phases are different. Despite of identical peripheral stimuli, the cortical network displayed a great variability of responses (latencies, amplitudes, firing probability) that depended on the firing pattern of thalamocortical cells and on the membrane potential of cortical neurons.

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0106.A

Dopamine Induces Excitation of the Basal Forebrain Cholinergic Neurons

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Introduction: The role of dopaminergic systems in maintaining wakefulness has only recently received emphasis. A wide variety of stimulant drugs that promote wakefulness have dopamine reuptake inhibition effects, while sedation is often induced by the neuroleptic drugs which activate dopamine autoreceptors. Our preliminary observations have identified a population of strongly wake-active dopaminergic neurons located in the ventral part of the periacqueductal gray matter (vPAG). These neurons widely project to sleep-wake related areas including the ventrolateral preoptic nucleus, the basal forebrain cholinergic cells, the hypothalamic orexinergic cells, the pontine cholinergic cells and the locus coreuleus noradrenergic cells. Here, we extend these studies by investigating the electrophysiological responses of dopamine application on one of the targets of the dopaminergic vPAG neurons, the subtantia inominata (SI) cholinergic neurons.
Methods: We performed patch-clamp recordings on SI cholinergic neurons in in vitro slices. SI cholinergic neurons were prelabeled in vivo with the fluorescent marker, Cy3-192IgG, which is selectively internalized by p75-receptor expressing basal forebrain cholinergic neurons. Cy3-192IgG was delivered by i.c.v. injection in rats (10-30 day-old). Five days later the animals were used for the preparation of in vitro slices (coronal, 0.4mm thick). Under fluorescent microscopy the prelabled neurons appeared bright red and were targeted for electrophysiological recordings. Whole-cell recordings were conducted under IR-DIC visualization using an Axoclamp-2A amplifier. Recorded neurons were marked by filling intracellularly with Lucifer Yellow and subsequently tested for ChAt immunoreaction.
Results: We found that bath application of dopamine (100microM) induced increases in firing rate (42% n=4) of the SI cholineregic neurons. The effect was reversible and no desensitization was observed. At least two mechanisms contribute to the dopamine excitatory effects in the SI cholinergic neurons. 1) Dopamine produced membrane depolarization (n=6), that persisted in the presence of TTX (1microM), suggesting a postsynaptic action (n=2), and was not associated with a change in membrane resistance (n=2), suggesting that more than one conductance mediated the depolarizing response. 2) Dopamine reduced the afterhyperpolarization (AHP) that follows single spikes (n=5) that reduces the interval between spikes and leads to an increase in firing rate. Dopamine reduced AHP amplitude (from 11.52 ± 2mV to 7.15 ± 1.7mV), AHP area (from 1465 ± 332mVmsec to 693 ± 175mVmsec), AHP duration (from 254 ± 29.7msec to 172 ± 26.3msec) and increased AHP latency (from 25.3 ± 3.7msec to 37.7 ± 8msec). Dopamine excitatory effects were found in both Cy3-192IgG-labeled neurons (n=9) and on cholinergic neurons from animals that had not received Cy3-192IgG (n=2).
Conclusions: Dopamine-mediated excitatory action on the cholinergic basal forebrain population may represent one of the mechanisms by which the dopaminergic systems maintain wakefulness. Our in vitro electrophysiological studies show that dopamine mediates two separate effects on SI cholinergic neurons and both effects contribute to the excitation of these neurons.

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0107.A

The Combination of HIVgp120 and Nicotine Affects Sleep

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Introduction: The glycoprotein 120 (gp120), derived from the human immunodeficiency virus (HIV) is highly neurotoxic. It induces apoptosis and several functional changes in the brain. Some of these effects involve changes in sleep architecture. For example, HIVgp120 increases NREM and REM sleep after a single icv injection within the following 4 hours after injection. Likewise, it reduces sleep after a simichronic treatment (5 days of administration). Although HIVgp120 induces all these changes the mechanism of action remains elusive. It has been reported that HIVgp120 affects several neurotransmission systems, including the glutamatergic, and VIPergic systems. It has been also indicated that HIVgp120 may be interacting with the cholinergic system, in particular affecting the nicotinic receptor.

Methods: In this study we pursued to determine if there is an interaction between nicotine and HIVgp120 to affect sleep. We used 4 groups: Control, received saline ip and icv. VIHgp120 (140 ng, icv) and saline ip. Nicotine systemic (1.5 mg/kg) and saline icv. Finally, HIVgp120 icv and nicotine ip. This treatment was given for 5 days. Nicotine was administered 15 min before HIVgp120. One day after the last injection sleep was recorded. We used the software ICELUS and we detected three sleep-waking cycle stages: waking, NREM and REM sleep.

Results: Our results indicated that HIVgp120 increased total sleep (both NREM and REM sleep), while nicotine increased waking at the expenses of REM sleep. The rats that received the combination of both molecules expressed a normal sleep-waking cycle.

Conclusions: These results suggest that nicotine may be antagonizing HIVgp120 deleterious effects.

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0108.A

The Effects of Adenosine on the Membrane Properties of Basal Forebrain Cholinergic Neurons

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Introduction: Adenosine has been proposed as a "sleep factor" that promotes the transition from waking to sleep by affecting several sleep-wake related areas. Investigations have also shown that adenosine when locally applied in the basal forebrain area promotes sleep and inhibits acetylcholine release in the cortex suggesting an inhibitory action on the basal forebrain cholinergic neuronal population. However, a direct action on the cholinergic neurons has not been established. Here we report an electrophysiological in vitro study that investigates the effect of adenosine on identified cholinergic neurons of the subtantia inominata (SI).

Methods: We performed patch-clamp recordings on SI cholinergic neurons in in vitro slices. SI cholinergic neurons were prelabeled in vivo with the fluorescent marker, Cy3-192IgG, which is selectively internalized by p75-receptor expressing basal forebrain cholinergic neurons. Cy3-192IgG was delivered by i.c.v. injection in rats (10-30 day-old). Five days later the animals were used for the preparation of in vitro slices (coronal, 0.4mm thick). Under fluorescent microscopy the prelabled neurons appeared bright red and were targeted for electrophysiological recordings. Whole-cell recordings were conducted under IR-DIC visualization using an Axoclamp-2A amplifier. Recordings were conducted both in current- and voltage-clamp modes. Recorded neurons were marked by filling intracellularly with Lucifer Yellow and subsequently tested for ChAt immunoreaction.

Results: Adenosine (50-100microM) reduced the SI cholinergic neuron firing rate by inducing membrane hyperpolarization and decreasing input resistance (n=4). Membrane hyperpolarization persisted in the presence of TTX (1microM), suggesting a postsynaptic action (n=2). In additional recordings, in voltage-clamp mode, we compared the currents evoked by a voltage ramp protocol (from –120 to –50mV) recorded in control condition and during adenosine application. These recordings were used to obtain current-voltage relationships for adenosine induced current by digital subtraction (adenosine – control). These experiments showed that adenosine inhibits the SI cholinergic neurons by activating an outward current at resting membrane potential that reverses at –75mV (n=4). Application of the adenosine A1 receptor antagonist 8-cyclopentyl-theophylline (CPT, 200nM) increased the current evoked by a voltage ramp protocol (n=3) consistent with removal of a tonic inhibition by endogenous adenosine.

Conclusions: We show that adenosine directly inhibits the SI cholinergic neurons by activating postsynaptic adenosine A1 receptors. Similar to the adenosine inhibitory action in other areas of the central nervous system, adenosine inhibits the SI cholinergic neurons by activating a potassium current.

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0109.A

P-waves Are Coupled To Long-Lasting Respiratory Disturbance Following Glutamate Stimulation Of The Pedunculo-Pontine Tegmental Nucleus (PPT)

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Introduction: Brainstem phasic events characteristic of REM sleep can be recorded as field potentials in the PPT of rats and have been implicated in many brain functions including learning, memory, cognition, dreaming and startle responses. They reflect endogenous activation of ascending arousal system, and are a useful index for anesthetic plane. Pharmacological stimulation of PPT can induce sustained increased wakefulness, REM sleep, and P- wave activity in conscious cat and rat. REM sleep-related clusters of phasic events have been associated with respiratory disturbance in man, bulldogs and rats, but the mechanisms underlying these associations remain undefined. Because the PPT is implicated in generating/propagating phasic events we performed the present study to probe the influence of PPT on breathing in anesthetized rats.

Methods: Thirteen spontaneously breathing adult, male Sprague-Dawley rats were anesthetized using ketamine/xylazine (80/5 mg/kg, respectively). A bipolar electrode and a 3-barrel glass pipette were targeted to the left and right PPT (A:-0.5; L:$\pm$2.0; H:7.0), respectively. Normal saline, glutamate (10 mM) or oil red-O dye were pressure injected from separate barrels, and we recorded: 1) pontine EEG (to detect P-waves); 2) a logic-level injection marker; and 3) respiratory movements monitored by piezo-electric strain gauge. The pipette was advanced ventrally in 100 µm increments and the responses following 2 - 10 nl glutamate injections were recorded. P-waves were detected and scored visually, while respirations were detected by computer algorithm.

Results: The baseline pontine EEG under ketamine anesthesia was characterized by the presence of clustered and/or single P-waves. P-wave clusters were most common: expressed as a series of monophasic spikes of the same polarity having an overall duration of less than 2 s and an interspike frequency of 6-12 Hz. The first response to glutamate was a

significant increase in P-wave expression ($p < 0.01$, $F = 14.2$) without respiratory disturbance. One to two hundred μm ventral to this site, glutamate injection produced long-lasting respiratory instability characterized by alternating periods of tachypnea and bradypnea and /or apnea. The total density of apnea increased from 0.0 s/min at baseline to 2.22 s/min ($p < 0.0001$; $X2 = 271.2$). Further, a significant association was observed between P-waves and respiratory pattern ($p < 0.0001$; $X2 = 33.3$) such that P-waves almost never occurred during apnea (2.6% of total apnea duration).

Conclusions: P-waves are spontaneously expressed in rats under ketamine anesthesia and can be potentiated in clusters by glutamate stimulation of the PPT without alteration of the ongoing respiratory rhythm. In contrast, stimulation at more dorsal PPT sites elicits sustained respiratory dysrhythmia. During this response, P-waves appear to have an excitatory coupling with respiration such that they characteristically occur only during tachypnea. These findings argue that PPT exerts a strong modulation over respiratory rhythm and that phasic events marked by P-waves may contribute to this effect.

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0110.A

Pontine Intertrigeminal Region Attenuates Spontaneous Sleep Apneas In Rats

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Introduction: Chamberlin and Saper have described neuroanatomical pathway of reflex apnea involving the pontine intertrigeminal region (ITR). Our experiments in anesthetized rats showed that blockade of ITR by kynurenic acid, tetracaine or HCL, increased the duration of reflex apnea induced by intravenous 5-HT bolus injection. Since peripheral administration of 5-HT in anesthetized rats produces instant reflex apneas and intraperitoneal injection of 5-HT in freely moving rats increases spontaneous sleep apneas, we hypothesized that reflex and sleep apneas may share a common central pathway. In view of these studies, we conducted the present experiment to determine whether the lesion of ITR by ibotenic acid in freely moving rats would affect sleep apneas in the same way as the blockade of that region affected reflex apneas in anesthetized animals.

Methods: Twelve adult Sprague-Dawley rats, maintained on a 12h/12h light/dark cycle, were instrumented for recording EEG and EMG and were allowed 7 days to recover. After that, polygraphic recording was done for 6h. Behavioral state was staged as wake (W), non-rapid eye movement (NREM) sleep or rapid eye movement (REM) sleep by computer algorithm. During polygraphic recording, respiration was recorded by single-chamber plethysmography. Spontaneous apneas were detected as cessations of respiration for more than 2.5 seconds and were observed to occur as pauses between tidal breaths. Breath by breath parameters were extracted by automated analysis. Afterwards, by surgical intervention under ketamine anesthesia, a unilateral lesion of the ITR by microinjection of ibotenic acid was performed. Following the surgical procedure rats were allowed 7 days to recover. After the recovery period, animals were polygraphically recorded on days 2, 7 or 14. They were sacrificed on day 14 and their ITR lesions were histologically verified.

Results: A unilateral lesion produced by microinjection of ibotenic acid into the left ITR significantly increased spontaneous apnea expression in NREM sleep on days 2 ($p = 0.01$) and 14 ($p = 0.02$). It is of interest that apnea frequency doubled at day 14 in comparison to baseline. However, following the ITR lesion, REM apneas were not statistically significant from baseline. There was no change in average respiratory rate either during NREM or REM sleep versus control. Post-lesion polygraphic recording revealed a decrease in W on days 2 ($p = 0.02$) and 7 ($p = 0.01$), an increase in NREM sleep on day 7 ($p = 0.03$) and no change in REM sleep.

Conclusions: It appears from the present experiment that a physiological role of the ITR is to attenuate sleep-state dependent spontaneous apneas. These observations are in accordance with our previously reported data on the role of ITR in attenuation of reflex apneas. Taken together, our studies suggest that both reflex and sleep apneas share the common central pathway.

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0111.A

Paradoxical Sleep and its Role in the Prevention of Apoptosis in the Developing Brain

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Introduction: It has been well documented that paradoxical sleep (PS) is the dominant state during early development in mammals. Previous studies have investigated the role PS may play in early brain development and suggest that PS deprivation during critical stages of development result in marked behavioral changes and reduced brain mass in adult animals. Additionally, studies investigating the effects of drugs (e.g., ethanol and benzodiazepines) that are known inhibitors of high levels of neuronal activity have shown that these drugs produce massive apoptosis in the developing rat brain. Rat pups between the ages of postnatal day 7 (p7) to 14 (p14) are in a critical period of development that requires a sustained high level of activity within the central nervous system (CNS). We proposed that PS deprivation during this period with induction of prolonged quiet sleep (QS) would precipitate an abnormal increase in apoptosis in the CNS, supporting the hypothesis that PS serves as a protective state for the activity-dependent development that occurs at these ages.

Methods: Six rat pups were injected with 25 m g/kg of clonidine twice daily, from ages p5 to p9. Six littermates were injected with a saline vehicle following the same schedule. On day nine, pups were perfused and prepared for histology. The brains were sectioned and prepared for Caspase-3 staining. An additional four rat pups were implanted for electrocorticographic and electromyographic recording on either p5 or p9. Of those four, two received a 25 m g/kg dose of clonidine and two received the vehicle control. All animals were recorded for a minimum of one hour after receiving the injection. The non-parametric Mann-Whitney U test was used to compare groups.

Results: The sleep records of the four implanted animals demonstrated that clonidine is an effective PS suppressant in animals at this age. The clonidine treated animals total time in PS was 1.8% with the majority of time spent in QS, while the controls spent 23% in PS ($p<.002$). Caspase-3 staining indicated that animals that are PS deprived during ages p5 to p9, have significantly more apoptosis than control animals. This data is consistent with prior research that demonstrates a marked decrease in brain mass 70 days after prolonged PS deprivation.

Conclusions: This data, along with similar studies, suggests that PS plays a critical role in the development of the central nervous system. Prior literature has shown that PS deprivation results in decreased brain mass in adults, and that certain drugs result in increased levels of apoptosis if administered during critical periods of development. This study demonstrates a specific mechanism for decreased brain mass resulting from PS deprivation, and that brief exposures are sufficient to significantly affect the developing brain. Taken together, this data suggests that a possible function of PS is to maintain the high level of CNS activity that is necessary during this critical period of development.

0112.A

High Inter-night Reliability of Monkey EEG

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Introduction: Rhesus monkey sleep strongly resembles human sleep in its diurnal pattern, REM/non-REM cycles, and temporal link to circadian core body temperature (Balzamo et al., 1977). Night to night variability of rhesus sleep has not previously been evaluated although it is an important consideration for designing animal studies that compare baseline to experimental conditions. Experimental condition effects on animal sleep typically use computer algorithms to measure changes in sleep EEG. This study evaluated the night to night stability of rhesus sleep EEG using spectral (FFT) and period amplitude analysis (PAA).
Methods: All night EEG, EMG, and EOG was recorded from 3 adolescent, male rhesus monkeys (Macaca mulatta) using radio telemetry (DSI, St.Paul, MN) in their home cages during 12 hour dark periods. Power spectral data and two measures of PAA (integrated amplitude (IAM) and time in band (TIM)) were extracted from 6 nocturnal EEG recordings spaced one month apart. A two-factor (animal x month) ANOVA was used to evaluate differences between animals and differences between months for each of the 3 extracted measures. A series of RM-ANOVA was then used to evaluate individual frequency bands (Delta (0.5-4Hz), Theta (4-8Hz), Alpha (8-12Hz), Sigma (12-17Hz), and Beta (17-35Hz)) within each measure (FFT, IAM, TIM) as a function of recording date.
Results: Significant differences between animals were found for all nocturnal EEG measures when compared across frequency bands (FFT: $p<0.0001$, IAM:$p<0.015$, and TIM: $p<0.001$). Main effects of month and animal by month interactions were non-significant ($p<0.99$) for all three measures. None of the individual frequency bands varied significantly as a function of recording date when evaluated using RM-ANOVA although IAM sigma approached significance ($F(5,10)=3.28$, $p=0.052$).
Conclusions: Spectral and period amplitude analytic measures of sleep EEG in human subjects have high inter-night reliability (Tan et al., 2000). The present study provides the first evidence that global measures of nocturnal monkey EEG show significant individual differences between animals while the power of individual frequency bands do not vary significantly across time. The only extracted measure from monkey sleep to approach significant variability across time was IAM sigma, the same measure Tan et al. found to have the lowest correlation between nights. Additional analysis using these computerized measures will explore the stability of frequency band contributions to monkey sleep EEG in separate sleep states. Rhesus monkey sleep in the laboratory appears to be a trait-like characteristic with robust reliability. This study provides additional evidence that rhesus monkeys are the optimal animal model for human sleep.

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0113.A

EEG, Behavioral and Neuronal Effects of Median Preoptic Nucleus Electrical Stimulation

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Introduction: The median preoptic nucleus (MnPN) contains a subset of neurons exhibiting sleep-related c-Fos immunoreactivity (Gong et al., 2000) and increased firing rates during both sleep phases compared to waking (Suntsova et al., 2002). The aim of this study was to examine the effects of MnPN electrical stimulation on EEG, behavior and neuronal activity in the dorsolateral hypothalamus (DLH), which is one of the targets of MnPN projections.
Methods: Rats were surgically prepared with frontal and parietal cortical EEG and EMG electrodes for sleep-wake states monitoring. Rostrocaudally oriented bipolar stimulating electrodes were implanted into MnPN. Two bundles of microwires, carried in microdrives, were aimed at the DLH bilaterally.
Results: During quite waking single pulses (50-150 muA, 200 ms) delivered to the MnPN evoked slow wave-spindle complexes in the EEG. These complexes followed the stimulation frequency at rates of 0.3-1 pulses/s. Both spindles and delta waves appeared in response to 3-15 pulses/s stimulation frequency. Waxing and waning responses were observed at stimulation frequencies 6-15 pulses/s. In most cases behavioral sleep was elicited in conjunction with EEG slow wave activity. High-frequency stimulation (100-200 pulses/s, 50-120 muA) provoked diffuse EEG-synchronization during quiet waking and did not cause behavioral activation or EEG-desynchronization during non-REM sleep. Both low- and high-frequency stimulation with current intensities above 150-200 and 100-120 muA, respectively, evoked hypersynchronous rhythmic EEG activity and, after a few seconds triggered absence-like seizures which continued after the end of stimulation. Repetitive seizure induction (6 seizures, 1/hour) was accompanied by a twofold decrease in time spent asleep. After 3-5 seizures, in response to stimulation animals developed absence seizure followed by myoclonic and, finally, generalized tonic-clonic seizures. All wakefulness/REM-active DLH neurons showed a dramatic reduction in their discharge rates in response to MnPN stimulation (3-200 pulses/s, duration of trains 5 s). The discharge rate fell to a minimum after 1-2 s stimulation. Recovery of pre-stimulus discharge occurred 10-20 s after the end of stimulation. During seizures these cells became virtually silent. State-indifferent, non-REM- and REM-active units did not respond to MnPN stimulation.
Conclusions: Both low and high frequency MnPN stimulation induced the appearance of EEG and behavioral correlates of sleep. Similar effects were observed previously (Sterman, Clemente, 1962; Benedek et al., 1979) in response to stimulation of ventrolateral preoptic area (VLPO), which also contains a cluster of sleep-active cells. The inhibitory response of DLH neurons to MnPN stimulation was similar to that exhibited by posterior hypothalamic cells to VLPO stimulation (Suntsova, Dergachyova, 2001). Like VLPO, MnPN stimulation may trigger generalized seizures. We hypothesize that sleep-promoting neuronal populations localized within preoptic area participate in sleep induction and maintenance via inhibition of major arousal system and, in the same way, contribute to the mechanisms underlying generalized seizures.

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0114.A

Effects Of Urotensin-II In The Regulation Of REM Sleep

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Introduction: Urotensin II (UII) is cyclic dodecapeptide with strong vasoconstrictive activity in the periphery. Autoradiographic binding experiments in rat brain have shown that 125I labeled-UII binds to the pedunculopontine tegmental (PPT) nucleus, the lateral dorsal tegmental area, and the lateral septal, medial habenular, and interpeduncular nuclei. Also, in situ hybridization reveals that UII receptor (UII-R) mRNA colocalizes with choline acetyltransferase (Clark et al., 01). The distribution of UII-R in cholinergic nucleus of the mesopontine tegmental area suggests the UII system may be involved in functions regulated by acetylcholine, such as the sleep/wake cycle. To determine the role of UII-R on

the sleep/wake cycle, we have analyzed the behavioral and physiological consequences of microinjection of UII in rats.
Methods: Eight male Sprague-Dawley rats were anesthetized with 2.5-3.0 % halothane and implanted for chronic sleep recordings as well as with a guide cannula in the lateral ventricle. Other group of ten 10 rats was also implanted for sleep recordings as well as bilaterally with guide cannulas in the PPT nucleus. One week after the surgery, rats were habituated to the recording conditions for at least 2 days. Rats implanted in the lateral ventricle were challenged with an icv microinjection of UII peptide [1 mg], whereas animals with cannulas in PPT nucleus received a bilateral microinjection of 1 ng of UII peptide. Polygraphic sleep recordings were analyzed for 6 hours following the injection. The SleepSign software (Kissei Comtec America, Irvine, CA) was used to score the EEG signal, and four stages were determined: wakefulness (W), slow-wave sleep 1 (SWS 1), slow-wave sleep 2 (SWS 2) and rapid eye movement (REM) sleep. Rats were housed individually with ad libitum access to food and water. The dark-light cycle was controlled (12:12). Statistical analysis of the data was carried out using an ANOVA and then a post-hoc Sheffé test.
Results: A significant increase in amount of REM sleep was observed both in rats injected icv (16.49% from total time of recording) and in rats with a cannula in the PPT nucleus (13.30% from total time of recording), compared to their respective controls (9.5% and 9.9%, respectively) [$p < 0.01$]. The increase in REM sleep was due to a significant increase in the number, but not the duration of REM sleep episodes ($p < 0.01$, compared to their respective controls). No significant changes were observed in W, SWS 1 and SWS 2.
Conclusions: In view of our results and taking into account that the UII-Rs are expressed in PPT nuclei, we conclude that UII peptide is involved in the regulation of the cholinergic mechanisms that control REM sleep.

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0115.A

Midbrain Modulation Of Arousal: Cortical Electroencephalogram Following Lesion Of Ventral Tegmental Area Neurons
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Introduction: A number of neurotransmitter systems (chief among them the monoaminergic and cholinergic cell groups) have historically been assigned major roles in modulating arousal. Recently, histamine, hypocretin/orexin and nitric oxide have also been recognized as having potential influences on arousal. The ventral tegmental area (VTA) has long been implicated in motivated behaviors, including drug-seeking. New evidence suggests that the VTA may also play an important role in modulating cortical desynchronization during wakefulness and REM sleep. In particular, our research (Lee et al, J Neurosci 2001) has recently suggested that the GABAergic component of the VTA may modulate arousal. In the current study the potential role of the VTA in modulating cortical electroencephalogram (EEG) activation was explored.
Methods: Adult male Sprague-Dawley rats were housed under standard colony conditions. Under sodium pentobarbital anesthesia, animals received either a sham operation or a single bilateral VTA injection of NMDA. Another group of animals received an intra-VTA injection of dermorphin conjugated to saporin (DERM-SAP) (Advanced Targeting Systems, San Diego). Animals were also surgically implanted with skull electrodes for recording the EEG and nuchal electrodes for recording the EMG. The EEG and EMG were recorded continuously for 24 hours beginning 14 to 28 days after surgery. Automated scoring software (Kissei-Comtec USA) was used to determine arousal state. Igor Pro software (Wavemetrics) was used to perform frequency analysis of the EEG during identified sleep states.
Results: Frequency analysis of the EEG in 4-sec epochs revealed differences in the distribution of relative power in the NMDA-lesioned animals, compared to controls. Specifically, higher frequency components of the EEG during slow wave sleep were attenuated following excitoxic destruction of neurons in the VTA. This attentuation was also observed after a DERM-SAP lesion specifically aimed at mu-opioid-receptor expressing cells in the VTA.
Conclusions: Lesion of the ventral tegmental area in rats leads to specific changes in EEG composition in the behaving animal. Specifically, the targeted inactivation of mu-opioid receptor-containing neurons in the VTA leads to a loss of higher frequencies in the cortical EEG. These results indicate that a selective inactivation of GABAergic cells in the VTA has specific effects on arousal mechanisms in the intact animal.

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0116.A

Triazolam Microinjections into the Peri-Fornicular Region Increase NREM Sleep in Rats
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Introduction: The hypocretin/orexin (Hcrt/OX) receptor-ligand system is critically involved in the pathophysiology of narcolepsy/cataplexy and may play a role in the pharmacological and physiologic regulation of sleep-wake states. The majority of Hcrt/OX neurons are located in the peri-fornicular region (PeF) of the posterior hypothalamus. In this study, we investigated the pharmacological regulation of the PeF by testing whether microinjections of the clinically used benzodiazepine hypnotic, triazolam (TR) into the PeF of rats would lead to alterations in sleep and wake activity.
Methods: Sprague-Dawley rats (male, 3-4 months old) were anesthetized with ketamine (70mg/kg) and xylazine (6mg/kg) intraperitoneally, and implanted with EEG and EMG electrodes. Microinjection guide cannulae (24-gauge) were stereotaxically positioned 1 mm above the PeF: A-P –3.14, M-L ±1.2, D-V –7.4 (Paxinos and Watson,1986). Nine rats accurately received bilateral microinjections (0.25ul each side) of vehicle and TR (0.25ug and 0.50 ug) into the PeF, in randomized order, followed by 4 hours of sleep/wake recordings. Data were analyzed by repeated measures ANOVA for dose (vehicle, TR 0.25ug and 0.50ug) and time (hours 1-4) factors. In five additional rats, TR (0.50 ug) was administered in combination with the GABAA-BZD receptor antagonist, flumazenil (0.95 ul). Rats received vehicle injections followed 30 minutes later by vehicle (VEH-VEH) or TR 0.50ug (VEH-TR) and FLU (0.95ug) followed 30 minutes later by vehicle (FLU-VEH) or TR 0.50ug (FLU-TR). Two days separated each injection trial. Animals were maintained on a 12L:12D cycle with food and water available ad libitum. Accurate cannulae placements were determined by cresyl violet staining of 40um coronal sections through the posterior hypothalamus.
Results: Wake, NREM, REM and TST: Wake time was decreased by TR (0.25ug) in hours 1 ($p £ 0.01$) and 2 ($p £ 0.05$) following microinjections, whereas NREM ($p £ 0.01$ and $p £ 0.05$) and TST ($p £ 0.01$ and $p £ 0.05$) were increased in the first two hours. TR (0.50ug) had similar effects for wake, NREM and TST in each of the first 2 hours following microinjection (all comparisons significant at $p £ 0.01$). Sleep latencies and intermittent wake time: NREM latency was significantly reduced by TR 0.25ug ($p £ 0.01$) and TR 0.50 ($p £ 0.01$). REM latency was decreased by TR 0.25ug ($p £ 0.05$). Intermittent wake time decreased with TR 0.25ug ($p £ 0.01$) and 0.50ug ($p £ 0.01$) injections. Combination of flumazenil and triazolam: Data were collected in 5 rats to test whether FLU (0.95ug) would block the effects of TR (0.50ug) in the PeF. TR (0.50ug) injections increased NREM and TST and decreased wake time, intermittent wakefulness and NREM sleep latency within the 2 hours following injections, replicating the data in the initial group of 9 rats (presented above). FLU (0.95ug), administered 30 minutes before TR (0.50ug) blocked the effects of TR (0.50ug), in that values from FLU-TR injections were similar to VEH-VEH and FLU-VEH trials. FLU

(0.95ug) administered alone had no effects on sleep and wake patterns.
Conclusions: These data indicate that neurons in the PeF are responsive to pharmacological input of a GABAA-BZD receptor agonist. These data are consistent with the hypothesis that the PeF region receives inhibitory projections from the anterior hypothalamus, which may form part of an intrahypothalamic system involved in sleep/wake regulation

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0117.A

Characterization Of The Sleep Patterns Of Fatty Acid Amide Hydrolase Knockout Mice

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Introduction: Fatty acid amides (FAAs) are endogenous lipids that have been related to neurophysiological functions, including promotion of sleep. FAAs are rapidly catabolized in vivo to the fatty acid amide hydrolase (FAAH), hindering efforts to determine their physiological properties. Recently, FAAH knockout (KO) transgenic mice were generated. To further characterize the behavioral and physiological profile of these mice, we examined the sleep/wake cycle, body temperature (Tb), and locomotor activity (LMA) in both FAAH KO mice and their non-transgenic littermates.
Methods: Adult homozygote FAAH KO mice (n= 10), heterozygote FAAH KO mice (n=10) and non-transgenic mice (n=10) were anesthetized with 1.0 % halothane and implanted for chronic sleep recordings, and telemetry transmitters for recording Tb and LMA. Two weeks after surgery, mice were habituated and recorded for 48 h for sleep and 129 h for Tb and LMA. SleepSign software (Kissei Comtec America, Irvine, CA) was used to score the EEG, and three stages were determined: wakefulness (W), slow-wave sleep (SWS), and rapid eye movement (REM) sleep. Results were statistically analyzed using an ANOVA and then a post-hoc Sheffé test.
Results: Our results demonstrate that homozygote FAAH KO mice spent more time in SWS (59.8 % of total time), compared to the control group (54.7 % of total time) during the light cycle [$p<0.01$]. On the other hand, both homozygote and heterozygote FAAH KO mice showed a well-defined circadian rhythm in Tb and LMA, with the highest peaks in temperature and activity during the dark period and lowest peaks during the light period. No significant differences were observed in Tb and LMA for any of the mice used in this study.
Conclusions: Our results indicate that the absence of FAAH produces an increase in the amount of SWS, suggesting that this enzyme may be a regulator of FAAs like oleamide, that promote sleep.

0118.A

Effect of the Endogenous GPR7/8 Ligand (Neuropeptide W) on Sleep/Wakefulness

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Introduction: Neuropeptide W (NPW) and its brominated form (NPB) have recently been described as the endogenous ligands of orphan G-protein coupled receptors GPR7 and GPR8. Intracerebroventricular infusion of NPW or its brominated form (NPB) enhance food intake in rats. GPR7 receptors in rats are distributed across all cortical layers and in several hypothalamic nuclei, including the preoptic nucleus and the lateral hypothalamic area. To determine whether NPW has a role in the modulation of sleep architecture, we have infused 0.4 and 2 nmoles of peptide into the brain ventricles and recorded the EEG/EMG to score states of vigilance. We have also analyzed the distribution of c-fos positive neurons 60 minutes after NPW infusion.
Methods: Adult rats were anesthetized with 1.0 % halothane and implanted for chronic sleep recordings. In addition, a stainless steel cannula was stereotaxically implanted according to the Paxinos's stereotaxic coordinates, in the lateral ventricle (AP -0.34, ML $\pm$ 1.0, DV +2.0). One week after surgery, rats were habituated to the recording conditions for at least 48 hours. Once the habituation period was completed, recordings were performed following microinjection of saline (5.0 ul), NPW peptide (1 ug; 400 pmoles), and NPW peptide (5 ug; 2 nmoles). During the experiment rats were housed individually, with ad libitum access to food and water and maintained on a normal 12-hr light cycle (on 06:00 hr, off 18:00 hr). Rats were perfused under anesthesia to perform c-fos immunocytochemistry and to verify histologically the microinjection sites. Statistical analysis was carried out using an ANOVA and then a post-hoc Scheffe test.
Results: Administration of 1 ug (400 pmoles) of NPW peptide, increased the amount of REM sleep (14.34%), 2 hours after its microinjection ($p < 0.05$, compared to vehicle [6.7%]), whereas injection of 5 ug (2 nmoles) increased REM sleep (16.51%), 3 hr after its administration ($p < 0.01$, compared to vehicle [12.61%]). Injection of NPW peptide induced c-fos immunoreactivity in the paraventricular and lateral hypothalamic nuclei, consistent with the distribution of GPR7/8 receptors.
Conclusions: Our results strongly support a role of NPW and its receptors GPR7 and GPR8 on the modulation of REM sleep.

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0119.A

Auditory Processing in Wakefulness and Sleep: Subsecond Brain Dynamics

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Introduction: The realization of a unified perception relies on the functional integration of specialized brain regions. The transition from wakefulness to sleep is characterized by alterations of attention and sensory processing. At sleep onset, loss of perceptual awareness is paralleled by the appearance of sleep spindles and K-complexes in the electroencephalogram (EEG), indicating brain electrical synchronization. Several lines of evidence suggest, however, that the sleeping brain may still show signs of response to auditory stimuli. Thus a brief tone delivered during nonREM sleep elicits K-complexes. To investigate the physiological basis for the interaction of attention, perception and vigilance level new statistical and signal processing methods were applied to single-trial event-related EEG responses in a simple auditory discrimination task at sleep onset.
Methods: The EEG was recorded from ten healthy subjects at 29 scalp sites during task presentation. The experimental manipulation consisted in an auditory 'oddball' discrimination task performed repeatedly during sleep onset periods. A series of 1000 Hz 'standard' tone pip stimuli (96%) was presented, while a 1500 Hz 'target' stimulus was presented infrequently (4%). The subjects were asked to press a button upon detection of the 'target' stimulus. The EEG was decomposed into spatially fixed, temporally independent components with different patterns of projection to the scalp channels (component topography). Both the EEG data and the resulting independent components were analyzed with a variety of statistical and signal processing methods including spectral and time-frequency analyses, inter-trial coherence (ITC), event-related 'ERP images'. For each component scalp distribution, an equivalent sin-

gle dipole source inverse solution was computed.
Results: The frequency spectrum and the scalp topography of the EEG and single-trial ERP showed dependence on vigilance state, as expected by EEG mapping studies. Inspection of the EEG signals acquired during nonREM sleep stage 2 confirmed the presence of K-complexes in response to both target and non-target stimuli. In contrast to conventional signal averaging methods, our approach allowed to determine that different mechanisms may underlie the generation of the various aspects of event-related potentials. Beside discrete stimulus-evoked brain events, the analysis revealed that stimulus-induced partial phase resetting of multiple electroencephalographic processes were involved in the generation of event-related responses. Separation of the signals in independent components revealed several common domains or epicenters of neural synchrony contributing to the averaged ERPs. Their spectral signature differed between waking and different sleep stages. Additionally analysis of the time course of the different components revealed that a number of those, common across subjects, contributed to the K-complexes evoked by the stimuli.
Conclusions: Our analyses demonstrated that ERP averaging and other classical approaches reveal only a portion of the event-related brain dynamics occurring in single EEG trials, and that these dynamics differed across wake/sleep states.

0120.A

Orexin and Melanin-Concentrating Hormone (MCH) Double Knockout Mice: Compensatory Role for MCH in Narcolepsy-Cataplexy

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Introduction: Orexin (hypocretin) and MCH neuropeptides are produced by distinct populations of neurons in the lateral hypothalamic area that independently project to arousal-promoting nuclei. While failure of orexin signaling in the brain has been linked to the sleep disorder narcolepsy, MCH is known to regulate feeding and energy balance. Anatomical similarities between the orexin and MCH systems suggest that MCH might also play a role in sleep-wake control. In this study we produced mice in which both orexin and MCH genes have been inactivated (double knockout mice) to investigate whether the MCH allele influences the narcoleptic-cataplectic phenotype of orexin knockout mice.
Methods: Orexin homozygous and MCH homozygous knockout mice (C57Bl/6J background, N5) were intercrossed to generate double heterozygous mice. Filial crosses generated littermates for use in experiments. Mice were genotyped by PCR. Experiments were performed with male mice (3-4 months old). Experiment 1: The frequency of novelty-elicited cataplexy-like arrests in orexin+/+;MCH+/+ and orexin+/+;MCH-/- littermates (5 pairs) as well as 7 orexin-/-;MCH+/+ and 8 orexin-/-;MCH-/- littermates was evaluated by infrared videophotography during the dark phase. Experiment 2: The frequency of spontaneous direct transitions from wakefulness to REM sleep was evaluated using polysomnographic recording over 2 consecutive days from 4 pairs of orexin-/-;MCH+/+ and orexin-/-;MCH-/- mice housed individually in home cages.
Results: Experiment 1: No orexin+/+;MCH+/+ or orexin+/+;MCH-/- mice displayed behavioral arrests of any kind. In contrast, orexin-/-;MCH+/+ mice exhibited cataplexy-like arrests during the filming period (4.0 $\pm$ 1.2 arrests/hour). By comparison, orexin-/-;MCH-/- mice showed a striking 5–fold increase in arrests (18.3 $\pm$ 1.8/hour, p=0.000002).Experiment 2: EEG/EMG records demonstrated spontaneous direct transitions from wakefulness to REM sleep in orexin-/-;MCH+/+ mice during the dark phase (4.8 $\pm$ 2.0 transitions/dark phase). No arrests were observed during the light phase when sleep-wake patterns of these mice are relatively normal. In contrast, orexin-/-;MCH-/- mice exhibited significant increases in direct transitions to REM sleep during both the light (2.4 $\pm$ 0.8 transitions, p=0.003) and dark (25.1 $\pm$ 7.3 transitions, p=0.006) phases.
Conclusions: Although loss of the MCH gene alone does not result in narcolepsy, inactivation of both orexin and MCH genes results in a phenotype that is much more severe than that observed with deficiency of orexin alone (genetic epistasis). These results suggest a compensatory role for MCH in the regulation of cataplexy and sleep-wake control. Further investigation of interactions between output pathways related to energy homeostasis and arousal are warranted. Our findings may suggest that MCH neurons of the lateral hypothalamic area play a role in the presentation of human narcolepsy, a genetically complex disorder.

0121.B

Change in Apnea Threshold in Response to Long-term Intermittent Exposure to High Ambient CO2 in Submarine Soldiers

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Introduction: During most of the cruise submarines are detached from their environment- this status is defined as closed atmosphere. Therefore, oxygen levels are relatively low (19 Kpa = 144mmHg) and CO2 levels are high (1 Kpa = 7.6mmHg). Breathing during sleep is controlled by the metabolic system responding primarily to high CO2 and low O2 levels. It is well known that in acute exposure to high altitude, where both O2 and CO2 levels are low, breathing becomes periodic (a form of central sleep apnea). The objective of this study was to determine whether there is sleep disordered breathing in submariners, in the acute and chronic exposure to gas changes.
Methods: Sleep of 8 healthy soldiers was assessed three times: 1. control night – in submarine docking; 2. at the beginning of cruise (reflecting acute exposure to gas level changes); and 3. at the end of cruise (chronic exposure to gas level changes). Each night was divided to three parts because of different CO2 levels (as a result of ventilation of the submarine). Sleep and breathing was measured using watchPAT100, a portable device that is used to determine breathing disorders during sleep.
Results: Oxygen levels remained relatively stable throughout the cruise. The sleep and breathing data were categorized according to 4 CO2 conditions: acute moderate (CO2 levels of 2.3-5mmHg during first 1-2 nights of cruise), acute high (C02 levels 5-9.2mmHg during first 1-2 nights of cruise), chronic moderate (CO2 levels 2.3-5 mmHg during last night of cruise), and chronic high (CO2 levels 5-9.2 mmHg during last nights of cruise). In the chronic condition, RDI was significantly higher in the moderate CO2 than high CO2 condition (18.9/h vs 8/h, $p<0.005$). RDI did not correlate with CO2 levels during the first nights of the cruise ($R= -0.2$, NS) but significantly negatively correlate with it during the last nights of cruise ($R= -0.56$, $p<0.05$).
Conclusions: We conclude that during an eleven day cruise submariners adapted to high CO2 levels, as evidenced by the significant dependence of RDI on CO2 during the final but not initial days of the cruise. This adaptation resulted in a significant increase in RDI when CO2 levels declined during the last nights of the cruise.

0122.B

1Hz Resolution Spectral Analysis Defines A Low Beta Band 14.5-18Hz In Sleep

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Introduction: Precise definitions of frequency band limits in the spectral analysis of sleep are important because several aspects of the signal change rapidly with frequency. This is particularly so over the higher range 14-30Hz that we examine here. Research in the past few years has generally adopted a single beta band with a lower limit around 15-17Hz and an upper limit 25-35Hz. Discordant results, however, and theoretical insights gained from the neuronal transition probability model, have led to the need for a reappraisal of these limits. We do this on the basis of changes in power time-course comportment.
Methods: The study uses data from 18 healthy subjects (24.6±2.8 years). Overnight sleep was recorded using three bipolar EEG derivations (F4-Cz, C4-T4 and Pz-O2), an EMG and an EOG. Sleep stages were visually scored using standard criteria and the F4-Cz signals were digitised at a sampling rate of 256Hz. Power spectra (mV2) were computed by FFT for consecutive 4-second epochs over the frequency range 14-30Hz. Power time-courses in this range were examined in 1Hz bins after appropriate smoothing. The lower limit for beta was set at 14.5Hz, since spindles are practically non-existent above this frequency. We examined the first 4 NREM-REM cycles using objective measures of discontinuity in time-course comportment as a function of frequency: we applied two independent criteria by determining that frequency where (a) the initial slope of NREM beta changes sign and (b) the ratio of average power in REM to average power in the NREM trough crosses unity. These analyses were done using the ERA software package from Phitools, France.
Results: Using 72 NREM-REM pairs, we identified one discontinuity at the start of NREM at 18.0±1.7Hz (SD): the time-course changes abruptly from a low start (positive slope) below this frequency to a high start (negative slope) above it. The time-course comportment also has a marked discontinuity at the NREM to REM transition: above the discontinuity frequency, a rising NREM beta flattens as it traverses REM while below, beta is falling in NREM and continues to fall in traversing REM. The ratio criterion gave us an independent second value for the discontinuity frequency at 18.2±1.5Hz. Combining these results gave a final result 18.1±1.6Hz.
Conclusions: For the first time, a sharp power-time-course discontinuity has been pinpointed and accurately measured in the beta range. It excludes considering the range as a single beta band since this can lead to distorted or misleading time-course results. We therefore propose the range be split into a low band 14.5-18Hz and a high band from 18Hz to at least 30Hz. Apart from this practical application, the discontinuity has a fundamental significance that can be understood in the light of the neuronal transition probability model: it occurs at that frequency below which neurons oscillate at frequencies characteristic of the NREM state.

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0123.B

Trait-Like Inter-Individual Differences In The Expression Of REM Sleep

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Introduction: Since the discovery of REM sleep 50 years ago, various studies have been devoted to the expression of REM sleep during normal sleep periods and in response to experimental challenges. Little is known, however, about systematic inter-individual differences in the expression of REM sleep. We investigated the magnitude and the stability of inter-individual differences in REM sleep expression among adults during baseline sleep and during recovery sleep after 36 hours of total sleep deprivation.
Methods: As part of a larger study, n=15 normal, healthy subjects (ages 23-38; 8 females) each completed two identical, strictly controlled laboratory experiments. Each experiment involved a 12-hour baseline sleep opportunity (22:00-10:00), a 36-hour behaviorally monitored sleep deprivation period, and a 12-hour recovery sleep opportunity (22:00-10:00). Sleep periods were recorded polysomnographically and scored blind to subject. Complete data were available for 11 subjects during both baseline sleeps, and 13 subjects during both recovery sleeps. The amount of REM sleep, REM sleep latency, and the mean duration of the nonREM/REM sleep cycle were compared between the first and second experiment, for baseline sleep and for recovery sleep. The intraclass correlation coefficient (ICC), defined as the ratio of between-subjects variance to total variance, was computed to quantify trait-like inter-individual differences. In addition, the correlations between subjects' averages over the two baseline nights and subjects' averages over the two recovery nights were assessed.
Results: The amount of REM sleep was 136.4 ± 47.3 and 144.0 ± 30.4 minutes, respectively, during the baseline and recovery nights (averages ± s.d. over subjects). The REM latency was 81.9 ± 37.4 and 76.0 ± 37.0 minutes, respectively, and the mean duration of the nonREM/REM sleep cycle was 94.5 ± 12.1 and 94.5 ± 11.3 minutes. For baseline REM amount, the ICC over the two experiments was 0.46; for baseline REM latency the ICC was 0.41; and for baseline sleep cycle duration it was 0.56. ICC values were lower for recovery sleep. Nevertheless, the correlation between baseline average and recovery average was 0.77 for REM amount, 0.84 for REM latency, and 0.90 for sleep cycle duration.
Conclusions: Substantial trait-like inter-individual variability (from 41% to 56% of total variance) was observed for the amount of REM sleep, REM latency, and the mean duration of the nonREM/REM sleep cycle during 12-hour baseline sleep opportunities. Moreover, these inter-individual differences in REM sleep expression were stable even after 36 hours of sleep deprivation. Although these findings might be secondary to trait variability in nonREM sleep expression, they may be important for studies of the waking neurocognitive functions of REM sleep. We are investigating whether age, gender, body weight, or other factors predict the trait-like inter-individual differences in the expression of REM sleep.

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0124.B

The Amplitude-Velocity Ratio of Blinks: A New Method For Monitoring Drowsiness

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Introduction: The peak closing velocity (PCV) and the amplitude (A) of blinks are usually highly correlated, but this changes with drowsiness. Such measurements are usually made by timing calibrated movements. However, the ratio A/PCV has the dimension of time, not distance (amplitude) or distance per unit time (velocity). So long as measurements of A and PCV involve the same units of distance, their ratio can be derived from uncalibrated measurements . The aim of this investigation was to measure the amplitude-velocity ratios of blinks (AVRB) when alert and when drowsy because of sleep deprivation.
Methods: The subjects were 12 healthy volunteers (7F, 5M:19-64yr). Eight had eye and eyelid movements recorded during 10-min psy-

chomotor vigilance tests (PVT), in both simple and choice reaction-time modes, in the afternoon/evening when alert, and again during the night after being awake for 20+ hr, or next afternoon after 32+ hr of wakefulness. The PVT required a push-button response to a change of shapes lasting 400 msec on a PC screen at random intervals of 5-15 sec. Four other Ss were tested for 30- min periods in a STISIM driving simulator, in the evening when alert, and during the night after being awake for 20+hr. One of the latter subjects was also tested at another time with the PVT, as in the first group. All subjects had practice runs. Eye and eyelid movements were recorded by an infrared reflectance method using 50-microsec pulses of infrared light every 500 microsec from light-emitting diodes, one pointing at each eye, the reflected pulses being detected by adjacent phototransistors. The effect of environmental light before each pulse was subtracted and the pulse height (position) and its first derivative (velocity) for each eye were displayed on a PC screen. Changes in position were linearly related to the calibrated amplitude of eye movements. Blinks, saccades etc were distinguishable, as confirmed by video recordings of the subject's face. The A and PCV of all blinks over a 3-min period in the middle of each test were measured from the PC screen.
Results: In all Ss when alert, the A and PCV of blinks were highly correlated ($r=0.82, n=202, p<0.001$). The mean of AVRBs for alert Ss was 4.1 ± 0.8 (SD), increasing after sleep deprivation to 6.4 ± 6.0 (ANOVA, $p<0.0001$). AVRBs > 6.0 then appeared in all Ss with a frequency of at least 2/min. In 4/9 Ss doing the PVT there were 23 lapses (no response within 1 sec), all when Ss were drowsy. There was a significant increase in AVRBs between the 60-30 sec and 30-0 sec periods before lapses ($p=0.003$).
Conclusions: The mean AVRB and the frequency of AVRBs >6 increased with drowsiness, particularly in the 30 sec before lapses in performance. This could provide a new method for monitoring drowsiness in people such as drivers. A patent is pending for a new device based on these methods.

0125.B

Eyelid Closure, Visual Suppression and Hypovigilance in the Drowsy State: Lapses in Performance With Eyes Open or Closed

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Introduction: Methods for monitoring drowsiness have been proposed that are based on long eyelid closures detected by video camera images of the subject's eyes. There is an implicit assumption that drowsy lapses in performance always involve eyelid closure, blocking light entry through the pupils. This is undoubtedly true for some lapses. However, it may be that central suppression of vision that normally occurs with saccadic eye movements (with eyes open), with blinks, and with the sleep onset process may cause lapses with the eyes open in drowsy Ss trying to stay awake. We cannot see when falling asleep, even if the eyelids are taped open. The aim of this investigation was to examine the role of eyelid closure during lapses in performance of a psychomotor vigilance test (PVT) in sleep-deprived subjects. This was facilitated by the development of a new PVT (the Johns Test of Vigilance) that enabled eye and eyelid movements to be monitored during the PVT.
Methods: Nine healthy volunteers (5F, 4M; 19-64 yr) had their eye and eyelid movements monitored while they performed a 10-min PVT 6-8 times each, half when alert and half when sleep-deprived for 20+ or 32+ hr. In total there were 66 PVTs involving 3631 stimuli. The infrared reflectance method for monitoring the eyes is described in a companion report. A PVT lapse was defined as either no response or a delayed response >1sec after the start of the stimulus which involved a change in patterns lasting 400 msec at random intervals of 5-15 sec on a PC screen. The data for eye movements and PVT responses, displayed together, were inspected to establish the relationship between them which was confirmed by video pictures of the Ss eyes.
Results: There were 23 lapses in 4 of the 9 Ss, none in the other 5. Lapses occurred only after sleep deprivation. The eyelids were closed throughout the stimulus for 5 lapses, open for the whole time in 9, and for most of the time, between blinks and/or saccades, in another 9 lapses, ie the majority of lapses (18/23) did not involve the eyelids being closed when the stimulus was present, a minority (5/23) did.
Conclusions: In drowsy subjects who are trying to stay awake, lapses in performance can occur whether the eyes are open or closed at the time. The central suppression of vision that occurs normally with saccades and blinks, and which is part of the sleep-onset process even with eyes open, must be considered, along with prolonged eyelid closures, as a cause of performance lapses in the drowsy state. In a companion report it is shown that the velocity of eyelid movements, assessed in relation to their amplitude-velocity ratios, became slower in the 30-sec before each lapse. This may provide a useful method for predicting imminent performance failure, whether or not the eyes are open.

0126.B

Sleep and High Altitude

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Introduction: Reduction in O2 tension in ambient air, associated with ascent to high altitude, gives rise to a series of central and peripheral responses to compensate hypoxemia. Insomnia, disruption of sleep, decrease in Slow Wave Sleep (SWS), more frequent arousals, awakening with a sense of suffocation are a common cause of discomfort after acute ascent to high altitude. Data about changes in Total Sleep Time (TST), Rapid Eye Movement (REM) sleep and SWS latency and decrease in REM sleep have been reported. Values of hypoxemia inducing arousal were believed responsible for sleep disturbances in altitude. At high altitude, given the prevalence of insomnia, some studies have been made about sleep during acclimatisation in natural conditions. Our aim was to study sleep, respiratory activity, heart rate, metabolic and temperature changes after 30-35 hours of acclimatisation at 3480m.
Methods: Polysomnographic variables (EEG, EMG, EOG, EKG, Respiration, Temperature (LabView-National-Instruments and Medcare-Flaga) and SpaO2% (8500Nonin-Med-Inc. and Medcare-Flaga) were recorded continuously during sleep at 122m and at 3480m above sea level in six male adult athletes (age: 37-44 years) in controlled standard for diet, acclimatisation, room temperature (°C) and relative humidity (%). Light-dark and jet-lag effects were excluded by location of the study. Polysomnographic data were amplified and acquired at sampling rate of 200-512 Hz for subsequent on-line and off-line analysis according to standard criteria. Changes in pH, pCO2, pO2, tCO2, HCO3-, Na+, K+, Ca++, tHb, O2Hb (OptiCCA, Roche-Diagnostics) were studied on capillary blood samples taken from the earlobe at rest and in comfort: a) close to sea level, 122m, b) on reaching 2050m and c) after 30-32 and 39-41 hours of acute acclimatisation at 3480m. Differences between conditions were assessed by Student's paired t-test. A probability level of less than 0.05 was accepted as significant.
Results: Significant reductions in TST (.5%; $p<0.0021$), REM sleep (.3%; $p<0.0226$) and SWS (.3%; $p<0.0151$) were observed after 32-35 hours at 3480m compared to 122m. A parallel increase in wakefulness (,8%; $p<0.01$) was detected. REM sleep episodes were shorter and fragmented at 3480m compared to 122m. SWS latency increased. SpaO2% recorded during sleep at 3480m was lower ($p<0.001$), consistent with higher heart rates ($p<0.05$) compared to 122m. High correlation was found between SpaO2 and REM sleep, total sleep time and heart rate. Periodic breathing was observed during stage 2 NREM, but this disappeared as soon as subjects entered in REM sleep.
Conclusions: The results of this study suggests that arousal at high altitude, could have a protective function in preventing excessive oxygen

deprivation during sleep, and can be due to direct and/or indirect stimulation of the mesopontine reticular activating system involved in the behavioural and metabolic integration of autonomic control and arousal.

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0127.B

A Gabor Transform Study of Time-dependent Sleep Spindle Characteristics

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Introduction: This study aims to investigate some time-dependent characteristics of human sleep spindles using the Gabor Transform.
Methods: The C3-A2 channel of six standard sleep studies pertaining to healthy young adults was subjected to a Gabor Transform in order to extract total number, mean frequency, time position and other characteristics of sleep spindles. All were recorded in an 18-channel analog Nihon-Kohden polygraph (Neurofax) with posterior digital conversion (12 bits, 128Hz).
Results: Total spindle count was above 2,500 for every subject. Mean spindle frequency was clearly U-shaped within NREM sleep for 3 subjects and ambiguous for the remaining cases. Correlation between mean spindle frequency and density ranged between 90.9% and 85.9% for five subjects and was 74.8% for one subject. This was the case with lowest spindle count. For the case with highest spindle frequency/density coherence, correlation with delta power was showed to be 85.6% and 84.2% respectively. In the few instances when spindles were detected within REM sleep, frequency variability tended to be higher than in NREM sleep.
Conclusions: We have found a consistent association between mean spindle frequency and density along the night that should be accounted for in systematic studies of sleep spindles. Sleep spindle modulation by homeostatic mechanisms needs further investigation.

0128.B

Sleep Quality And Metabolic Changes At An Altitude Of 3480 Metres

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Introduction: Metabolic changes were considered responsible for sleep disturbances at high altitude, with frequent awakenings during acute acclimatisation. It has been suggested that measurement of peripheral arterial oxygen saturation (SpaO2) during sleep could be useful in monitoring such alterations. We considered the relationships between metabolic changes and sleep quality variations after 30-40 hours of acute acclimatisation at 3480m above sea level.
Methods: Observations were made in domestic location on 5 adult male athletes (age: 37-44 years) in controlled for diet and acclimatisation. SpaO2 (Sapio-Life) was recorded continuously at sea level and 3480m above. Changes in pH, pCO2, pO2, tCO2, HCO3-, Na+, K+, Ca++, tHb, O2Hb (OptiCCA, Roche-Diagnostics) and blood lactate concentration were studied on capillary blood samples taken at rest and in comfort from the earlobe: a) at about sea level, 122m, b) on reaching 2050m and c) after 30-32 and 39-41 hours of acute acclimatisation at 3480m. Sleep perception was evaluated by sleep quality indicators. Differences between data (mean ± S.D.) were assessed by Student's t-test and p values <0.05 were accepted as significant.
Results: At high altitude, 65% of the athletes took a longer time to fall asleep; 30% of them woke up 2 hours before the expected time and 60% woke up more than once. Sleep quality was perceived as significantly ($p<0.025$) poorer, duration of sleep was shorter and 60% of subjects felt poorly restored on waking up. SpaO2 % during sleep was lower ($p<0.0001$) at 3480m compared to sea level. A significant ($p<0.0059$) correlation between total sleep time and SpaO2% was observed. Compared to sea level, pH increased in all conditions at high altitude ($p<0.01$-0.003). After 30-32 hours of acute acclimatisation, pH was significantly increased at 3480m compared to 2050m ($p<0.049$), consistently with pCO2 and HCO3- variations. At high altitude, pO2 and SpaO2 decreased ($p<0.0005$) compared to sea level, and pO2 was higher ($p<0.024$) after 39-41 hours than after 30-32 hours of acute acclimatisation at 3480m. Moving from 2050m to 3480m, both pO2 and SpaO2 significantly decreased ($p<0.003$).
Conclusions: This study demonstrates that metabolic variations during acute acclimatisation at high altitude might be responsible for poor sleep quality. Excessive oxygen deprivation during sleep at 3480m may be prevented by frequent arousal which could be due to stimulation of the mesopontine reticular activating system, involved in the behavioural and metabolic integration of autonomic control and arousal. The measurement of SpaO2 during sleep can be an objective tool for the diagnosis of sleep alteration at high altitude. Our data also demonstrates that, at intermediate altitude, the peripheral metabolic pathway used by these athletes at rest is aerobic, even during acute acclimatisation.

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0129.B

Influence of Early Maternal Behavior on Sleep-Wake Cycle and Sleep Response to Stress in Adult Rats

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Introduction: Early life events have long-lasting influences on behavior and may be involved in individual differences in stress responses in adults. For example, offspring of mothers presenting with high (HL) and low (LL) Licking/grooming and arched-back nursing differ in their response to acute stress, HL pups showing lower plasma ACTH and corticosterone responses to stress compared to LL pups. Stress exposure induces important alterations in sleep architecture. For example, acute restraint at the beginning of the active period is followed in rats by increased sleep duration, mostly REM sleep. This study aimed at evaluating the influence of maternal HL and LL behavior on sleep and sleep response to stress in offspring.
Methods: Thirty-five Long-Evans rats were selected according to maternal behavior. At 7-months, these 15 HL and 20 LL rats were implanted chronically for sleep recordings under halotane anaesthesia. After a 5-day habituation period to recording equipment under standard housing conditions (12:12 light:dark cycle; lights on at 8h AM), baseline sleep was recorded for 24h. The following morning (one hour after lights-on), rats were submitted to a 1-h immobilization stress and recovery sleep was recorded for the next 22h. Comparisons between groups were made using t-tests for independent samples.
Results: No difference was observed on sleep architecture between HL and LL rats on baseline sleep. Recovery sleep following 1-h acute immobilization stress showed more time in wakefulness ($p<.05$) and increased REM sleep latency ($p<.05$) in HL compared to LL offspring.
Conclusions: Baseline sleep architecture is similar in adult rats born from HL and LL mothers. Exposure to acute restraint stress, however,

produce a greater disturbance in the sleep of HL than LL offspring. It may be hypothesized that sleep of HL offspring is more sensitive to acute restraint stress than that of LL offspring. This contrasts with neuroendocrine results showing that LL present more plasma corticosterone and ACTH following acute stress compared to HL. Difference in HPA axis reactivity to stress is probably involved in the different response of the sleep-wake cycle observed in those animals.

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0130.B

Chronic Mild Stress in Rats Increases REM sleep and Sleep Fragmentation and Decreases Sucrose Intake

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Introduction: In an animal model of depression, chronic mild stress(CMS) has been demonstrated to cause behavioral and hormonal changes which often is associated with depression in humans. Reduced sucrose intake has been postulated as one of the core symptoms of depression, anhedonia. However, findings on sucrose intake are inconsistent. In humans, depression is associated with sleep abnormalities like shortened REM latency, increased REM sleep, fragmented sleep and reduced delta sleep. In the present study we investigated if the CMS procedure in our hands would decrease sucrose intake, and give sleep changes similar to what is found in depressed patients.
Methods: Male SPD rats were implanted under anesthesia with electrodes for recording EEG (fronto-frontal and fronto parietal) and with silver wires in the neck muscle for EMG recording. Stages scored were waking, SWS1, SWS2 and REM sleep. After recovery and adaptation to recording situation, sleep was monitored for 8 hr Following this baseline sleep recording, the rats were divided into two groups: a control group (n=7) and a CMS group (n=7). The CMS group was then exposed to daily stressors (e.g. periods of soiled cage, reversed light/dark cycle, grouped housing, food and/or water deprivation) for 4 weeks. Sleep was then monitored again in both groups. Sucrose intake (1 % sucrose solution) was tested weekly during the 4 week period.
Results: CMS rats spent more time in REM sleep (F(1,6) = 11,20, p = 0.038) and showed more fragmented sleep (F(1,6) =27,88, p =0.002) compared to their baseline recording. Increased sleep fragmentation in CMS rats was particularly evident by increased number of arousals, REM sleep and SWS1 episodes. The overall duration of sleep stages was decreased (F(1,6) =15,25, p =0.008). The amount of SWS2 was not decreased, however SWS2 in percent of total SWS was reduced (F(1,6) =12,32, p =0.013). Compared to the control group, CMS rats reduced their latency to REM sleep (-77%, p=0.043). Correlation analysis showed that animals which had less consumption of sucrose spent more time in REM sleep (r=-0,54, p=0.044) and had increased number of REM sleep episodes(r=-0,58, p=0.031). Chronic mild stress decreased sucrose intake in our experiment. The largest effect was obtained on day 3, 10, 17 and 24, but returned to normal levels after 28 days (F(1,12) = 5,54, p =0.036). The rat's bodyweight was not affected by CMS (F(1,12) = 1,44, p =0.253).
Conclusions: The CMS rats had increased REM sleep, increased fragmentation and a relative reduction of SWS2 compared to their own baseline values. Sucrose intake was decreased. The findings support the use of CMS as an animal model of depression.

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0131.B

Increased NREM Sleep Heart Rate Variability In REM Sleep Deprived Men Supports The Covert REM Sleep Model

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Introduction: Variability of RR intervals for normal to normal beats (SDNN) varies between wakefulness and sleep, and across NREM and REM sleep stages. The increased SDNN associated with REM sleep can be observed before the actual onset of REM sleep as scored by standard criteria. This phenomenon can be explained by the covert-REM model which stipulates that different physiological REM sleep processes can dissociate into NREM sleep. We tested if an increase in REM sleep pressure caused by REM sleep deprivation would further increase the dissociation of the heart rate variability into NREM sleep, and this more specifically in the 20 minutes prior to REM sleep.
Methods: Healthy subjects slept 3 consecutive nights in the laboratory. Following the adaptation/baseline night, one group [REMD: n=11, 4 men, 7 women] was deprived of REM sleep (awakened after 5 min of REM sleep starting at the 3rd cycle) while a second group [CTL: n=10, 4 men, 6 women] was control deprived (awakened after 25 min of REM sleep starting at the 3rd cycle). All subjects were then recorded a third night for a sleep onset study (2 hrs) and then slept undisturbed. Mean SDNN was assessed for the 20 min prior to the 1st REM sleep period of recovery sleep in blocks of 5 min prior to REM using a 2 x 2 x 4 ANOVA with Group (REMD, CTL), Gender (M, F) and Block (1-5 min, 6-10 min, 11-15 min, 16-20 min before REM).
Results: A main Block effect (F(3,51)=6.07; p<.001) indicated that mean SDNN increased with approaching REM sleep. Post-hoc Tukey HSD tests showed that SDNN 1-5 min prior to REM was higher than either 11-15 min (p<.001) or 16-20 min (p<.004) prior. A marginal Group main effect (F(1,17)=3.33; p<.09) indicated that SDNN was higher for REMD than CTL whereas a Group x Gender interaction (F(1,17)=4.35; p<.05) clarified that only men showed this REMD-sensitive SSDN increase. Simple effects analyses showed higher SDNN for REMD than CTL men (F(1,17)=6.19, p<.02) and no comparable difference for women (F(1,17)=.045; p<.84).
Conclusions: The findings support and extend previous work showing that cardiac variability in NREM increases as REM approaches. They also suggest that cardiac variability reflects deprivation-induced REM pressure in NREM sleep, but only in men. Although further study with men is needed, this evidence, together with the recent finding that REM deprivation also increases muscle atonia in NREM sleep, is consistent with the notion that multiple covert REM sleep signs may occur in NREM sleep up to 20 min prior to a REM episode—and possibly elsewhere during sleep. The observed link with gender is consistent with known gender differences in cardiac variability, i.e., that SDNN increases in REM sleep for men but not women.

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0132.B

Processing Of Acoustic Stimuli During NREM Sleep: Results From A Simultaneous FMRI And EEG Study

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Introduction: The apparently reduced reactivity to external stimuli is a basic feature of sleep, and the changes of information processing during sleep are still to be disclosed. Using the novel approach of combining functional magnetic resonance imaging (fMRI), which provides the

highest anatomical resolution of all in vivo brain mapping techniques, and EEG in sleep, the objective of the present study was to explore regional activation patterns upon different kinds of acoustic stimulation in NREM sleep.

Methods: Eleven healthy volunteers (6 m, 5 f, mean age 23.8 years, age range 22-28) participated in the study following partial sleep deprivation for two days. FMRI sessions were performed on a clinical 1.5 T scanner (Signa Echospeed, GE, USA) and started between 10:00 and 11:00 pm while continuously presenting scanner noise via headphones. During fMRI, echo planar images (EPI) (TR=3000ms/TE=60 ms, 5 mm thick) were acquired. Each dataset contained 7 slices running parallel to AC-PC allowing to cover the primary and secondary auditory and visual cortices as well as the thalamus. Four different stimuli (text, text reversed, beep, piano music) were presented in a block design with four periods of rest interleave with three periods of continuous stimulation lasting 30 s each. Polysomnographic recordings were performed using a MR compatible device (Schwarzer, Munich, Germany). Sleep recordings included an EEG according to the international 10-20 system, an EOG and an EMG. Once unambiguous NREM sleep stages according to Rechtschaffen and Kales were visible in the on-line polysomnography, scans were started applying one of the stimuli. Sleep stages were reevaluated following post processing (artifact correction).

Results: Visual on- and off-line analysis of the PSG recordings showed that 8 subjects (4 male, 4 female) reached at least stage 2 sleep, with three of them reaching slow wave sleep. Three subjects were not able to fall asleep. During all sleep stages, BOLD (blood oxygenation level dependent) signal increases in the auditory cortex were abolished or markedly reduced. In contrast, a negative BOLD response was observed during sleep stage 2 most consistently located in the visual cortex, precuneus and neughbouring the auditory cortex. Additional negative responses were variably seen in the anterior and posterior cingulum and preforntal cortices. No stimulus effect emerged on a significance level. Comparison between the different stimulus types was hampered by the high intrasubject variability.

Conclusions: The data revealed a negative BOLD signal responses within sensory and non sensory cortical areas in NREM sleep, which was shown to be independent of the type of acoustic stimulation including meaningful or meaningless simple or complex stimuli. This finding excludes a major effect of stimulus properties and makes processing of the informational content of the stimulus type an unlikely source of the observed negative BOLD signal.

0133.B

Gender Differences In Sleep Architecture In Healthy Young Adults

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Introduction: The sleep literature on gender differences shows controversies, part of which can be explained by methodological issues. The matter of how early such differences appear is one notable issue. In the present study, young (18-25 y.o.) adults were investigated and efforts were devoted to control for confounding variables.

Methods: Twenty-nine young right-handed healthy participants (15 women, age: 21.4± 1.7 years, range = 19 to 25; 14 men, age: 22.0 ± 2.0 years, range = 18 to 26) were recruited through public announcement. Selection interviews excluded candidates with personal or familial (first-degree) history of psychiatric or neurologic disorders, alcohol, medication, caffeine, extreme chronotypes, sleep disorders, and napping. Participants were asked to keep a regular sleep-wake schedules for two weeks before coming to the laboratory and filled an agenda during that period. Participants spent two consecutive nights in a sleep laboratory. Night 1 served as an adaptation night and further screening of sleep disorders. Data was collected during night 2. Sleep stages were determined using 20-second epochs according to Rechtschaffen & Kales, 1968. The following sleep variables were compared using t-tests (level of significance = .05): total sleep time (TST); latency to sleep onset and sleep stages; duration (minutes) and proportion (% of TST) of sleep stages (1, 2, SWS, REM) and wakefulness after sleep onset (total and thirds of night); number of REM sleep fragments; number of stage shifts.

Results: Men showed the following statistically significant differences compared to women: less sleep time in the last third of the night, increased number of REM sleep fragments in the 3rd and 4th period. Notably, there were no statistically significant differences gender differences on slow-wave sleep variables.

Conclusions: These results indicate that young healthy adults show few but significant gender differences in sleep architecture. The fact that men showed decreased sleep time in the latter part of the night is congruent with previous studies in this age group. The finding of increased REM sleep fragments is congruent with increased duration of REM sleep periods reported by others in older participants. The absence of significant differences on SWS variables is compensated for by literature on sleep EEG delta activity in this age group. Overall, the present results suggest that some of the gender differences reported previously in sleep architecture of middle-aged and elderly adults are found in young adults of 18-25 years old.

0134.B

Suppression Of Fetal Movement During Maternal REM Sleep In Preeclampsia Is Reversed With Nasal CPAP

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Introduction: Preeclampsia occurs in 7% of human pregnancies. While hypertension is the most significant clinical sign found in preeclampsia, the reversal of the normal circadian blood pressure rhythm is also commonly reported. We have recently reported that sleep is specifically responsible for episodes of marked hypertension in preeclampsia, and this is reversed with the use of nocturnal nasal CPAP treatment, which limits maternal partial upper airway obstruction induced by sleep. Preeclampsia is the predominant cause of fetal morbidity and mortality. We therefore aimed to investigate fetal well-being during maternal sleep by assessing fetal movements during maternal polysomnography.

Methods: We performed full overnight polysomnography (PSG) on 10 normal pregnant women at a mean gestational age of 32 $\pm$ 1.2 weeks, and 10 women with severe preeclampsia at a mean gestational age of 33 $\pm$ 1.1 weeks ($p = 0.93$ compared with normal subjects). We placed 4 specially designed piezo electric sensors on the maternal abdomen, one placed in each quadrant of the uterus, in order to record fetal body movements. These signals were amplified and recorded simultaneously with maternal PSG onto the Compumedics S-series recording system. Maternal sleep was scored according to standard criteria, and the number of fetal movements during maternal sleep were counted by two scorers. These studies were repeated in 2 of the preeclamptic subjects during maternal treatment with nocturnal nasal CPAP.

Results: Amounts of both non-rapid eye movement (NREM) sleep (273 $\pm$ 15.3 min and 273 $\pm$ 16 min, in control and preeclamptic subjects, respectively, $p = 0.97$) and rapid eye movement (REM) sleep (70 $\pm$ 6.2 min and 53 $\pm$ 7.7 min in control and preeclamptic subjects, respectively, $p = 0.11$) were similar between control and preeclamptic subjects. However, while the number of fetal movements per hour of sleep was similar between the groups in NREM sleep (107 $\pm$ 12 in control subjects and 83 $\pm$ 18 in preeclamptic subjects, $p = 0.30$), there was a marked suppression of fetal movements in preeclamptic subjects during REM sleep (140 $\pm$ 15 per hour and 37 $\pm$ 5 per hour, in control and preeclamptic subjects, respectively, $p < 0.001$). In the two subjects who were subsequently treated with nocturnal nasal CPAP, there was a marked increase in the number of movements during sleep (from 249 $\pm$ 34 per hour of sleep during the non-treatment study to 455 $\pm$ 55 per hour of sleep during the treatment study).

Conclusions: The number of fetal movements during maternal sleep is markedly suppressed specifically during maternal REM sleep in women with preeclampsia. This suppression is reversed with maternal nocturnal nasal CPAP treatment. The reduction in fetal movements may reflect severe maternal peripheral vasoconstriction induced by snoring and partial upper airway obstruction, which thereby limits placental blood flow. Nasal CPAP reduces maternal upper airway obstruction, thereby limiting peripheral vasoconstriction and increasing placental blood flow.

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0135.B

Reduced Cardiac Output During Maternal Sleep In Preeclampsia Is Associated With Intrauterine Growth Restriction

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Introduction: Preeclampsia is a disease specific to humans and occurs in approximately 7% of all pregnancies. Intrauterine growth restriction (IUGR) occurs commonly in preeclampsia. Recent studies have suggested that there is a specific association between IUGR and decreased cardiac output (CO) in preeclampsia. Sleep in preeclampsia is associated with partial airflow limitation and resultant marked hypertension, and this is reversed with the use of nocturnal nasal continuous positive airway pressure (CPAP) treatment. While hypertension is one of the clinical signs of preeclampsia, other hemodynamic changes are associated with this disease including marked peripheral vasoconstriction, reduced plasma volume and reduced cardiac output. We therefore aimed to investigate the impact of maternal sleep on these other hemodynamic parameters.
Methods: We studied 24 women with severe preeclampsia and mean gestational age of 33 $\pm$ 4 wk, and 15 control pregnant subjects with a mean gestational age of 32 $\pm$ 2 wk p = 0.49 compared with preeclamptic subjects). We performed full polysomnography (PSG) with beat-to-beat blood pressure recording. From the blood pressure waveform, stroke volume (SV), heart rate (HR), CO, total peripheral resistance (TPR) and ejection duration were calculated utilising customised software (Beatscope). In 12 of the 24 preeclamptic subjects, this study was repeated on a subsequent night while subjects were treated with nasal continuous positive airway pressure (CPAP).
Results: Cardiac output did not differ between control and preeclamptic subjects during wakefulness (8.0 $\pm$ 0.2 l/min and 7.7 $\pm$ 0.3 l/min in control and preeclamptic subjects, respectively, p = 0.43). There was a small reduction in cardiac output during sleep in control subjects. In contrast, there was a marked reduction in cardiac output in preeclamptic subjects (7.7 $\pm$ 0.4 l/min and 5.7 $\pm$ 0.3 l/min in control and preeclamptic subjects, respectively, p < 0.001). Total peripheral resistance was markedly elevated in preeclamptic subjects during wakefulness (830 $\pm$ 40 dyne.sec.cm\super-5\/ and 1080 $\pm$ 50 dyne.sec.cm\super-5\/, p = 0.001), and while this was reduced during sleep in control subjects (790 $\pm$ 42 dyne.sec.cm\super-5\/) it was further elevated during sleep in preeclamptic subjects (1570 $\pm$ 108 dyne.sec.cm\super-5\/, p < 0.001 compared with control subjects). When preeclamptic subjects were treated with CPAP, reductions in cardiac output during sleep were minimised (7.2 } $\pm$ 0.4 l/min, p = 0.012 compared with untreated preeclamptic subjects during sleep), while there was a reduction in TPR (1030 $\pm$ 57 dyne.sec.cm\super-5\/, p = 0.02 compared with untreated preeclamptic subjects during sleep). Cardiac output during sleep was highly correlated with fetal birth weight (r = 0.79, p < 0.001).
Conclusions: Maternal cardiac output decreases markedly during sleep in preeclampsia and is associated with fetal growth restriction. Nasal CPAP prevents these sleep-induced hemodynamic changes in preeclampsia and could potentially be utilized to reduce the problem of fetal growth restriction.

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0136.B

Effects Of Continuous 60 Hz Magnetic Fields On Melatonin And Sleep In The Rat

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Introduction: This project was designed to examine the effects of long-term electromagnetic fields on the production of melatonin and the subsequent sleep structure of rats. Electromagnetic fields (EMF) occur around any wire conducting electricity, from everyday appliances as hair dryers and toasters to large overhead transmission lines. All people encounter EMF every day of their lives. There are different types of EMF. One of the most famous examples is visible light. The form of EMF discussed here is considered extremely low frequency EMF, such as that described above emitting from common appliances and electrical wires. Electricity used in the US cycles 60 times a second (60 Hz). This frequency has been deemed safe by chemists and physicists, due to the very small amounts of radiation produced. However, biologists and experimental psychologists have uncovered a variety of possible health related ramifications due to long-term exposure. Scientific investigations have found that 60 Hz EMF may have direct or indirect effects on the pineal gland production of melatonin. For example, melatonin production decreased in rats and humans after exposure to EMF. Melatonin is a hormone produced in the pineal gland that has well-established effects on circadian timing of sleep in most animals.
Methods: To investigate these findings further, we exposed 9 male Sprague-Dawley rats to a 1000 milligauss magnetic field and 9 sham exposed for one month. Electrodes for electorphysiological recording of sleep were implanted according to standard procedures. Urine was collected for the final 3 days of the exposure period for analysis of 6-sulphatoxymelatonin.. When exposure was completed and urine collected, sleep was analyzed for 24 hours. Independent t-tests were performed to analyze differences in melatonin between the exposed and sham exposed animals. Total sleep time during the dark and during the light, low-voltage sleep, high voltage sleep, and paradoxical sleep were all analyzed by Mann-Whitney U non-parametric test. Independent t-tests were performed to analyze differences in melatonin between EMF exposed and sham exposed groups.
Results: Data indicated that melatonin production was significantly increased increased (t=1.75, p=.10 [two-tailed] in the exposed animals as compared to the sham exposed.. Paradoxical sleep was slightly decreased in the exposed animals (U=24.5, p=.18). Sleep analysis revealed no other significant changes in the sleep structure of EMF exposed animals as compared to the sham-exposed animals.
Conclusions: While our results support the notion that pineal gland melatonin production can be altered by power frequency electromagnetic fields, this effects had minimal effects on sleep stages. Further study, using different parameters of EMF stimulaltion in relation to melatonin and sleep, is warranted.

0137.B

Disappearance of Sleep Inertia is associated with Distal Vasoconstriction

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Introduction: Even though alertness should be highest at the end of sleep, there is always sleep inertia upon awakening, which usually takes about one hour to dissipate. There is no known physiological correlate

of this sleepiness. We have previously shown that a rise in sleepiness is associated with induction of vasodilatation and body heat loss, and thus it might be predicted that a fall in sleepiness is associated with the converse thermoregulatory mechanisms. An estimate of body heat loss can be derived from the distal-proximal skin temperature gradient and core body temperature decline.

Methods: This analysis used data from healthy subjects (8 men and 8 women) studied 4 times over 4 weeks, following an afternoon nap from 16-18h. Core body temperature (CBT), distal (DIST) and proximal (PROX) skin temperatures were continuously registered in a constant routine protocol (supine position, small isocaloric meals, ambient light <8 lux during wake, 0 lux during sleep, constant temperature 23°C). The distal-proximal skin temperature gradient (DPG) was used as an estimate of vasodilatation and body heat loss. Subjective ratings of sleepiness were assessed at 30 min intervals using the Karolinska Sleepiness Scale (KSS). Statistical analysis of each time course (10min bins) was calculated with ANOVA for repeated measures. The intra-subject relationship between the time course of DIST, PROX, DPG, CBT and KSS was analyzed by multiple regression analysis, whereby the inter-subject differences were taken into account by dummy coding. The time course of mean DPG and KSS values was fitted to an exponential function.

Results: Immediately after beginning the nap, DIST and PROX increased rapidly, whereas CBT declined but slowly. PROX peaked 50 min after lights off, DIST and DPG at the end of the 2-h nap, and CBT reached a minimum 30 min after lights on. Sleepiness ratings were highest in the first assessment 1 min after lights on and reached lowest values after 60 min. DIST and DPG also declined, attaining minimum values 60 min after lights on. PROX declined after the maximum within the nap and reached a minimum 40 min after lights on. Both the DPG and KSS decline after lights on could be fitted to an exponential cooling-out function with similar time constants ($0.29h \pm 0.05h$ vs. $0.33 \pm 0.05h$). The intra-individual time course of DPG after lights on was significantly correlated with KSS ($r=0.49$, $p<0.0001$, N=16 subjects, 320 time points), whereas CBT was not.

Conclusions: The intra-subject correlation analysis indicates a close association between subjective ratings of sleepiness and distal vasodilatation after lights on. Sleep inertia on waking showed a similar rate of dissipation as the cooling-out rate of the extremities, which had been warmed up by redistribution during the dark period. Thus, as the readiness to fall asleep is correlated with distal vasodilatation, so is the waking-up process (or disappearance of sleep inertia) correlated with distal vasoconstriction.

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0138.B

Serotonergic Antidepressants Increase Oculomotor Activity During Both Wake and Non-REM Sleep

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Introduction: Fluoxetine produces excess eye movements (EMs) during all stages of Non-REM, and possibly, REM sleep. This effect may be correlated with fluoxetine dose, and increasing doses may be associated with EM intrusion into deeper stages of Non-REM sleep. There have no systematic investigations of the effects of other serotonergic antidepressants on EMs in Non-REM sleep. It has also not been determined whether EMs during wake are modified by this class of medications.

Methods: All individuals (N=42; flouxetine=15, citalopram=8, venlafaxine=8, paroxetine=6, sertraline=5) on a serotonergic antidepressant referred for polysomnographic evaluation over a three month period were included. Consecutive individuals (N=53) during the same time period who were not on any antidepressant were used as controls. Subjects had to have full-night recordings without CPAP. Eye movements were automatically detected by Alice 3 (Respironics) software, and were characterized as rapid if the slope between the maximum and the beginning/or end was greater than 366 microV/sec, or if within the movement there was a slope greater than 219 microV/sec. Otherwise, EMs were classified as slow. Slow and rapid EM densities were computed for each sleep stage, and for wake, by dividing the total number of EMs in each sleep stage by the number of minutes spent in that stage. Age, gender, sleep architecture, and Apnea/Hypopnea indices were recorded as potential confounding variables.

Results: Eye movements were substantially and significantly increased during both wake and all stages of Non-REM sleep in individuals taking serotonergic antidepressants. Mean slow EM indices (SD) in the SSRI group were: 8.1 (4.6), 6.2 (4.3), 1.9 (2.7), 1.0 (1.3), 1.2 (2.0) and 3.5 (1.7) in wake, Stages I through IV, and REM respectively. Indices for the non-SSRI group were: 3.2 (2.2), 2.6 (2.5), 0.4 (0.5), 0.3 (0.5), 0.3 (0.5) and 2.7 (1.3). All comparisons between the SSRI and non-SSRI group were significant at $p < 0.001$ using two-tailed t-tests. Elevations in EMs were observed for all individual serotonergic antidepressants. Statistical comparisons for rapid EMs were the same as slow EMs for Non-REM and wake, though not as statistically robust for Stages II and IV, where $p<0.01$. No statistical differences were observed between the two groups for rapid EMs in REM. Correlations for slow EM indices between wake and Non-REM stages were high ($r>0.6$), as were correlations between slow EM and rapid EM indices within sleep stages. There were trends for signficiant correlations between eye movement indices and both apnea/hypopnea index ($r=0.19$, $p=0.07$) and sleep efficiency ($r=-0.19$; $p=0.06$) for Stage II only; all other stage-related correlations for these potential confounders were not significant. No effects of gender or age on slow or rapid EMs were observed .

Conclusions: We confirm and extend previous findings that not only fluoxetine, but all serotonergic antidepressants, increase the density of eye movements during Non-REM sleep. In addition, we found that such eye movements were similarly increased during wake. These data were true for eye movements characterized as rapid and slow. It is possible that such eye movements are related to confounding variables, such as microarousals, though common causes of microarousals (eg obstructive respiratory events) correlated only weakly, and only in Stage II, with eye movement indices. It is also possible that depression itself is associated with elevations in eye movements during wake and sleep. The functional significance of increased eye movements is unclear. It is not known whether such eye movements are a consequence, or potentially, a cause, of the sleep disruption and/or increased vividness of dreams seen with such agents.

0139.B

Sleep In Rats Born From Chronically Mild Stressed Mothers

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Introduction: A healthy, uneventful pregnancy is an essential prerequisite for optimal fetal development as well as for adapted, healthy offspring. Animal studies have repeatedly shown that the fetus is sensitive to perturbations occurring during perinatal period including environmental, nutritional, social or pharmacological factors. Actually, rats born from females that were stressed during pregnancy are characterized by physiological, neuroendocrine and/or cognitive deficits at the adult age. We have undertaken a series of studies using chronic mild stress, administered during the whole perinatal period and recorded the sleep of offspring at the adult age.

Methods: Rats were mated in our facilities. Control pregnant females were housed in standard conditions. From day 1 of pregnancy, stressed pregnant females were housed close to a kernel where frequent, unpredictable and unavoidable barking occurred (average noise level: 62.5 dB; range: 50 to 75dB), a condition known to be stressful. Treatment lasted throughout the whole pregnancy up to postnatal day 15. Fourteen

adults Long-Evans rats (8 from controls mothers (C), 6 from stressed mothers (S)) were selected for sleep recording. Following surgery and habituation to the recording equipment, baseline sleep was record for 24 hours; we now report only on the first four hours of the light period (subjective night). Statistical comparison were made using Mann-Whitney U tests.

Results: Compared to controls, S rats showed the following significant differences: increased time spent in wake ($p<.005$), increased number of awakenings ($p<.01$), decreased sleep efficiency ($p<.005$), and lower percentage of deep slow wave sleep ($p<.05$). Percentage of REM sleep was similar in the two groups.

Conclusions: At the adult age, rats born from mothers submitted to chronic mild stress during perinatal period show sleep disorders comparable to what is found in the literature on directly stressed animals. Two possibilities can explain the present results: 1) chronic mild stress induces impairments in maternal care, which in turn could induce lasting sleep disorders in pups; 2) chronic mild stress during pregnancy interferes with the normal development of the brain of the fetus. Interestingly, rats born from mothers with low occurrence of Licking/grooming and arched-back nursing, a model of altered reactivity to stress, do not present spontaneous sleep alteration (see Gaudreau et al., this meeting). We conclude that stress during pregnancy interferes with brain development and induces lasting alterations of sleep in offspring.

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0140.B

Actions Of Both Orexin A And Orexin B In The Myenteric Plexus Of The Guinea-Pig Small Intestine

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Introduction: Orexin A and orexin B (ORX A and ORX B) are known to regulate sleeping as well as feeding and energy homeostasis by their central and possibly peripheral actions. Recently, a subset of enteric neurons and gut endocrine cells are reported to display orexin-like and orexin receptor-like immunoreactivity. Since the myenteric plexus is mainly involved in the control of gut motility, electrophysiological observations were made to examine actions of orexins on neuronal properties and synaptic transmission in the myenteric plexus.

Methods: The myenteric plexus-longitudinal muscle preparations were made from the isolated ileum of the guinea-pig after an 18 hours fasting period. The preparations were placed in a recording chamber and superfused with a modified Krebs solution at about 36oC, gassed with 95%O2 and 5%CO2. Intracellular recordings were made from myenteric neurons using sharp glass capillary microelectrodes filled with 2M KCl by means of a conventional preamplifier. Myenteric neurons were classified into two types (S/Type 1 and AH/Type 2) according to criteria proposed by Nishi & North (1973) and Hirst et al (1974). Synaptic responses were evoked by focal electrical stimulation to the surface of myenteric ganglia and nerve strands connecting the ganglia. Orexins were applied by superfusion at concentrations from 10 nM to 1,000 nM.

Results: Both orexins caused membrane depolarizations in a proportion of S and AH neurons in the presence (control) and absence of extracellular Ca2+, and the depolarizations were associated with an increase in input neuronal resistance, sometimes eliciting action potentials. The responses induced by ORX A were usually larger than those by ORX B at the same concentration. Indeed, the lowest concentration for depolarizing action of the former was 30 nM and that of the latter was 100 nM, respectively. Slow after-hyperpolarizations characteristic of AH neurons could be observed in the presence of orexins at 100 nM. Furthermore, both orexins at concentrations higher than 100 nM often augmented cholinergic fast EPSPs recorded from S neurons. When the orexin-induced depolarization and augmentation of the fast EPSPs were simultaneously observed, the augmentation was confirmed by nullifying the orexin-induced depolarization by the manual clamp method. Orexins did not affect the postsynaptic sensitivity to ACh mediating the fast EPSPs.

Conclusions: Actions of ORX A and ORX B (both at 30-1,000nM) in the myenteric plexus of the guinea-pig ileum were investigated in vitro with intracellular electorphysiolgical methods. Both orexins caused membrane depolarizations associated with an increase in input neuronal resistance in a subset of myenteric neurons via their direct action, and also facilitated cholinergic ganglionic transmission possibly by increasing presynaptic release of ACh. It is concluded that orexins can modulate intestinal motility by acting on the activity of myenteric neurons.

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0141.B

Pattern of Paradoxical Sleep Occurrence After an Acute Restrain Stress

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Introduction: In various species, including human, PS occurs in the form of episodes separated by long intervals (single PS episodes, SIPSEs) and in the form separated by short intervals (sequential PS episodes, SEPSEs). In the rat, the pattern of PS occurrence can be profoundly altered when the needs for thermoregulation are high. Thus, SEPSEs almost disappear in rats exposed to low ambient temperature (Ta) which induces sleep deprivation. At the inverse, SEPSEs reappear during the PS rebound observed in the recovery period. To date, it is not known how a PS rebound can be temporally reorganized in a non sleep deprived rat living under unmanipulated environmental (standard) conditions. This issue is presently investigated by examining the temporal organization of the PS rebound occurring after an acute restrain stress.

Methods: Eight adult male Sprague-Dawley rats were indivually caged in a climatic chamber in which the photoperiod (12h:12h light-dark cycle, light off 18:00) and the Ta ($24 \pm 0.5°C$) was regulated. They were implanted under total anaesthesia with EEG and EMG electrodes. The recovery period lasted two weeks. Sleep was polygraphically studied in control (C, no stress) and after a 90 min restrain (rat placed in plastic tube) stress (S) starting at light off. 23h recordings (beginning at light off) were performed in C and S conditions. PS was visually scored according classic criteria and four parameters were assessed : (1) number ; and (2) duration of PS episodes ; (3) the total amount of PS ; (4) the interval from the end of one to the beginning of the next (PS interval). The criteria of this scoring followed the rules extensively validated by Amici et al., (1994). Thus, SIPSE and SEPSE were respectively separated by intervals < and > 3 min. Comparisons between C and S conditions were tested by Student paired-t test.

Results: As expected, a significant ($p<0.05$) PS increase (+53%), confined to the nocturnal period, was found after an acute restrain stress. This increase began after 21:00 and lasted until the end of the night. From 21 :00 to 06 :00, PS was augmented by 79% ($p<0.001$). During this 9 hours period, the total duration of SIPSE was increased by 40% ($p<0.05$). This increase was more obvious for SEPSEs (+300%, $p<0.05$%). Interestingly, both increases of the total durations of SIPSEs and SEPSEs were mainly due an increase of episode number ($p<0.05$).

Conclusions: After an acute restrain stress, the increase of PS was actually associated with an increase of SEPSEs. This result corroborates the fact that the occurrence of PS in clusters of sequential episodes would be a relevant mechanism to increase the amount of PS. Since homeostatic regulations are depressed during PS, this adaptative process would be of paramount importance.

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0142.B

Different Dynamics Of Heart Rhythm And Arterial Pressure Evoked Responses To Acoustic Stimulation During Sleep

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Introduction: Changes in cardiovascular regulation, as well as in responses to different stimuli, occur during the wake-sleep cycle (W, Wake; NREMS and REMS, non-REM and REM sleep, respectively). Heart Period (HP) and Mean Arterial blood Pressure (MAP) undergo spontaneous fluctuations, which are also affected by the wake-sleep state, as well as other factors, e.g. respiration. MAP fluctuations, in their turn, influence HP through the baroreflex loop. The aim of this work was to analyze the dynamics of integrated cardiovascular regulation during the wake-sleep cycle by means of "impulse" acoustic stimuli.

Methods: Six male Sprague-Dawley rats (250-300g) under general anesthesia were instrumented with EEG and EMG electrodes and an arterial catheter for blood pressure measurement and withdrawal of blood samples. Acoustic stimuli (50 ms, 90 dB, 1000 Hz) were delivered through a computerized system during W, NREMS and REMS. Epochs starting 30 s before and ending 30 s after acoustic stimulation were considered, the time origin being placed at the occurrence of acoustic stimulus. In each interval, the following variables were evaluated: a) the correlation coefficient of HP vs MAP fluctuations (rHM), taken as an index of peripheral vs central balance in HP control: in fact, prevailing fluctuations in peripheral resistance and MAP establish a positive HP vs MAP correlation, while prevailing parallel changes in centrally driven influences to the heart and vessels determine a negative HP vs MAP correlation; b) HP and MAP evoked responses to acoustic stimulation; c) the sympathovagal index (LFHP/HFHP).

Results: In all wake-sleep states, following acoustic stimulation rHM increased, in algebraic sense, with respect to baseline (W: 0.247±0.039 vs 0.078±0.034; NREMS: 0.412±0.022 vs 0.253±0.020; REMS:-0.0253±0.040 vs -0.160±0.031; $p<0.001$, $p<0.001$ and $p<0.01$, respectively). Evoked responses in NREMS consisted of an early increase in MAP and HP, followed by a larger decrease in MAP and HP and the return to control values. When MAP started returning to baseline, HP continued dropping and returned to baseline with a delay significantly different from zero (1.95±0.53s, $p<0.001$) and also different among states ($p<0.001$). After acoustic stimulation, LFHP/HFHP increased with respect to baseline in NREMS (4.88±0.41 vs 2.59±0.20, $p<0.001$) and decreased in W (4.19±0.51, $p<0.05$).

Conclusions: Acoustic stimulation increases the contribution of baroreflex drive to HP control. The main cardiovascular response to acoustic stimulation occurs at the level of peripheral resistance: an early rise in peripheral resistance, causing a MAP increase, baroreflexly determines the initial bradicardia; the following drop in peripheral resistance and MAP determines a significant tachycardia. The increase in LFHP/HFHP following acoustic stimulation suggests a rise in sympathetic drive to the heart. The delay in HP return to baseline is not baroreflex in origin, but on the contrary reflects a non-linear HP response to baroreflex demand.

0143.B

Arousal Frequency In Non-patients Is Related to Changes in Lipid Metabolism and Increased Cortisol Levels

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Introduction: Experimentally reduced sleep duration, sleep apnea and insomnia are associated with increased lipid levels, insulin intolerance, increased cortisol and other changes of potential long term impact on health. The present study attempted to study such changes in non-patient "normals" differing in the number of arousals during sleep.

Methods: A sample of 24 individuals (half were male), in an IT company were recruited based on high (>2.75) and low mean scores (<1.5) on a revised Melamed Burnout Questionnaire (min=1, max=4). The subjects were recorded for a two-week period using daily ratings of sleep (1=poor -5 good sleep), actigraphy, polysomnography (EEG) at home, ambulatory blood pressure recordings (24h), and repeated saliva samples (for analysis of cortisol), and a one morning blood sample was obtained the day after EEG. Based on the EEG the participants were divided at the medium (8arousals/h) into groups with 8h many (> 8/h) and few (< 8/h). The arousals were scored according to the international classification of sleep disorders (American Sleep Disorders Association), and sleep was scored conventionally. The results were analysed using a one-factor ANOVA with arousal frequency as factor.

Results: The results showed that the group with a high frequency of arousals had more awakenings during sleep (8.6 ± 1 vs.5.2 ± 7/hr, $p<.05$), higher sleepiness ($3.6\pm.2$ vs $4.2\pm.1$; $p<.01$) and more difficulties awakening ($2.6\pm.3$ vs $3.7\pm.2$; $p<.05$). The group with more arousals showed an increased: diastolic blood pressure (82 ± 1 vs 73 ± 3 mmHg: $p<.05$), heart rate (82 ± 3 vs. 70 ± 2 beats/min; $p<.05$), lipids (LDL; $3.3\pm.2$ vs$2.6\pm.3$ nmol/l; $p<.05$) and cortisol levels in blood (573 ± 25 vs 395 ± 19 mmol/l; <.01) and saliva ($17.1\pm.2$ vs. $10.0\pm.1$ nmol/l; $p<.01$). Stepwise multiple regression ananlyses indicated that the number of arosals was the main predictor of each of the metabolic parameters. The best predictors of arousals was tension (42% of variance explained), wheras burnout, fatigue, depression did not enter the regression.

Conclusions: The results suggest that frequent arousals during sleep in non-patients are associated with increased levels of metabolic parameters that may be significant in long-term health.

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0144.B

Cerebral Circulation During REM Sleep: A Major Regulatory Role For Nitric Oxide

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Introduction: Nitric Oxide (NO) is the major determinant of the cerebral blood flow (CBF) differences that exist between sleep-wake states, with its vasodilating action most evident during REM sleep when CBF substantially exceeds that in non-REM sleep and also that in wakefulness. While NO tonically elevates CBF during REM, further large phasic increases of CBF occur during the transient blood pressure surges that characterize this sleep state. This study addressed the hypothesis that NO does have an important vasodilating role also in the phasic circulatory disturbances of REM sleep.

Methods: Newborn lambs (N = 6) were anesthetised and instrumented with electrodes for EEG, EMG and EOG recordings, and a ultrasonic flow probe positioned around the superior sagittal sinus to measure CBF. Non-occlusive catheters were inserted into the carotid artery for blood pressure monitoring (Pca), into the jugular vein for drug infusion, and under the dura to record intracranial pressure (Pic). Studies began 72 hr after surgery: we examined dynamic changes of CBF, Pca, Pic, cerebral perfusion pressure (CPP = Pca - Pic) and cerebral vascular resistance (CVR = CPP/CBF) during spontaneous sleep-wake cycles. Data were recorded for 3 hr periods before (Control period) and during infusion of N-nitro-L-arginine (L-NNA), an inhibitor of NO synthase (L-NNA infusion period). L-NNA was given as a loading dose (25/mg/kg over 70 min), and then infused continuously during the 3 hr L-NNA infusion period (20 mg/kg/hr, total dose of 85 mg/kg). Using the onset of the Pca upswing as a zero time reference, we assembled coherent averages of

CPP, CBF, and CVR during spontaneous arterial pressure surges in Control (n = 17) and L-NNA infusion periods (n = 17), and for each variable we calculated changes from the -30s value.
Results: In the Control period an early decrease in CVR, beginning before the onset of blood pressure and CPP surges, begins the phasic CBF increase which is then further incremented as CPP rises. This pattern of cerebral circulatory events during the L-NNA infusion period is substantially altered in four critical aspects: 1) the early onset of the of the CVR decrease and CBF surge is abolished; 2) the extent of the CBF surge is markedly reduced; 3) the CPP elevation is significantly prolonged; 4) there is a late and prolonged increase in CVR.
Conclusions: These experiments show that NO regulates levels of CVR and CBF during REM phasic events, and appears to be the primary vasoactive determinant of the characteristically high and variable CBF of this stage of sleep. We speculate that both endothelial and neuronal NO synthase may be important sources of vasoactive NO in the brain in sleep and that NOS dysfunction could augment the extent of arterial pressure disturbances of REM sleep while coincidentally impairing cerebral perfusion.

0145.B

Effects of Early Manipulations on Basal and Stress-Induced Alteration in Sleep

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Introduction: Manipulations of the mother-infant relationship alter the development of the litter. Early handled (EH) rats exhibit reduced stress response, whereas maternal separated (MS) ones present increased stress reactivity. Other important central nervous system alterations are also observed. The purpose of the present study was to evaluate baseline and stress-induced sleep patterns of EH and MS rats.
Methods: Throughout the whole study, animals were maintained in 12:00h light/dark cycle and had free access to food and water. Early handling consisted of daily removal (from day 2 to 14 of life) of the litter from the home-cage for 15 min. For maternal separation, litters were removed from the home-cage for 3 h in the same period of life as EH pups. When 3-month olds, rats were implanted with cortical and muscle electrodes for sleep recording and staging. After surgical recovery (at least one week), animals were adapted to the system (for at least 24h). Baseline recordings lasted 22h (from 9:00h to 07:00h of the next day). On the following day, animals were submitted to cold (4C) for 1h and again recorded for another 22h period. Sleep was analysed and classified as waking, slow wave sleep 1 (SWS1), slow wave sleep 2 (SWS2), preparadoxical sleep (PPS) and paradoxical sleep (PS). Sleep analysis was performed in the light (9:00h - 19:00h) and dark (19:00h - 07:00h) phases of the diurnal cycle and sleep was evaluated in 2h blocks. Statistical analysis was performed by the 3 way ANOVA for repeated measures (2 groups: EH, MS x 2 situations: Baseline, post-stress x 5 [light phase] or 6 [dark phase] blocks).
Results: In the light phase, sleep efficiency and time of PS where augmented in MS animals from 09:00h-11:00h than in EH rats in the same period. Number of spindles during PS was higher in MS than EH animals from 09:00h to 13:00h and number of PS episodes, from 13:00h to 15:00h.In the dark phase, there was a reduction of sleep efficiency, time spent SWS1, SWS2, PPS and PS from 21:00h to 23:00 and a subsequent increase from 23:00h to 01:00h during baseline recording. In response to stress, these time differences were abolished for both EH and MS rats.
Conclusions: Despite the physiological and behavioural differences described for EH and MS rats, the sleep pattern and especially after cold stress does not seem to be remarkably different between these groups.

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0146.B

Is Sleep-Onset REM Sleep An Exceptional Feature Of Sleep?

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Introduction: Sleep onset REM sleep (SOREMS) episodes are rarely observed in normal nocturnal sleep. Recently periods of low muscle tone in NREMS have been reported. The distribution of the latency to the first occurrence of episodes with low muscle tone in NREMS was bimodal with a first mode shortly after sleep onset and a second mode 40 minutes later. As low muscle tone is a prerequisite for scoring REMS, episodes with low muscle tone might represent a window for REMS. The aim of the present study was to investigate whether there might be a window for SOREMS.
Methods: We analysed the data of 16 healthy young men who slept four times at weekly intervals for 4 h at night (23-03 h) and 3 h in the subsequent morning (10-13 h). Between the sleep episodes the subjects remained in the laboratory under constant supervision. Polysomnographic recordings were performed and sleep stages were scored according to standard criteria. SOREMS episodes were defined as REMS episodes with a latency < 20 minutes. Episodes of low muscle tone at sleep onset were determined based on visual inspection of the EMG.
Results: The distribution of REMS latency was unimodal in night sleep and bimodal in morning sleep. Seven out of 16 subjects showed SOREMS episodes in all four morning sleep opportunities. A total of 40 SOREMS episodes were observed during morning sleep (mean duration 12.0 ± 2.3 min, SEM) and only one episode occurred at night. In the 24 morning sleep opportunities without SOREMS additional 14 episodes with low muscle tone at sleep onset were detected with a mean duration of 15.6 ± 5.7 min. In contrast, only 22 out of 63 nocturnal sleep episodes started with low muscle tone (mean duration 17.0 ± 4.4 min). Sleep propensity in the morning was reduced due to the preceding 4-h nocturnal sleep. episode. Simulations with the two-process model revealed a reduced level of S (sleep propensity) of 77.5 % at sleep onset in the morning compared to night sleep.
Conclusions: Nearly half of our healthy young subjects had a SOREMS episode in every morning sleep period. Only two subjects had not a single SOREMS episode and even they had one and two episodes with low muscle tone at sleep onset, respectively. Taken together, 84 % of the morning sleep episodes (SOREMS included) started with low muscle tone. In nighttime sleep this proportion was 36 %, which is much less than in morning sleep, but still considerable. We conclude that there is a window for SOREMS and that full expression may occur in the morning in combination with low NREMS pressure. Therefore, SOREMS episodes seem to be a normal feature of sleep that are observed under specific conditions.

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0147.B

Abnormal Sleep Responses to Light-Dark Transitions in Light-Reared Rats

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Introduction: Postnatal exposure to atypical lighting conditions causes anatomical and functional deficits in the image forming visual system. Little is known about how light affects the non image-forming visual system, a collection of subcortical retinorecipient nuclei that are involved in light-mediated behaviors, including sleep-wakefulness. Previous work from our laboratory has suggested that dark-rearing increas-

es the magnitude of the REM-sleep triggering response following lights off, but is not associated with other significant changes in sleep architecture in rats. In the present study, we characterize the sleep-wakefulness patterns of rats reared in continuous light (LL) or in a normal 12:12 light-dark (LD) cycle.
Methods: Albino rats (F344) were reared in LD or LL from before birth until adulthood. At postnatal week 8, four male rats from each condition were implanted with EEG and EMG electrodes, and baseline sleep patterns were recorded in a 12:12 LD cycle and in a shorter 3:3 LD cycle at two light intensities each (65-0 and 500-0 lux). An automated scoring system calculated mean rectified amplitudes for EEG, EMG, and midline ("theta") EEG recording electrodes. 30 second epochs were classified using the PASS algorithm as waking, REM, or non-REM sleep.
Results: Electrophysiological recordings from control and light-reared rats suggest that light-rearing significantly attenuates the magnitude of the REM-sleep triggering response following lights off, but does not alter mean daily percentages of wake, sleep, and non-REM sleep. In a 12:12 LD cycle at 65-0 lux, both groups demonstrated strong nocturnal patterns. Both groups spent more time awake in the dark than in the light (30.6 % more time awake for LD, and 26.1% for LL). This effect was magnified at the 500 lux level (36% and 34% more time awake, respectively). In the shortened 3:3 LD cycle, both groups spent more time awake during the dark phases than the light phases (19.9% more time for LD, and 10.7% more time for LL at 65-0); this effect was magnified at the 500 lux level (26% more time awake during dark for LD and 20.9% more time for LL). In a 3:3 LD cycle, control rats spent significantly more time of total sleep in REM sleep during the dark phases than the light phases (9.1% more time at 65-0 and 12.6% more time at 500-0). In light-reared rats, this REM-sleep enhancement during lights-off was significantly attenuated (2.1% at 65-0 and 2.2% at 500-0).
Conclusions: These data suggest that rearing rats in continuous light does not cause significant changes in sleep architecture, but may compromise sleep-wakefulness responses to acute light-dark shifts. In contrast to dark-rearing, which exaggerates the REM-sleep triggering response to lights-off, light-rearing attenuates this behavior. A greater understanding of how early exposure to light affects the developing retina and retinofugal targets in the non image-forming visual system may provide insight into etiology of this disruption.

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0148.B

Evidence For Different Brain Reactivity To External Stimuli During Phasic And Tonic REM Sleep: A Simultaneous FMRI And EEG Study

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Introduction: Studies using functional magnetic resonance imaging (fMRI) have recently described changes of brain activity upon stimulation in NREM sleep. The changes of information processing especially in stage REM with intensified mental activity are still to be disclosed. Making use of the novel approach of combined EEG and fMRI investigations in sleep, the objective of the present study was to explore regional activation patterns upon acoustic stimulation in REM sleep.
Methods: Eleven subjects (6m/5f, mean age: 24.9y) underwent partial sleep deprivation two days prior to study night in order to enhance REM sleep probability. After positioning of the MR compatible EEG (frontal, central, parietal and occipital), EOG, EMG and ECG electrodes, fMRI sessions of up to 3 hours from 03:00 onwards were performed at 1.5T (GE Signa Echospeed) while continuously presenting scanner noise via headphones. For fMRI a multi-slice EPI sequence (7 slices, 5 mm thick, 96x96 matrix, resolution 2 mm, TE=60 ms, TR=3 s) parallel to the AC-PC line covering visual and auditory cortical areas was used. Additional acoustic stimuli were presented in a block design (3 on, 4 off periods of 30 sec each). Once unambiguous stage REM was established in the online polysomnography for at least one minute, scans were started. An offline artefact correction was applied to the EEG. FMRI data were analyzed using SPM99 and thresholded at $p<0.001$ uncorrected.
Results: REM sleep scans could be obtained in seven subjects. After EEG post-processing and sleep staging, scans with apparent arousals or intermittent sleep stage 2 during the 3.5 min block duration were discarded. This resulted in 14 scans. Within these, activation maps strongly differed between periods with REM scans containing mainly tonic REM sleep and those dominated by phasic activity. A deactivation in the thalamus was only seen in phasic REM scans, along with deactivation of large cortical areas. Using the activity in the thalamic region as regressor revealed strong connectivity patterns. No such correlations could be identified during NREM sleep or wakefulness. In contrast, task-dependent activation patterns in tonic REM sleep were often similar to wakefulness and show no thalamic deactivation.
Conclusions: This first fMRI study on information processing in stage REM shows a difference in brain reactivity between tonic and phasic REM sleep: Activation maps during tonic REM sleep resemble maps obtained during wakefulness. During phasic REM sleep, a negative BOLD response in cortical areas as shown previously in NREM sleep was obtained, and in addition a strong thalamic deactivation was obvious. We were able to identify a stable synchronization of thalamo-cortical networks that maybe specific to phasic REM sleep.

0149.B

Normal Sleep and Sleep Stage Patterns: Effects of Age, BMI and Gender

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Introduction: The purpose of this study was to establish the effects of age, BMI and gender on sleep and sleep stage patterns in a large random sample of the general public without sleep disordered breathing or sleep complaints.
Methods: Our analysis was based on a two-stage random sample of men and women. In the first phase, 16,583 men and women were interviewed ranging in age from 20-100 years. In the second phase of this study, 1,741 men and women who participated in the first phase were further evaluated in the sleep laboratory. From this sample we excluded subjects with sleep disorders that were assumed to have a possible effect on sleep or sleep stage patterns. Specifically, we excluded those with a complaint of excessive daytime sleepiness, insomnia and those with an A/HI³ 5. This resulted in a sample of 1,324 (609 men and 715 women). This polysomnographic evaluation consisted of a single night recording using a fixed protocol of eight hours. The sleep variables of interest in this study for sleep efficiency were percent sleep time (%ST) and sleep latency (SL). For sleep stage patterns the variables of interest were percent stage 1 (%S1), percent REM sleep (%REM) and percent slow wave sleep (%SW). These data were evaluated controlling for age and BMI using the General Linear Model and multiple regression.
Results: Sleep efficiency worsened with age in terms of both %ST ($P<0.001$) and SL ($P<0.001$). For sleep stage patterns %S1 increased ($P<0.001$) while %SW ($P<0.001$) and %REM ($P<0.001$) decreased with increasing age. Sleep efficiency was not associated with BMI (%ST [$P=0.74$] and SL [$P=0.63$]). However, increasing BMI was associated with increased %S1 ($P<0.001$), decreased %REM ($P<0.001$) but not with %SW ($P=0.64$). Women compared to men had significantly more %ST ($P=0.02$) while there were no significant differences for gender in terms of SL ($P=0.42$). Women compared to men had less %S1 ($P<0.001$), more %SW ($P<0.001$) and %REM ($P=0.01$).
Conclusions: This study is the first study to evaluate the effects of age,

BMI and gender on sleep in a random sample of adults without sleep disordered breathing or sleep complaints. Aging was associated with declining sleep efficiency, increasing %S1, and decreasing %SW and %REM. Obesity was associated with increased %S1 and decreased %REM. Women compared to men had better sleep efficiency, lower %S1, as well as higher amounts of %SW and %REM. This gender difference was not accounted for by sleep disordered breathing or other common sleep complaints. Finally, this gender difference could be at least partially associated with the increased longevity of women.

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0150.B

Slow Wave Activity Levels Are Correlated With Insulin Secretion In Healthy Young Adults

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Introduction: Sleep duration and quality have been shown to play an important role in metabolic and endocrine functions. Slow wave activity (SWA), the primary marker of sleep wake homeostasis, is the most accurate measure of sleep depth or "intensity". In the present study, we examined the relationship between the amount of SWA during sleep and glucose metabolism, in particular pancreatic beta cell responsiveness in healthy young adults.
Methods: : Data obtained from 10 men (mean age: 22 $\pm$ 1 years) were used in the present analysis. Each subject had a baseline (8-hour in bed) polygraphic sleep recording preceded by one adaptation night in the laboratory. All subjects had regular bedtime habits without sleep complaints. Sleep EEG was visually scored in 20-second epochs and spectrally analyzed in the delta frequency range (0.75-4.50 Hz) by fast Fourier transform (FFT) on consecutive artifact-free 4-sec epochs. The central EEG lead (Cz- A1) was selected for analysis. Power spectra of five consecutive 4-sec epochs were averaged and matched with the sleep scores. All night delta power spectra were then averaged in each subject to give mean absolute SWA in NREM (stages 1, 2, 3 and 4) sleep. Pancreatic beta cell responsiveness was measured in each subject by the amount of insulin secreted in response to a standard morning intravenous glucose tolerance test (ivGTT) after an overnight fast. Acute insulin response to glucose (AIRg) was derived from minimal model analysis of the ivGTT. Second phase insulin secretion was calculated as the total area under the curve of insulin profile between the 19\superthand 40\superthminutes of blood sampling (total AUC 19-40 min).
Results: Mean absolute SWA (mV\super2) in NREM sleep was positively correlated with both first phase insulin secretion quantified by the AIRg ($r = 0.83$, $p = 0.003$) and second phase insulin secretion defined as total AUC 19-40 min ($r = 0.70$, $p = 0.03$).
Conclusions: In healthy young adults, 50 to 70 % of individual variability in pancreatic beta cell response to intravenous glucose stimulation is predicted by the amount of SWA during a normal 8-hour baseline sleep period. This remarkable association suggests that individual differences in SWA may be a predictor of individual differences in diabetic risk, quantified by the "disposition index", calculated as the product of insulin sensitivity by AIRg. Thus, in young adults, our data suggest that the ability of pancreatic beta cells to compensate for various degrees of insulin resistance may be dependent on sleep quality. This interesting relationship could be mediated by sympatho-vagal balance, which is markedly affected by sleep intensity and modulates pancreatic beta cell function.

0151.B

Hypocapnia Reduces The Amount Of REM Sleep In Cats

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Introduction: Sleep disturbances at high altitude are common. Low partial pressures of oxygen (Os2s) at high altitudes cause hyperventilation which increases Os2s levels in the body. However, this hyperventilation simultaneously reduces arterial carbon dioxide (COs2s) levels. Thus, it is unclear whether sleep disruption at altitude is caused by hypoxia, hypocapnia or both. Our objective was to investigate the role of COs2s in sleep disruption at high altitudes.
Methods: Intact adult cats were recorded during: 1) normocapnic normoxia (breathing room air); 2) hypocapnic hypoxia (breathing 10% Os2s in Ns2s); 3) isocapnic hypoxia (breathing hypoxic gas with end tidal COs2s maintained at the normal NREM level); and 4) hypocapnic normoxia (mechanically hyperventilated with end tidal COs2s maintained by computer control at either 65, 75 or 85% of the normal NREM level. Recording sessions lasted approximately 3 hours. Treatment orders were assigned to correspond to a Latin Square design. Electroencephalographic data were recorded on paper and tape. Epochs of sleep and wakefulness were determined at 1.57 minute intervals. Statistical significance was determined using a repeated measures ANOVA with Bonferroni's post-test with an alpha level of 0.05.
Results: REM sleep was reduced in all conditions of hypocapnia. Hypocapnic hypoxia significantly increased REM sleep latency and reduced total amount of REM sleep by 80%. Decreased REM sleep was the result of significant reductions in both the duration and the number of REM sleep periods. In contrast, isocapnic hypoxia significantly reduced REM sleep by only 30% and did not alter REM sleep latency. Hypocapnic normoxia significantly reduced the duration and the number of REM sleep periods, total sleep, and sleep efficiency, and it significantly increased the amount of wakefulness. Therefore, hypocapnia whether caused secondarily by the response to hypoxia or directly by mechanical hyperventilation reduced the amount of REM sleep. Furthermore, the REM sleep reductions in both cases were a function of the extent of the hypocapnia and were similar at similar levels of hypocapnia.
Conclusions: Low levels of COs2s cause a significant reduction of REM sleep. We hypothesize that the alkalinization caused by low COs2s levels inhibits, by unknown mechanism(s), the initiation and maintenance of REM sleep.

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0152.B

Sleep Spindles and the First Night Effect

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Introduction: The detrimental effect in healthy participants of having to sleep for a first night in a laboratory is a well-known phenomenon. Sleep spindles are considered as a representing a sleep protective mechanism.

The aim of the present study was to verify whether sleep spindles are sensitive to the first-night effect (FNE).
Methods: Twelve right-handed healthy participants (6 men, 6 women, 25.0 ± 4.9 years) were recorded for two consecutive nights in a sleep laboratory. All were free from sleep disorders and from a personal or a familial (first-degree) history of psychiatric or neurologic disorders. Subjects were asked to keep a regular sleep-wake schedule for 14 days before coming to the laboratory. Napping was not allowed on days prior to recordings. Both nights were scored according to Rechtschaffen & Kales (1968). Bilateral prefrontal (Fp1, Fp2) and central (C3, C4) monopolar EEGs referred to linked ears were recorded. Sleep spindles were selected visually using the following criteria: duration between 0.5 and 2 seconds, frequency between 12 and 15 Hz. Data is expressed as means ± S.D. Sleep parameters and Stage 2 spindle density from night 1 and night 2 were compared using T-tests. Antero-posterior distribution of Stage 2 spindle density and the lateralization of Stage 2 spindle density were evaluated using a 2 (nights) X 2 (frontal electrodes, central electrodes) ANOVA.
Results: Sleep architecture showed a typical FNE (significantly longer sleep latency, increased awakening, decreased sleep, decreased SWS and REM sleep). Duration of stage 2 was not significantly affected. On the other hand Stage 2 spindle density was significantly decreased on night 1 relative to night 2 for Fp2 (141.2 ± 99.4; 185.41 ± 97.0; $p<.05$), C3 (210.1 ± 131.4; 323.9 ± 136.8; $p<.01$) and C4 (227.9 ± 108.5; 328.9 ± 118.8; $p<.01$) but not for Fp1 (154.0 ± 108.3; 190.3 ± 97.1; $p<.07$). There were no significant lateralization effects. The Anova showed that Fp density was lower than Central ($F=34.4$; $p<.01$) but this antero-posterior effect not sensitive to FNE ($F=3.2$; $p<.09$) and no interaction was observed ($F=3.5$; $p<.08$).
Conclusions: These results support the notion that sleep spindles are associated with a successful sleep protective mechanism. The fact that the antero-posterior effect (Frontal pole < Central) resists to FNE is noteworthy.

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0153.B

Influence Of Nialamid On Sleep-Wakefulness Cycle And Correction Of Side Effects Through The Regulation Of Brain Metabolism

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Introduction: Introduction: Brain energetic balance is significantly influenced by external impacts, which reflect in the CNS integrative activity. One of such influences represents the antidepressants' action, resulting elevation of the brain monoamines' level and reflecting in the brain integrative activity. This is manifested essentially in Sleep-Wakefulness Cycle (SWC) changes. Accompanying PS suppression is regarded as essential for depression therapy. However, in a majority of cases, there occurs a long-lasting PS elimination, which is not expedient, considering its biological importance. Consequently, the aim of present investigation was the multi-factorial analysis of antidepressants' impacts on the SWC and correction of the side effects of these drugs.
Methods: Methods: Experiments were carried in cats (n=5), with chronically implanted electrodes for SWC recording. Brain metabolism regulation with changes of the circulating glucose level has been chosen for correction. Nialamid (N), (5,10mg/kg) and Glucose (Gl), (200, 300mg/kg) were administered intraperitoneally.
Results: Results: N administration induced the total disorders of SWC phase's ultradian alternations. Within 1-1.5h the animals stayed in the waking state. Than dissociation processes developed and within 7 –8h during behavioral waking the EEG patterns of passive waking and light slow wave sleep (LSWS) was alternating. Deep slow wave sleep (DSWS) EEG pattern was initiated 9-10h since N administration. Dissociation between behavioral and EEG parameters of DSWS was retained within 24-26h with significant increase of DSWS mean duration. Correlation between behavioral and EEG patterns of DSWS would restore from 50-55h. The first PS occurred with 55-58h.latency. Normalization of SWC was continued within 90-100h. Despite the long-lasting deprivation of PS, its significant rebound during recovery was absent. However, the remarkable qualitative PS alterations: notable decrease of hippocampal theta rhythm, PGO-spikes, and REMs frequency were found. Thus, during the N action and in the recovery period significant suppression of both PS and the level of emotional tension were observed. Concomitant administration of Gl and N didn't induces significant changes in sleep onset and dissociation between behavioral and EEG parameters of LSWS and DSWS. Ultradian structure of SWC was maintained. PS latency equaled to 1-1,5h. However, the incidence and total volume of PS were significantly lower against the baseline. Increased indices of emotional tension were found within PS, though they were still attenuated against the baseline. Thus, simultaneous administration of Gl and N resulted in significant decrease of PSs incidence and these phases maintained a moderate level of emotional tension in difference of N separated action, when the emotional tension in PS was suppressed almost completely.
Conclusions: Conclusion: Brain metabolism regulation with changes of circulating Gl level corrects significantly the undesirable SWC disorders elicited by MAO inhibitor. This fact has a certain therapeutic implication in the antidepressant's administration.

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0154.B

Changes In The Antidiuretic Response To Osmotic Stimulation During REM Sleep

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Introduction: A view on REM sleep phylogenesis is that it would represent, in mammals, the result of a transition from the nervous organization of reptiles, which is related to the development of endothermy. This view is supported by the finding that REM sleep is characterized by an impairment of thermoregulation, induced by a more general impairment in the hypothalamic integration of autonomic activity. However, a possibility to cross the apparent phylogenetic border of REM sleep may be given by the study of a hypothalamic regulation that reptiles and other phyla share with mammals. With respect to this, we have studied the osmoregulatory control of water balance, which is sustained by the release of the antidiuretic hormone (ADH). To this end, the release of ADH induced by osmotic stimulation has been determined during REM sleep (REMS) and, as a control, during wakefulness (W).
Methods: Adult male albino rats were implanted under anesthesia with electrodes for EEG recording and a cannula was inserted in a lateral cerebral ventricle. By means of a micrometric pump, different animals received, during W and REMS, an intracerebroventricular (ICV) injection (2.5µl in 60s) of artificial cerebrospinal fluid (aCSF), which was either isotonic or made hypertonic by adding 0.5M NaCl. After 20s from the end of ICV administration, animals were sacrificed using a mobile guillotine and the trunk blood collected. The correct placement of the cannula was verified, following the sacrifice, by the ICV injection of 2.5µl of a methylene green solution. ADH was extracted from plasma by reverse phase chromatography; fractions were lyophilized and then immunoassayed using [125]I-ADH as a tracer.
Results: The results (mean±S.E.M., pg/ml) concern 16 experimental animals and 5 animals which were not injected. Since the number of cases was small, the significance of differences ($P<0.05$) was assessed

by means of a non parametric test (Mann-Whitney). The administration of isotonic aCSF did not significantly change plasma ADH content (W: 1.45±0.09, n=3; REMS: 2.39±0.39, n=3) with respect to non injected animals (2.78±0.37). Hypertonic aCSF significantly increased ADH concentration, with respect to the isotonic administration, during both W (58.22±12.49, n=4) and REMS (22.47±7.55, n=6); however, the concentration of ADH in W was significantly different from that in REMS.
Conclusions: The results of this study suggest that ADH regulation of water balance is active during REMS, if challenged, but at a lower level of response than during W. This result may help in extending the observation that in humans spontaneous ADH release is not related to any wake-sleep stage. Moreover, a reduction in sensitivity of a mechanism phylogenetically older than thermoregulation, may be tentatively taken as an indication that the impairment of hypothalamic integration observed in REMS may have some deeper roots in the evolutionary origin of mammals.

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0155.B

Influence Of Darkness On The Transition From NREM To REM Sleep

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Introduction: From a physiological view-point, the transition from NREM to REM sleep (NRT) is a critical moment since physiological regulation is shifting from an homeostatic to a non-homeostatic modality. When this shift does not occur the transition period is followed by either NREM sleep or, more often, by wakefulness. In the rat, this period lasts 30-60s and has been quantitatively characterized by an analysis of the EEG by Benington and Heller. They proposed a quantitative index (NIV), which appears to be positively related to the probability to enter REM sleep. On this basis, we have analyzed the NRT elicited by the delivery of a dark pulse (DPD), a stimulus which has been shown to induce REM sleep with a high percentage of success.
Methods: Twelve male Sprague-Dawley rats (250g), adapted to a 12h:12h Light-Dark cycle, were implanted under general anaesthesia with EEG electrodes and a thermistor for hypothalamic temperature recording. Animals underwent two 24-h experimental sessions, one for the baseline (BL) and the other (DPD) in which twenty DPs (3min light-off, each) were delivered during the first 6h of the L period. The EEG power density (PW) in the Delta (0.75-4.0Hz), Theta (5.5-9.0Hz), and Sigma (11.0-16.0Hz) bands (4s epochs)was measured and the NIV was calculated according to Benington and Heller's criteria [NIV: max(ThetaPW)*max(SigmaPW)*max(sqrt(d-DeltaPW))], but only for a fixed time (30s) before REM sleep onset. Moreover, in order to better emphasize the tonic aspects of the EEG pattern during NRT we have introduced a modified index [NIV2: average (ThetaPW)*average (SigmaPW)*max(sqrt(d-DeltaPW))]. Paired T test and repeated measure ANOVA were used for the statistics. Data are given as mean±SEM.
Results: For both NIV and NIV2 the data are referred to the respective average value in the 12-h Light period of BL, taken as 100. NRTs triggered by DPD were divided in two groups on the basis of REM sleep onset latency (Lat): i) Short-Lat, 30-60s; ii) Long-Lat, 60-90s. Results were compared with those of the first 6h of BL. Both NIV and NIV2 were significantly higher ($p<0.05$) in NRTs triggered by DPD with respect to BL (NIV: BL, 104.0±2.5; Short-Lat, 113.9±13.5; Long-Lat, 161.5±18.0; NIV2: BL, 105.4±2.1; Short-Lat, 117.1±10.8; Long-Lat, 141.6±10.6). The influence of darkness on NRTs was confirmed by the comparison of the average NIVs in the Light and Dark period of BL (NIV: Light, 100±0; Dark, 107.2±6.1; NIV2: Light, 100±0; Dark, 121.2±7.5). However, the difference was significant ($p<0.05$) only for NIV2.
Conclusions: The results of this study indicate that NIV is increased by DPD. This effect might be related to the high probability for a REMS episodes to occur following a DPD. However, the significant increase of NIV2 during the Dark period of BL would emphasize the presence of a more general effect of darkness on the NRT.

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0156.B

The 1st Sleep Cycle as a Whole Sleep Hologram (Sleep Matrix)

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Introduction: Holographic model of information storage and processing had been already used in neurophysiology to account for the functioning of afferent systems (Pribram, 1975) and right hemisphere (Zenkov, 1978). We propose the hypothesis that operating of 1st sleep cycle can be seen from the viewpoint of holographic model.
Methods: To test this hypothesis we have evaluated 30 routine (latencies periods and duration of sleep stages) and segmental (average duration of stage segment, number of segments, maximum duration of a segment) parameters of sleep structure in 32 healthy subjects, 44 insomnia patients (before and after the treatment) and 42 patients with stroke by means of regression and factor analysis. The study was carried out in two directions: 1. possibility of using the 1st cycle parameters for prediction of parameters of the rest of sleep (excluding 1st cycle) and 2.possibility of using the 1st cycle parameters for prediction of parameters of the total sleep (including 1st cycle).
Results: 1. 1st sleep cycle contains the information about parameters of the total sleep; 2. holographic function of 1st cycle is tolerant enough to the disturbing influences (insomnia, stroke) and it works even in conditions where severe cerebral pathology occurs; 3. parameters of 1st cycle can predict the similar ones of the total sleep; 4. there is a possibility of "cross" prediction of parameters of the total sleep using parameters of 1st cycle; 5. factor structure of 1st cycle and the total sleep are absolutely identical; 6. the 2nd and the following sleep cycles are necessary for tuning the main matrix of the 1st cycle for accommodation the sleep structure in accordance with current needs of an individual.
Conclusions: The results of our study let us to propose a novel view on sleep organization estimating the 1st sleep cycle as a whole sleep hologram (sleep matrix).

0157.B

Short-Term Regulation Of REM Sleep Occurrence In The Rat During Cold Exposure And In The Following Recovery Period

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Introduction: In the rat, REM sleep (REMS) occurrence appears to be regulated according to different time scales. Short-term regulatory aspects have been evidenced in animals kept under normal laboratory conditions. In fact, the duration of the interval between two consecutive REMS episodes (INT) appears to be directly related to the duration of the preceding REMS episode but does not show any relationship with that which follows. Long-term regulatory aspects have been evidenced by means of sleep deprivation studies. In particular, the exposure to a low ambient temperature (Ta) has been shown to be a powerful physiological tool to induce a REMS deprivation. The degree of the REMS loss is directly related to the thermal load and it is followed by a proportional REMS rebound when the animal is returned to normal laboratory Ta. The aim of this study has been to evaluate whether, in the rat, short-term regulation is influenced by long-term regulation during cold exposure and in the following recovery period.

Methods: Twenty-four male Sprague-Dawley rats (250g), acclimated to 23±0.5°C and to a 12h:12h LD-cycle were used. Animals were implanted under general anaesthesia with electrodes for EEG recording and with a thermistor for hypothalamic temperature recording. Following two days of baseline recording (BL) the animals were exposed for 24h to Tas ranging from +10°C to –10°C (E) and were subsequently returned for 24h to Ta 23°C (R).
Results: The analysis refers to data relative to the 12-h L periods and to INTs <21 min. REMS episode (REP) duration was defined as that of either single REPs (episodes separated by long INTs, >3min) or REMS clusters (sequence of episodes separated by short INTs, <3min). Long INTs were grouped in 2min classes. The relationship between the duration of the long INT (midpoint value for each of the nine 2min classes) and the average duration (pool of single REPs and REMS clusters) of either the previous (REP-PRE) or the following (REP-POST) episode has been studied in BL, E, and R. The Pearson correlation between INT and REP-PRE was statistically significant ($p<0.01$) in both BL ($r=0.873$) and R ($r=0.957$), but not in E ($r=0.213$). No significant correlation between INT and REP-POST was found in either BL ($r=0.130$), E ($r=-0.572$), or R ($r=0.087$).
Conclusions: The results of our analysis confirm that under normal laboratory conditions the duration of the interval between two consecutive REMS episodes is directly related to the duration of the previous REMS episode but not to that which follows. Such a short-term modality to regulate REMS occurrence appears to be maintained during the REMS rebound which follows REMS deprivation but not during cold exposure, when the need for REMS is counteracted by the need to regulate body temperature.

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0158.B

Dynamics Of REM Sleep Enhancement Due To Dark Pulse Triggering

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Introduction: The delivery of a dark pulse (DPD) when the light is on triggers REM sleep (REMS) with a high percentage of success in the albino rat. The enhancement of REMS occurrence due to a rhythmical DPD does not increase the daily amount of REMS, due to an apparent compensatory decrease in REMS occurrence during lights-on. However, at present no studies have quantitatively analyzed the dynamics of REMS enhancement caused by a non-rhythmical DPD. The aim of this study was to investigate such a dynamics under a protocol in which non-rhythmical DPD was limited to a period of the day and to analyze the post-effects on REMS occurrence during the following unstimulated part of the day.
Methods: Thirteen male Sprague-Dawley rats (250g), adapted to a 12h:12h light-dark (LD) cycle, were implanted under general anaesthesia with EEG electrodes and a thermistor for hypothalamic temperature recording. Animals underwent two 24-h experimental sessions, one for the baseline (BL) recording and the other (DPD) in which twenty DPs (3min light-off, each) were randomly delivered (max. 4 per hour) during the first 6h of the L period. The recordings were visually scored to assess REMS amount and the number and duration of REMS episodes, according to the partition into Single episodes (both preceded and followed by an interval >3min) and Sequential episodes (separated by at least one interval <3min), which has been proposed by our laboratory. Paired T test and repeated measures ANOVA, with Bonferroni's correction for post-hoc comparisons, were used for the statistics. Data are given as mean±SEM.
Results: DPD significantly increased the total amount of REMS ($p<0.01$) in the first 6-h period of delivery (BL: 2039±139s; DPD: 2568±97s). However, no differences in the daily amount of REMS were observed (BL: 7535±370s; DPD: 7623±221s), since an apparent compensatory negative rebound occurred in DPD during the following 18-h period. The analysis of REMS dynamics in the first 6h showed that 7.5±1.0 Single and 4.7±0.5 Sequential episodes were triggered by DPD with a latency < 90s. However, in this period no significant differences in the total number of both Single (BL:12.7±0.9; DPD:12.4±0.9) and Sequential (BL:13.5±1.7; DPD:15.7±1.5) episodes were observed. Thus, the increase in total REMS in DPD was due to a significant increase ($p<0.01$) in the duration of both Single and Sequential episodes triggered by DPD (Single:135±7s; Sequential:90±7s) with respect to spontaneous episodes in both BL (Single:92±7s; Sequential:65±5s) and DPD (Single:85±8s; Sequential:62±5s).
Conclusions: A non-rhythmical DPD increases total REMS amount during the delivery period due to an increase in the duration of the triggered episodes. This REMS enhancing effect is not compensated for by a short-term mechanism during the delivery period but, apparently, through a long-term regulation in the following unstimulated period.

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0159.B

Autoregulation Of The Cerebral Circulation In Sleep

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Introduction: Autoregulation is a fundamental protective mechanism that maintains cerebral blood flow (CBF) constant as cerebral perfusion pressure (CPP) changes. Our previous work provided the first evidence that the vasoactive mechanisms that underlie autoregulation of the cerebral circulation function during sleep. Intriguingly, our data also revealed that the speed and the magnitude of the vasodilatory reserves available for autoregulation are significantly less in active sleep (AS) than in quiet sleep (QS). As little else is known about autoregulation of the cerebral circulation during sleep, we sought to further determine the effectiveness of autoregulation during hypotension in sleep.
Methods: Nine lambs (16 ± 5 days, 7.8 ± 1.1 kg, Mean ± SD) were instrumented under general anesthesia (1.5% Halothane, 50% Os2s, balance Ns2s0) with electrodes to record ECoG, EMG and EOG and catheters to record CPP (CPP = Arterial pressure minus intracranial pressure). CBF was recorded using a transit-time ultrasonic flow probe positioned around the superior sagittal sinus and held in place with dental acrylic. Following a minimum of 72 hours post-operative recovery, autoregulation curves (plots of CBF versus CPP) were generating in AS, QS and in Wakefulness (W). To do this, CPP was lowered for one-minute periods by inflating an occluder cuff around the brachiocephalic artery. Cuff inflations were repeated to collect data over a range of CPP. A bilinear regression was fitted iteratively to these data to determine the breakpoint of the curve as indicated by the value of CPP that corresponded to the minimal residual sum of squared deviations from the bilinear prediction.
Results: During control periods, CBF was higher (P£0.05) and cerebral vascular resistance lower (P£0.05, repeated measures ANOVA) in AS (25 ± 9 mL/min, and 2.6 ± 0.8 mmHg/mL/min, Mean ± SD) than in W (19 ± 7 mL/min, 3.5 ± 1.0 mmHg/mL/min) or QS (16 ± 6 mL/min, 4.1 ± 1.4 mmHg/mL/min), and greater in W than in QS (P£0.05); CPP did not differ. The autoregulation curve in AS was shifted upward relative to W and QS; the breakpoint was higher in AS (50 mmHg) than in QS (45 mmHg) or W (46mmHg) and the slope of the descending limb was greater in AS ($y = 2.5x + 34$, $R2 = 0.74$) than in QS ($y = 1.4x + 36$, $R2 = 0.84$) or W ($y = 1.45x + 52$, $R2 = 0.66$).
Conclusions: We conclude that although autoregulation functions in AS,

the higher breakpoint and greater slope of the descending limb may place the brain at risk for ischemia should hypotension occur.

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0160.B

Sympathetic Control of the Cerebral Circulation in Sleep

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Introduction: Active sleep (AS) is characterized by a tonic increase in cerebral blood flow (CBF) upon which are superimposed phasic increases in CBF associated with arterial blood pressure (Pa) surges, a decrease in cerebral vascular resistance (CVR) and an increase in extra-cerebral sympathetic nervous system (SNS) activation. In the newborn, the cerebral vessels are richly invested with sympathetic nerves and the SNS has been proposed to play a key protective role in the cerebral microcirculation when blood pressure increases. Yet no study has systematically investigated the role of the SNS in regulating the cerebral circulation in sleep, particularly during AS when large transient Pa surges are common.
Methods: We studied 5 newborn lambs undergoing spontaneous sleep-wake cycles before and after bilateral superior cervical ganglionectomy (SCG). Lambs were instrumented under general anesthesia (1.5% Halothane, 50% Os2s, balance Ns2sO) to record CBF, Pa, intra-cranial pressure (Pic), cerebral perfusion pressure (Pcp = Pa-Pic) and CVR. Five additional lambs acted as a sham-operated control group. A minimum of 72 hours post-operative recovery was allowed before each lamb was studied as it spontaneously cycled between sleep-wake states over a 24 to 48 hour period.
Results: Prior to SCG, CBF was significantly higher in AS than in Quiet Wakefulness (QW) and Quiet Sleep (QS) (16.8 ± 0.8 ml/min, 14.1 ± 1.3 ml/min, 13.0 ± 1.2 ml/min respectively, one way repeated measures ANOVA, P £ 0.05). CBF increased significantly following SCG in tonic AS, QW and QS (32.9 ± 7.4%, 26.2 ± 13.7 %, and 27.3 ± 13.8 % respectively, [one way RM ANOVA, P £ 0.05 vs before SCG]), coincident with a decrease in CVR (-24.4 ± 2.4%, -25.3 ± 7.7%, and -26.9 ± 8.8%, p £ 0.05). During the phasic arterial pressure surges of AS, CBF was higher and CVR was lower after SCG (one way ANOVA, P £ 0.05). No significant changes were observed in tonic or phasic Pa or Pcp between pre-SCG and post-SCG, nor was the sham control group affected by the surgery.
Conclusions: We postulate that SNS protects the cerebral micro-vessels of the newborn from pressure surges, particularly during AS when the cerebral circulation is maximally dilated and when large arterial pressure increases are common.

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0161.B

Repeated Awakenings from REM Sleep Shorten NonREM Sleep Episodes

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Introduction: The average length of nonREM/REM sleep cycles in humans equals 90-100 minutes. The underlying mechanism is unknown. Kleitman proposed a sleep-independent, basic rest-activity cycle to generate the periodic alternation between nonREM and REM sleep. Other authors suggested a sleep-dependent process to keep track of elapsed time within the sleep cycles. We analyzed the effects of awakenings from nonREM and REM sleep on cycle duration and cycle content.
Methods: Eight healthy men aged 24.1±0.6 years participated in two sessions of nine consecutive nights starting with an adaptation night followed by two baseline nights, three sleep intervention nights and three recovery nights. Time in bed was 8 hours starting at 2300 h. In the first session subjects were awakened upon appearance of REM sleep, or after at least 20 seconds of desynchronized EEG and minimal submental EMG amplitude (REM sleep deprivation, RD). Awakenings occurred in clusters alternating with consolidated nonREM sleep periods. The clusters were considered as REM sleep episodes that ended when an awakening was followed by 15 minutes of nonREM sleep stages 1-4, spontaneous wakefulness and movement time. In the second session subjects were awakened from nonREM sleep (control sleep deprivation, CD). It was attempted to match the number of interventions and the stages with high vigilance (waking + movement time + stage 1). Each nonREM sleep episode contained at least 15 minutes of nonREM sleep and, except for the first REM sleep period where no criteria were applied, each REM sleep episode at least 5 minutes of REM sleep (or of cluster duration). Differences were investigated by repeated measures ANOVA.
Results: The number of cycles did not differ between the nights in RD. Nevertheless, cycle duration decreased from 105.7±7.6 (SEM) min in baseline to 90.7±5.1 min in deprivation night 1 (D1), 66.9±2.8 min in D2, and 75.2±2.4 min in D3 ($p<0.03$ for all nights). This reduction resulted from shortened nonREM sleep episodes (stages 2, 3 & 4) in cycles 2 (in D2) and 3 (in D1, D2 and D3), and shorter REM sleep episodes (= clusters) in all cycles in all deprivation nights. In CD the number of cycles was reduced and their duration prolonged. Cycle length increased from 99.7±4.7 min in baseline to 128.6±5.9, 137.0±10.6 and 135.4±5.0 min in the control deprivation nights C1, C2 and C3 ($p<0.01$ for all nights). The longer cycle duration was due to prolonged periods of high arousal while the duration of nonREM and REM sleep episodes was not altered.
Conclusions: Interruption of REM and nonREM sleep has opposite effects on sleep cycles. Awakenings from nonREM sleep did not alter the duration of nonREM sleep. Thus a sleep-dependent process may keep track of the elapsed time within the cycle. Disruption of REM sleep, however, shortened the nonREM sleep periods. The data suggest that disrupting REM sleep inhibits nonREM sleep-maintenance.

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0162.B

Increased REM Density Induced by Anodal Transcranial Direct Current Stimulation Over the Left Premotor Cortex During Post-Training REM Sleep

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Introduction: One function of sleep is hypothesized to be the reprocessing and consolidation of memory traces. Using positron emission tomography, it was shown that during REM sleep in humans previously trained on an implicit motor learning there are cortical reactivations in the left premotor cortex, bilateral supplementary motor cortex and left posterior parietal cortex. Excitability elevation of the primary motor cortex induced by anodal transcranial direct current stimulation (tDCS) improves performance in the acquisition and early consolidation phase of implicit motor learning. Objectives: We aimed to investigate if anodal

tDCS over the left premotor cortex during post-training REM sleep period does influence REM sleep and memory processing.
Methods: 14 healthy, right handed, good sleepers (mean age: 36, range from 19 to 56 years) underwent complete polysomnographic recordings with one adaptation night and two nights of randomized anodal tDCS or placebostimulation. During the second and third polysomnographic night each subject, previously trained on a serial reaction time task (SRTT), received either 15 minutes of anodal tDCS or placebo stimulation over the left premotor cortex during the second REM sleep period. If the REM period was less than 15 minutes, a further tDCS was applied in the following period. 7 subjects were wakened and retested immediately after stimulation, and 7 subjects were retested in the morning.Polysomnography was scored according to standardized criteria. REM density was measured as the frequency of REMs (expressed in REM/30 second in each REM period). Comparisons between the nights in each period of REM sleep were performed using ANOVA and post hoc Tukey tests and separate ANOVA for SRTT for reaction time, errors and variability.
Results: The following main differences between stimulation night and placebo night were found: REM density was significantly increased in each anodal tDCS period in comparison with the corresponding placebo stimulation period ($p<0.04$ for 2.REM period, $p<0.01$ for 3. REM period, $p<0.05$ for 2.+3.REM period). Reaction times of the SRTT were significantly shorter immediately after stimulation (interaction of block and TDC and time period $p<0.02$ for absolute values $p<0.04$ for standardized values). There was no significant difference in sleep macrostructure data between both nights and for other SRTT reaction times values.
Conclusions: The high increase in REM density during anodal stimulated post-training REM sleep and lower reaction times immediately after tDCS, suggest that the brain areas reactivated during post-training REM sleep participate in the optimization of visuomotor response network, e.d. influenced by tDCS.

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0163.B

ROC Characteristics Of Autonomic Arousals Detected by Pulse Transit Time For Diagnosis Of OSAS

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Introduction: Pulse transit time (PTT) is the time it takes the pulse-wave to travel from the heart to a peripheral site on the body. Therefore it is a non-invasive measure of beat-to-beat blood pressure (BP) changes and can be used as a measure of autonomic arousals (Pitson and Stradling, 1998). OSAS is associated with sleep fragmentation, hypertension and tiredness. Autonomic arousals measured by means of PTT are shown to be sensitive to OSAS and tendencies to hypertension. Previously various parameters of arousal detection by PTT where discussed (Xio, Y. et al. 2002). In this document we present normative values of one of those parameters.
Methods: PSG recordings of 150 males (with suspected OSAS) were randomly selected from a pool of data recorded in a clinic. Periods with movement time or artifacts were ignored in analysis. Desaturation, apneas/hypopneas, limb movements and autonomic arousal by PTT were scored and indexes were calcuated. Patients with a high limb movement index were excluded.Arousals from PTT were analyzed automatically with the Rembrandt system. A decrease of 5msecs in PTT compared to 10 second baseline was identified as an autonomic arousal. In the previous study we found that a 5msec decrease of PTT was more sensitive to respiratory distrubances than the 15msec used in literature.The subjects were divided in groups on the basis of an AHI lower or higher than 5. ROC curve of this PTT drop detection is calculated to show the sensitivity (true positive rate) and specificity (1 - false positive rate) tradeoff of different thresholds compared to the AHI. Based on this ROC curve optimal PTT threshold values are discussed.
Results: The threshold to distinguish between individuals with an AHI lower (normals) or higher than 5 (patients) was between 14 (False Positive rate=0.5, True Positive rate=0.96) and 26 (False Positive rate=0.2, True Positive rate=0.69). A threshold of 14 identified 96% of the patient group correctly but only 50% of the normal group. A threshold of 26 still identified 69% of the patient group correctly and 80% of the normal group.
Conclusions: This and the previous study showed that PTT-arousals differentiated OSAS patients from a fairly mixed group of non-patients and patients. Autonomic arousals indicated by a decrease of PTT by 5 ms compared to a baseline of 10sec is sensitive to sleep disordered breathing.

0164.B

Sleep-Waking Cycle And EEG Rhythmic Activities In Mice Lacking M2, M3, M4 Or M2/M4 Muscarinic Receptors

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Introduction: A large number of studies indicate that the cholinergic activation of muscarinic receptors plays a crucial role in the cortical activation, the generation of theta rhythms during wake and paradoxical sleep (PS) and the onset and maintenance of PS per se. In order to determine the contribution to these events of the different muscarinic receptor subtypes, we analyzed the sleep-waking cycle and the EEG power spectrum of mice lacking functional M2, M3, M4 or M2/M4 receptors.
Methods: For each strain studied, 4 knockout (KO) and 4 wild type (WT) male mice (20-30 g, 10-14 weeks old) were conventionally implanted under anesthesia with electrodes for polygraphic sleep monitoring. They were allowed 10 days of recovery and habituation to the standard laboratory experimental conditions: 12-12 h light/dark, 22-24°C ambient temperature, food and water ad libitum. Continuous polygraphic recordings were performed during 72 h and collected on a computer via a CED interface using the Spike 2 software. Vigilance states were scored visually for 10 s epochs as waking (W), slow wave sleep (SWS) or PS according to the classical criteria. Finally, the power spectra were analyzed by fast Fourier transform (FFT) only using recordings with the best EEG signal quality.
Results: For all KO mice, no significant change in the distribution and quantities of each vigilance state was observed compared to WT. Strikingly, the daily amounts of PS were not statistically different from those encountered in WT. The same observations were made for the daily percentage, number and duration of PS bouts. An analysis hour per hour during the light and dark phases indicated that the circadian distribution of PS, SWS and W was not affected in the M2—, M3—, M4— and M2/M4— mice compared to WT. OT. Our preliminary FFT analysis however showed that rhythmic EEG activities were altered in the different KO mice, except M4—. In M2/M4— mice, theta rhythm was decreased during PS compared to WT, whereas both delta and theta activities were strongly depressesed during W in the M3— mice. In M2— mice, only theta rhythm during PS was increased compared to WT. In order to quantitatively analyze these events, an additional series of experiments was recently done for M2/M4— and M3— mice (4 KO and 4 WT for each lih line).
Conclusions: The present study clearly indicates that the different muscarinic receptors are not essential for PS onset and maintenance, as well as the ultradian and circadian regulation of vigilance. In contrast, the power spectra appear modified in M2, M3 and M2/M4 KO versus WT mice. Experiments are in progress to clearly quantify these modifications in order to precise the physiological roles of individual muscarinic receptors in the control of the EEG rhythmic activities.

0165.B

Localization Of The Neurons Responsible For The Inhibition Of Locus Coeruleus Noradrenergic Neurons During Paradoxical Sleep In The Rat

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Introduction: Unit activity of locus coeruleus (LC) noradrenergic neurons is closely linked to the vigilance states. These neurons are tonic during wakefulness (W), demonstrate a slow discharge rate during slow wave sleep (SWS) and stop firing during paradoxical sleep (PS). Our electrophysiological study in rats indicates that GABA is responsible for the PS-specific cessation of activity of LC neurons. By means of CTb/GAD double-immunostaining, we further demonstrated that the main brainstem GABAergic inputs to the LC arise from the ventrolateral part of periaqueductal gray (vlPAG) in the pons and the dorsal paragigantocellular nucleus (DPGi) within the dorsal medulla oblongata. To determine whether the vlPAG and/or DPGi are involved in the inhibition of LC neurons during PS, we examined in the rat the distribution of CTb and c-Fos double-immunostained neurons following CTb injection in the LC and PS rebound obtained after selective deprivation with the classical flowerpot technique.
Methods: Each experimental series (n=4) was constituted of 3 rats. First, each rat received under anesthesia an iontophoretic CTb injection in the LC (15 min, 1µA) after control electrophysiological recordings of several LC units. The rats were then conventionally implanted for chronic EEG and EMG recordings. After one week habituation to the recording conditions, 2 rats were placed on a flowerpot surrounded by water for 3 consecutive days, the third one staying for the same duration in its recording jar (control rat). At the end of the deprivation, one rat was immediately sacrificed (deprived rat), while the second one was put back in its recording jar for 180 minutes of recovery sleep before perfusion (rebound rat). Coronal sections were immunostained for CTb with DAB-Ni followed by c-Fos with DAB histochemical technique.
Results: Physiological data showed that during the recovery period after sleep deprivation, PS quantities increased more than 350% in rebound rats compared to control rats, while PS was absent in deprived rats. Following PS recovery, a strong c-Fos expression was specifically observed in numerous areas thought to play a crucial role in PS onset and maintenance. The number of c-Fos+ neurons was significantly increased in the tegmental laterodorsal (LDT), dorsal subcoeruleus (SubCD) and ventral reticular gigantocellular (GiV) nuclei within the brainstem. Surprisingly, numerous c-Fos+ neurons were also encountered within the lateral hypothalamic area, which is classified as W area. With regard to LC inputs, the most important number of double labeled CTb/c-Fos+ neurons was found in the DPGi and to a lesser extent the lateral paragigantocellular nucleus (LPGi) and the vlPAG.
Conclusions: Our data confirm at cellular level the role of the LDT, SubCD and GiV in PS onset and maintenance. Moreover, they suggest that other structures such as the DPGi, LPGi and vlPAG could contain the GABAergic neurons responsible for the tonic inhibition of LC noradrenergic neurons during PS.

0166.B

Sleep Disturbances in a Rat Model of Chronic Renal Failure

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Introduction: Sleep disturbances, including daytime sleepiness, sleep disordered breathing, periodic limb movement disorder, and restless legs syndrome, are common in patients with chronic renal failure. However, an animal model examining sleep in uremia remains to be described. We therefore explored the feasibility of preparing a rat model for the study of sleep in uremia and compared the sleep data obtained before and after induction of chronic renal failure (CRF).
Methods: CRF in male Sprague Dawley rats (n=5) was induced in a three stage procedure. Stage 1: A unilateral nephrectomy was performed. One week later, rats were implanted with electrodes for sleep recording, including cortical and theta EEG, nuchal muscle EMG, and left and right gastrocnuemius muscle EMG. Stage 2: Seven days later, a ¾ nephrectomy of the remaining kidney was performed. Rats were placed on a reduced protein diet and ¼ normal saline for 1 week. Baseline sleep was then recorded for 48 hours. Stage 3: Rats were placed on a high protein diet and ¼ normal saline for 7-10 days to induce uremia. Tail blood was then drawn to document blood urea nitrogen (BUN) levels, and sleep was studied for an additional 48-hours.
Results: Following induction of CRF, BUN values increased approximately 400% over baseline levels. During the major sleep period, uremic animals spent an increased percentage of time awake [43.74 $\pm$ 10.44 (SD) versus 29.40 $\pm$ 8.70 in baseline, $p = 0.031$]. Of the total sleep time, there was an increased percentage of non-slow wave sleep (NSWS; 49.43 $\pm$ 12.00 vs. 30.30 $\pm$ 3.94, $p = 0.008$), while the percentage of slow wave sleep (SWS) decreased (37.42 $\pm$ 12.53 vs. 57.07 $\pm$ 2.42, $p = 0.016$). Rapid eye movement (REM) sleep did not change but the number of sleep stage transitions decreased significantly (402.4 $\pm$ 115.05 vs. 530.6 $\pm$ 53.45, $p = 0.024$). An increase in limb movement frequency was not readily apparent, but is currently being quantified. During the major wake period, REM-sleep increased two-fold over baseline (13.14 $\pm$ 2.63 vs. 5.49 $\pm$ 1.29, $p = 0.010$) while the percentage of SWS decreased (44.01 $\pm$ 9.01 vs. 50.97 $\pm$ 12.28, $p = 0.047$). No other abnormalities were noted during the wake period.
Conclusions: The rat has been used independently in sleep and nephrology research. Based on this work, we attempted to integrate appropriate techniques to develop the first animal model for the study of sleep in uremia. Our preliminary data suggest that uremic-induced sleep/wake changes can be expressed in this model and that these alterations are comparable to those obtained in uremic humans, including increased wake and decreased SWS during the major sleep period and an increased REM-sleep propensity during the major wake period. This model may represent an important vehicle for the study of uremic-induced sleep disturbances and the development of clinical interventions.

0167.B

Intra-Suprachiasmatic Nucleus (SCN) Microinjection of a Nitric Oxide (NO) Donor and NO Synthase Inhibitor Affects Sleep in Rats

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Introduction: Nitric oxide (NO) has been implicated in the regulation of the sleep-wake cycle. Our previous studies suggest that the effects of NO synthase (NOS) inhibitors on sleep depend on the dose and the circadian timing of the treatment. High doses of the NOS inhibitor L-NAME, decrease non-rapid-eye-movement sleep (NREMS) when injected during the light period, whereas NREMS and rapid-eye-movement sleep (REMS) are enhanced when L-NAME is administered at night. These suggest that, in addition to playing a role in homeostatic sleep regulation, NO-ergic mechanisms may also be involved in the circadian regulation of sleep. The presence of NOS-positive neurons in the suprachiasmatic nucleus (SCN) and the finding that manipulations of the NO system in the SCN elicit phase-shifts, further support this idea. To study the role of NO-ergic mechanisms of the SCN in sleep regulation, we tested the effects of microinjecting NOC-12, a NO donor, and L-NAME into the SCN, on sleep in rats.
Methods: Male rats (250-300 g) were implanted with EEG electrodes, a brain thermistor and bilateral microinjection cannulae targeted at the SCN. Sleep was recorded on a baseline day, when the animals were only handled, a second baseline day when saline was injected, on a test day [1 ug (n = 4) NOC-12 or 10 ug L-NAME (n = 10)], and on a recovery

(saline) day. In addition, 1 ug NOC-12 (n = 5) was tested after the solution had been kept at room temperature overnight, a procedure known to cause the loss of the NO-releasing capacity of NOC-12. All injections were performed at dark onset and volumes were 50 nl. REMS and NREMS amounts were determined, and FFT analysis of the EEG was performed.
Results: Bilateral microinjection of saline in the SCN induced a transient increase, lasting for 3 - 4 h, in both NREMS and REMS, compared to handling. During this time, NREMS amounts were increased by 44.7% , and REMS amounts were increased by 116%. Sleep amounts were unchanged thereafter. In the 6-h period following NOC-12 administration, REMS was reduced by 75.4%, from 54.6 to 13.4 min. This REMS loss was restored, in part, during the light period, when REMS was above baseline levels. On the saline recovery day, REMS was 40% below baseline during the first 6-h. Sleep responses to NOC-12 were due to the release of NO, since NOC-12 void of NO-releasing capacity failed to elicit any changes in sleep. Bilateral SCN microinjection of L-NAME increased NREMS by 26% in the 12-h dark period (approx. 52 min), while REMS amounts remained unchanged.
Conclusions: The present findings support a possible role for NO in the circadian regulation of physiological sleep.

0168.B

Effects of Electroacupuncture on the Sleep State-dependent P50 Midlatency Auditory Evoked Potential

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Introduction: A measure of arousal, the sleep state-dependent, midlatency auditory evoked P50 potential is generated, at least in part, by the reticular activating system (RAS), and is present only during cortical EEG "desynchronization". The amplitude of the P50 is decreased in conditions involving RAS downregulation, e.g. narcolepsy, autism, Alzheimer's Disease. The P50 is upregulated (increased amplitude/decreased habituation) in diseases marked by RAS upregulation, e.g. schizophrenia, anxiety disorder, late stage Parkinson's Disease. The use of acupuncture for treatment of neuropsychiatric disorders is coming into greater use, including mood and sleep disorders. The aim of this study was to develop a protocol for the use of electroacupuncture stimulation of specific points through surface electrodes instead of needles.
Methods: Subjects (25-55 yo) without history of neurological or psychiatric disorders and medication-free underwent Control recordings followed by 1) recordings during one or more 20 minute episodes of electroacupuncture stimulation through surface electrodes, using 2) high (100 Hz), medium (60 Hz) or low (5 Hz) frequency applied at 1, 2, or 3 acupuncture points (Pc6, Ht3, Li3) known to affect CNS activity, or 3) 3 control points (Si3, Li11, Gb34). The P50 potential was recorded, normalized and analyzed as previously described using a paired stimulus paradigm with a 250 msec interstimulus interval (1). Statistical differences were analyzed using 2-way ANOVA, repeated measures, and Newman-Keuls tests. 130 subjects were tested, among them 63 female, 23 African-American, 7 Hispanic and 5 Asian. Results were not significantly different for subjects grouped by race or gender.
Results: Electroacupuncture using surface electrodes instead of needles was found to decrease P50 potential amplitude when applied at three specific points (Pc6, Hi3, Li3), compared to no stimulation ($p<0.001$) or compared to stimulation of 3 control points ($p<0.01$). Stimulation at low frequency (5 Hz) was more efficacious ($p<0.001$) than stimulation at medium (60 Hz) or high (100 Hz) frequencies in decreasing P50 potential amplitude. Bilateral stimulation of the three specific points described was more effective in decreasing P50 potential amplitude than stimulation of the same three points unilaterally ($p<0.001$). Repeated episodes of stimulation showed a non-significant tendency to have additive effects on decreasing P50 potential amplitude.
Conclusions: Based on its demonstrated effectiveness in modulating the amplitude of the P50 potential, a non-invasive measure of RAS function, the possibility of using surface electrodes instead of needles broadens the clinical applicability of electroacupuncture. However, only specific points were found to have positive effects. These results suggest that it may be possible to use this treatment methodology as an adjunct/replacement therapy for disorders of arousal.1) Garcia-Rill, E. and R.D. Skinner 2001 The sleep state-dependent P50 midlatency auditory evoked potential. In Sleep Medicine, T.L. Lee-Chiong, et al. (Eds.), Hanley & Belfus, Philadelphia, pp. 697-704.

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0169.B

Effects of Music on the Sleep State-Dependent P50 Midlatency Auditory Evoked Potential

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Introduction: The "Mozart Effect" is used to describe 1) that listening to music composed by Mozart heightens performance on certain spatial tasks, effectively raising the IQ of the subject, or 2) the intellectual advantage conferred by formal musical training, with the greatest effect seen in those whose training is initiated at an early age. It was postulated that the first, more transient, "Mozart Effect" can be attributed to the effect of the music to heighten the subject's state of arousal. The midlatency auditory evoked P50 potential is generated, at least in part, by elements of the reticular activating system (RAS) and is considered a "preattentional" process (1). P50 potential amplitude can be used as a measure of arousal, while the ratio of the second P50 potential to the first, in a paired stimulus paradigm, can be used as a measure of habituation, a process involved in sensory gating, and consequently, distractibility. We also used a Psychomotor Vigilance task (PVT) to assess reaction time, as a basic attentional measure.
Methods: Subjects (18-54 yo) with no musical training (NoTr, n=7) or with musical training beginning before the age of 7 (Tr, n=9) underwent Control recordings followed by recordings during either 10 min of Mozart piano concertos (M) or of silence (S), in random order. The P50 potential was recorded and analyzed as previously described (1). At a second session, subjects underwent PVT testing following Control, M or S conditions.
Results: There was no difference in age between groups. The amplitude of the P50 potential for both NoTr and Tr groups together (n=16) was Control 1.5±0.2; M 0.9±0.2; and S 1.3±0.3 (mean±SE in mV); while habituation was Control 23±8; M 31±9; and S 28±8 (mean±SE in %). The Tr group showed that P50 potential amplitude (Control 1.5±0.2; M 0.9±0.3; and S 1.1±0.3) and habituation (Control 19±8; M 26±9; and S 28±9) were similar to the NoTr group P50 potential amplitude (Control 1.6±0.4; M 0.9±0.1; and S 1.5±0.5) and habituation (Control 28±13; M 38±18; and S 28±15). Reaction time means and number of lapses did not differ between groups or across condition.
Conclusions: Our results show that exposure to music (Mozart piano concertos) 1) does not increase arousal, and may decrease it marginally, 2) has little effect on habituation to repetitive stimuli, and may decrease it marginally, and 3) has no effect on reaction time. These effects were similar in untrained and musically trained subjects, indicating that, if there is a "Mozart Effect", it is unrelated to arousal level, preattentional or basic attentional function.1) Garcia-Rill, E. and R.D. Skinner 2001 The sleep state-dependent P50 midlatency auditory evoked potential. In Sleep Medicine, T.L. Lee-Chiong, et al. (Eds.), Hanley & Belfus, Philadelphia, pp. 697-704.

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0170.B

Acute Normobaric Hypoxia and its Effects on Measures of Sleep Quality in Recreational Athletes

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Introduction: Historically, athletes who live at sea level have achieved performance benefits from acute exposure to high altitude environments. The development of normobaric hypoxic tents allows for the utilization of nitrogen dilution techniques to reduce ambient pO2 within the immediate environment, enabling athletes to benefit from high altitude exposure whilst at sea level. Fragmentation of sleep is a common feature among the cluster of symptoms following acute ascent to high altitude. A study was carried out to evaluate the effect upon sleep quality of normobaric hypoxia at a simulated altitude of 2,500m in recreational athletes.
Methods: 8 healthy male recreational athletes (mean age 34.5; BMI 24.2, VO2 max = 56.4) participated in the study. Subjects were exposed to normobaric hypoxia (NH – pO2=110mmHg), placebo hypoxic conditions (PH - in hypoxic tent under normoxic conditions) or normal air (baseline), on three consecutive nights with a double blind, randomized design for NH and PH conditions only. EEG recordings were performed using Vitaport 3 recorders (TEMEC, Netherlands) with analysis of sleep quality based upon R&K scorings of total sleep time (TST), sleep period total (SPT), sleep latency (SOL) and sleep efficiency (SE%), with subjective assessment of the ease of "getting to sleep" (GTS), behaviour following waking (BFW) and sleep quality (QS) measured using the Leeds Sleep Evaluation Questionnaire. Actigraph measures of sleep were also recorded using actiwatches (Cambridge Neurotechnology, UK). The variables measured were; actual wake time, actual sleep time, sleep efficiency, fragmentation index, wake bouts, mean wake bout duration, mean sleep bout duration and sleep latency.
Results: Although there were no statistically significant differences in TST, SPT SOL and SE%, a reduction SL was observed under both NH than PL conditions compared to baseline, suggestive of increased ease of sleep initiation, supported by subjective measures (GTS) within the normal range of variability. TST, SPT and SE% were all higher under NH than PL, although TST and SPT baseline measures were substantially lower than under other conditions. QS and BFW also failed to achieve significance, although observations revealed baseline measures to be worse than both NH and PH, which was strongly indicative of a situational effect upon baseline measures. No significant differences were found between PH and NH for any of the actigraphy variables, however, large inter-individual variations were observed.
Conclusions: Acute NH at a stimulated altitude of 2,500m did not affect sleep quality compared to PH conditions. However, the situational effect of sleeping in an unfamiliar environment considerably influenced first night baseline measures. Because of this future research in thids area need a more complex design e.g. acclimatization study or 3-way crossover design should be employed in future investigations.

0171.B

EEG and Vigilance State Responses to Naps as Indicators of Sleep Homeostasis

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Introduction: The relationship of NREM delta EEG intensity to prior waking duration is seen as an indicator of sleep homeostasis. NREM delta increases following sleep deprivation and decreases on post-nap nights. This relationship may not be specific for NREM delta. Low frequency EEG up through the theta band increases in NREM sleep following sleep deprivation. Also, the large increase in REM after sleep deprivation in rats has been cited as evidence that REM sleep is restorative. We use a nap protocol to evaluate NREM and REM duration and EEG power in various frequency bands as indicators of homeostasis. We hypothesize that measures that are reliable indicators of homeostatic recuperation should be reduced post-nap and that the amount accumulated in the nap ought to be precisely subtracted on the post-nap night.
Methods: Sleep EEG was recorded from 19 young adults and 19 elderly subjects who passed health and sleep screening. All subjects completed 4 recording sessions consisting of a baseline night, a daytime nap, and a post-nap night. Nap times were 0900, 1200, 1500, and 1800 with the order varied. Using Pass Plus software, EEG was digitized and analyzed with both spectral and period amplitude analysis. Homeostatic regulation of NREM and REM durations and regulation of EEG intensity in the delta, theta, alpha, sigma, and beta frequency bands was evaluated as follows: Was the variable's level significantly reduced on the post-nap night and was the sum of the nap and post-nap levels equal to the baseline night level?
Results: In young adults only the 1500 and 1800 naps produced significant responses on the post-nap night. Only the 1800 data for the young adults are presented here. NREM duration was significantly ($p<0.0001$) reduced by 11% on the post-nap night compared to baseline, however, addition of the nap NREM mins produced a sum significantly exceeding baseline levels. REM duration was enhanced rather than reduced on the post nap night. Within post-nap night NREM sleep, delta power was reduced by the greatest amount (28%), although theta (25%) and alpha power (19%) were also significantly reduced. Adding the power accumulated during the nap to the post-nap values returned delta power to 100% of the baseline level. The sum of nap and post-post nap power was between 105 and 110% of baseline for theta, alpha, and sigma, and was 117% of baseline for beta. For all bands, EEG power during REM on the post nap night equaled or exceeded that of the baseline night.
Conclusions: According to the criteria proposed in the introduction, NREM delta EEG best reflects the recuperative processes of sleep. Although other NREM EEG frequencies approached the criteria, NREM delta was the variable most reduced on the post-nap night and whose sum of nap and post nap values most closely approximated baseline levels. REM and REM EEG variables increased following a nap, contrary to what would be expected if they reflected the restorative processes of sleep.

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0172.B

K-complex Elicitation And Amplitude Are Independent Of ISI

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Introduction: The sensitivity of the K-complex elicitation and amplitude to variations in stimulus properties remains unclear. Several studies have reported larger N550 and an increased K-complex elicitation rates to rare rather than frequent stimuli. These findings have been interpreted as consistent with the ISI effects previously reported by Bastien and Campbell (1994) who reported that tone pips presented every 30 seconds produced a larger N550 response than those presented every 10 or every 5 seconds. Alternatively, they may reflect some novelty processing that persists into sleep. We hypothesized that both K-complex elicitation rate and amplitude would vary as a function of ISI between 15 and 30 sec-

onds.
Methods: Ten healthy adults (6 women) aged 21-70 (mean = 46.3, S.D. = 15.2 yrs) spent a single night in the sleep laboratory. EEG was recorded from six gold plate electrodes (Fz, Fcz, Cz, Cpz, Pz and O2) referenced to A1 + A2. Auditory stimuli were 80 dB, 1000Hz tone pips having 52 ms duration and a rise and fall time of 2 ms presented with a variable inter-stimulus interval (ISI) of 15 - 30 second. Data were collected during stage 2 sleep in the first two sleep cycles. Responses to stimuli were classified based on whether they produced: a K-complex or some other response, and averaged separately for each ISI.
Results: A repeated measures ANOVA revealed no significant differences between ISI categories for either K-complex amplitude $F(15,135) = 0.87$, $p > 0.05$ or the probability of a K-complex being elicited $F(15,135) = 0.72$, $p > 0.05$. Linear regression analysis revealed no significant relationship between ISI and either K-complex amplitude ($r = 0.16$, $F(1,15) = 0.37$, $P > 0.05$) or probability ($r = 0.00$, $F(1,15) = 0.00$, $P > 0.05$).
Conclusions: The data clearly indicate no difference in either the amplitude or likelihood of elicitation of K-complexes as a function of ISIs ranging between 15 and 30 sec. Previous differences in these variables in the responses to rare and common tones, and between tones and inspiratory occlusions were interpreted as being due to ISI differences within the range tested. In light of the present data, interpretation of oddball effects during sleep needs to take other factors, such as habituation and novelty effects, into consideration. The data also indicate that if K-complexes do indeed show a refractory period as previously suggested, it is shorter than 15 seconds.

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0173.B

Morphology Of Slow Eye Movement At Sleep Onset
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Introduction: Trajectories of slow eye movement at sleep onset are classically described as "rolling," "pendulous," or "looped." Moving beyond these descriptions, recent work has shown that (1) the amplitude, peak velocity, and duration of horizontal bidirectional slow eye movement (SEM) differ, on average, according to stage of sleep onset as defined by T. Hori and colleagues; (2) the SEM "main sequence"—thee proportion of variance in peak velocity or duration accounted for by eye movement amplitude—differs among sleep onset stages and locally within stages; and (3) within stages, successive peak-to-peak amplitudes of SEM approximate sequences of evenly distriibuted random numbers. Again using the Hori et al. EEG stage scoring system, this study examines in greater detail the morphology of SEM during sleep onset.
Methods: Using BIOPAC™ hardware and software, DC electrooculography (EOG) was completed in four young adult subjects during nighttime sleep. Using established measurement criteria for the EOG and the EEG, SEMs were counted at opposed, inversely matched deflections of the right and left EOG tracings during Stages 3 through 8 of sleep onset; owing to its rarity in this sample Stage 4 was omitted. To remove EEG artifact the raw signal was FIR low-pass filtered at 1Hz. EOG waveforms were then displayed as (1) eye position, (2) eye velocity (the derivative of eye position), and (3) the integrand of curve length, which assigns positive values to velocity in either direction of eye movement. To assess the structure of SEM, each tracing was then segmented according to successive segments' goodness of fit to any of various mathematical descriptors.
Results: As if operating on "prototype" functions $y = f(x)$, local trajectories of eye position could be described as approximating specific waveform transformations. These included (1) reflection around the y axis: $y = f(-x)$; $c>1$; (2) vertical translation: $y = f(x) + c$ or $y = f(x) – c$; $c>0$; (3) horizontal translation rightward: $y = f(x - c)$; $c>0$; (4) stretching: $y = cf(x)$ or $y = f(x/c)$; $c>1$; and (5) horizontal compression: $y = f(cx)$; $c>1$. Values of eye velocity (the derivative, which crosses zero for bidirectional eye movement, or the curve length integrand, which remains positive) produced transformation categories 1, 3, 4, and 5. In addition, the derivative could reflect a prototype around the x axis ($y = -f(x)$). More generally, waveform transformations (a) could operate singly, serially, or by superposition; (b) could be static, with y axis fixed, or dynamic, with a rightward-shifting axis of reflectional symmetry; and (c) were locally optimal and globally most dynamic in Stage 5/6 of sleep onset, in association with high values of the coefficient of determination (amplitude x velocity).
Conclusions: The morphology of SEM evolves distinctively over the course of sleep onset and reaches an apex of spatiotemporal complexity in Stage 5/6. Thus at the height of hypnagogic hallucinatory experience, the activity of oculomotor neurons is most highly organized, both locally and globally.

0174.B

The Role Of Oxytocin In The Paraventricular Nucleus In Yawning And Penile Erection
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Introduction: The role of the hypothalamus in the control of vigilance has recently been re-emphasized. Beside the circadian and homeostatic controls, other physiological mechanisms, such as brain ischemia and hypoxia are also known to significantly affect the vigilance. A series of animal studies has demonstrated that paraventricular nucleus (PVN) in the hypothalamus is involved in the induction of yawning. Yawning response in the hypothalamus is typically associated with the induction of penile erection, and intracerebroventricular (ICV) and /or local administration into the PVN of oxytocin, dopamine D2 agonists, ACTH and alpha-MSH induce both yawning and penile erection in rats. The PVN contains various neuropeptides, such as oxytocin, vasopressin, corticotropin releasing factor, dynorphine, as well as dopamine, and projects to various brain regions such as the brainstem, hippocampus and spinal cord. It has also been recently demonstrated that the PVN also receives hypocretin inputs from the lateral hypothalamic area. The PVN is thus likely to coordinate various functions (including vigilance control) in relationship to the replenishment of nutrients and water, and also the sexual and maternal behaviors that assure survival of the species. In order to further the understanding of the basic function of the PVN, we have investigated the cellular mechanisms involved in the induction of yawning and penile erection with double-staining for c-fos and oxytocin in the PVN after ICV oxytocin administration.
Methods: Male Wistar rats (weighing 300-450 g), were used for all experiments. They were individually placed in cages, and either oxytocin (50 to 200 ng) or apomorphine (5 to 10 µg) was injected into the lateral ventricles (ICV), in a volume of 10µl, via the ICV cannula connected by polyethylene tubing to a 10-µl Hamilton syringe. Immediately after the injection, the number of yawning and penile erections was counted by direct observation and recorded for a period of 60 minutes. Since it is known that lithium chloride (LiCl) activates oxytocin neurons in the PVN, the effects of LiCl (0.5 to 2mEq. ip) on spontaneous yawning and penile erection as well as oxytocin and apomorphine (D2 agonist) induced yawning and penile erection were also investigated. In order to identify and localize the neurons activated in the PVN by oxytocin administration, the double-staining for c-fos and oxytocin were performed.
Results: ICV injection of oxytocin induced yawning and penile erections in a dose dependent manner. Similarly, ICV injection of apomorphine also dose-dependently increased yawning and penile erections. It is widely believed that central administration of oxytocin and apomorphine activates the descending oxytocin projection to mediate yawning

and penile erection. Double-staining for c-fos and oxytocin experiments, however, revealed that ICV injection of oxytocin did not induce c-fos expression in the PVN oxytocin neurons, including the caudal portion of the PVN, from where descending oxytocin projection initiates. In contrast, injection of LiCl (0.5 to 2mEq, ip) did not induce yawning and erection, but dose-dependently induced c-fos in oxytocin neurons in the PVN. Interestingly, we observed that pretreatment with LiCl counteracts the oxytocin-induced yawning and penile erection.

Conclusions: Previous studies suggested that the activation of oxytocin neurons in the PVN mediates the induction of yawning and penile erection. In the present study, however, ICV oxytocin, doses that induced yawning and penile erection, did not induce c-fos in the oxytocin neurons in the PVN. In addition, LiCl that potently activated PVN oxytocin neurons and enhanced c-fos expression, counteracted the oxytocin-induced yawning and penile erection. These results raise the possibilities that (1) activation of the oxytocin neurons are not required for the induction of yawing and erection or (2) phasic activation rather than tonic excitation of oxytocin neuron is involved in the induction of yawning and penile erection.

0175.B

Alpha Intrusion: Prevalence and Association with Sleep Complaints in the Sleep Heart Health Study

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Introduction: The polysomnographic finding of alpha intrusion has been reported in association with complaints of non-restorative sleep or fibromyalgia. However, the prevalence of this finding in healthy or disease populations is unknown. Thus, the true association of alpha intrusion with non-restorative sleep or other sleep complaints is uncertain. This study examines the relationship of alpha intrusion to measures of sleep complaints in a community-based population.

Methods: Participants were enrolled in the multi-center Sleep Heart Health Study (SHHS). The sample (n=2027; 53% women; 80% white, mean age 62 $\pm$ 11 years) was restricted to participants with polysomnograms of the highest technical quality scored by the most reliable scorers. Alpha intrusion was identified when alpha activity accounted for >40% PSG sleep time. Sleep complaints were measured using the Epworth Sleepiness Scale (ESS) and the SHHS sleep habits questionnaire (for frequency of daytime sleepiness, feeling unrested, difficulty initiating and maintaining sleep, insufficient sleep, frequent awakening from leg cramps or joint pain, sleeping pill use). ESS scores >10 were categorized as elevated. Sleep habits questions were dichotomized such that 'almost always' and 'frequently' indicated presence of the specific sleep complaint, while 'sometimes', 'rarely', and 'never' indicated its absence. Key covariates included age, gender, and race/ethnicity. Potential confounding variables included medication, alcohol, or caffeine use and chronic disease states (sleep-disordered breathing, cardiovascular disease, chronic lung conditions, diabetes, and hypertension). The associations between alpha intrusion and sleep complaints were modeled using logistic regression and adjusted for key covariates and potential confounding variables.

Results: The overall prevalence of alpha intrusion in this sample was 3.6% (73/2027). Women (p=.017) and whites (p=.008) were more likely to have alpha intrusion. Twenty-five percent of subjects had an elevated ESS and other sleep complaints were reported by 10-20%, but 51% of participants with alpha intrusion had no sleep complaints. Female gender was strongly associated with feeling unrested, not getting enough sleep, leg cramps, joint pains, difficulty falling and staying asleep, and sleeping pill use. The only sleep complaint associated with alpha intrusion was "waking too early and being unable to get back to sleep". This relationship persisted after adjusting for gender, age, and race (odds ratio=1.8; 95%CI=1.1, 3.1). Specifically, alpha intrusion could not be shown to be significantly associated with complaints of non-restorative sleep, difficulty falling or staying asleep, joint pains, or leg cramps; elevated ESS scores; psychotropic medication, alcohol, or caffeine use; or chronic health conditions.

Conclusions: In contrast to reports from clinical case series, in the SHHS cohort alpha intrusion was associated with early morning waking, but not complaints of non-restorative sleep.

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0176.B

Interferon Receptor Type I Deficient Mice Have Reduced Spontaneous REM Sleep

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Introduction: While type I IFNs are undetectable by conventional assays in the blood of uninfected animals and humans, numerous observations suggest that type I IFNs are produced continuously by the body, appear in the lymph and could possibly serve as physiological regulators. It has previously been shown that pharmacological doses of IFNa enhance NREM sleep in rabbits and total sleep time in humans. In addition, IFNa has been shown to alter protein regulators of the circadian output rhythm. Our objective was to determine if type I IFNs might play a role in normal physiological processes by assessing spontaneous Tb and sleep states in mice lacking the IFN type I receptor.

Methods: Mice (control 129 SvEv; IFN-RI knockouts on a 129 SvEv background) were implanted with intraperitoneal Minimitters for recording Tb. Stainless steel EEG electrodes were positioned on the dura over the parietal and occipital cortices for sleep/wake determinations. Following surgery, mice were placed in individual cages in a sound-attenuated chamber on a 12:12-h L/D cycle (29 °C) and given at least 7 days to recover. Mice were then connected to lightweight recording cables for habituation to the experimental conditions. After 3 days of habituation, spontaneous Tb and sleep were recorded for 48 hrs and the data from these two days were averaged to determine normal baseline values of Tb and sleep states in control and IFN-RI KO mice. NREMS, REMS and wakefulness were visually scored off-line in 10-s epochs. The average amount of time spent in each vigilant state was calculated in 2-h intervals for graphical representation. Telemetry receivers were placed under individual cages for recording body temperature using VitalView data acquisition software. Following sleep and Tb recording, brainstems were harvested from control and IFN-RI KO mice for analysis of NO synthase levels by real-time PCR.

Results: Body temperatures of control and IFN-RI KO mice did not differ significantly over the 12:12 hour light-dark cycle under normal conditions. Similarly, NREM sleep was not significantly affected at any point in the cycle by the lack of IFN-RI. In contrast, REM sleep in IFN-RI KO mice was significantly reduced (up to 40%) compared to control mice throughout most of the light-dark cycle except during the last 2 hours of the light period and the second 2 hour block of the dark period. Real-time PCR analysis of brainstem NOS showed that IFN-RI KO mice had approximately 2-fold more of each of the three NOS isoforms (I, II, and III) compared to control mice.

Conclusions: IFN-RI is not involved in regulating body temperature or NREM sleep under normal conditions, but the IFN-RI does appear to play a significant role in maintaining normal REM sleep. In addition, the reduced REM sleep observed in IFN-RI KO mice does not appear to be due to reduced NO activity in the brainstem.

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0177.B

Maternal Separation Alters Sleep and Hormonal Responses to Restraint Stress in Adult Mice

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Introduction: In animal models of early life stress, postnatal stress can alter the development of behavioral and endocrine responses to stress. The maternal separation paradigm is frequently used to simulate early life stress in rodents and has been shown to adversely affect neural systems mediating stress reactivity. For instance, rats and mice that were subjected to a maternal separation paradigm as neonates display increased stress-induced corticosterone (CORT) secretion and elevated levels of anxiety. Sleep disturbances may also be among the diverse consequences of early life stress. Therefore, we studied the effects of maternal separation on the sleep-wake cycle and plasma CORT levels under both baseline and acute stress conditions in the in adult mice.
Methods: This study involved male C57Bl/6J mice maintained on a 14:10 light:dark cycle (lights on 4:00) that were divided in three groups. Maternally separated (MS) mice (n=7) were separated from their mother for 3 hours per day from postnatal day 1 through day 14. Handled (H) mice (n=4) were subjected to a neonatal "handling" paradigm for 1 min per day during the same period. Control (C) mice (n=4) remained undisturbed until weaning. At the age of 3 months, the mice were implanted with chronic EEG and EMG electrodes for standard sleep monitoring. After recovery from surgery, sleep was recorded in all animals under baseline conditions and after a 1 hr-period (11:00-12:00) of restraint stress. A 1hr-session of sleep deprivation by gentle handling performed the day before restraint stress served as a control procedure. Two weeks later, plasma CORT levels were determined under baseline conditions and in response to an acute restraint stress.
Results: Preliminary data obtained under baseline conditions indicate no major difference on sleep-wake patterns between the three groups of mice. In response to 1 hr restraint stress, MS mice exhibited an initial decrease in both NREM (-23%, p=0.01) and REM (-54%, p=0.01) sleep time during the remaining 6 hr of the light phase compared to the handling session. This effect was not observed in C and H mice. During the following dark phase, all groups of mice showed significantly increased amounts of NREM (C: +38%; H: +50%; MS: +54%; p=0.001) and REM (C: +159%; H: +90%; MS: +148%; p=0.001) sleep compared to handling. Basal CORT levels in C, H and MS animals were not different but stress-induced CORT secretion differed between the groups. Higher CORT values were observed in both MS (p=0.04) and H (p=0.01) mice relative to C mice, 30 min after the initiation of the stress procedure.
Conclusions: These data indicate that as adults, maternally separated mice show an abnormal sleep response to an acute stress challenge relative to handled and non-handled mice. This may not be specifically related to the stress-induced CORT secretion, since CORT levels are similarly increased in both maternally separated and handled mice.

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0178.B

The Existence Of 'Super-fast' Spindles In Adolescent Girls

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Introduction: The stage 2 sleep spindle in human adults is normally considered to be of a frequency between 12 and 16Hz. The purpose of this study was to investigate and describe sleep spindle characteristics in young adolescent girls.
Methods: Twenty-eight females between the ages of 10 and 14 years (M = 13.5, SD = 0.9) participated in the study. Participants spent two nights in the sleep laboratory, the first being an acclimatization night and the second being used as a baseline night for spindle counts. Sigma power (uV2) was assessed and sleep spindles were counted from the C3 and PZ leads for each page of Stage 2 sleep. Epochs which contained large body movements or artefacts were excluded. Spindles were counted as falling into one of two categories: 1) 11 – 16Hz or 2) greater than 16 Hz. The criteria which had to be met in order to be counted as a spindle were as follows: 1) minimum 0.5 seconds in length; 2) minimum 20uV in amplitude; 3) a frequency of between 11 and 16 Hz or greater than 16 Hz.
Results: Sleep spindles (11 – 16Hz) were found to have durations of between 0.5 and 3 seconds, with the majority (83%) lasting between 0.5 and 1 second. Power spectral analyses suggested that there is more spindle activity in the frontal and parietal regions than in the central regions. This was partially confirmed by the spindle counts themselves which showed a higher spindle density in the parietal region (2.55/min) than in the central region (1.48/min). Spindle activity was also found in the 16 – 19Hz range. These spindles exhibited a similar pattern of activity to the 11 – 16Hz spindles. Again, the majority of these spindles (80%) had a duration between 0.5 and 1 second. A higher spindle density appeared in the parietal region (0.82/min) than in the central region (0.49/min).
Conclusions: The most interesting finding to emerge was the existence of 'super-fast' spindles. These spindles were above the normally assessed range of 11 – 16 Hz with frequencies as high as 19 Hz. In fact, 25% of the observed spindles had frequencies higher than 16 Hz. We have called these EEG events spindles because they correspond with the accepted definition of a sleep spindle in terms of both their shape and sleep stage, differing only in their frequency.

0179.B

Scalp Topography Of The <1Hz Oscillation In The Human Sleep EEG

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Introduction: Studies have shown the existence of a <1Hz. oscillation in the human sleep EEG, which is most prominent during SWS, and is thought to relate to delta activity and K-complex (KC) production. Both KCs and delta frequency (1-4.5Hz.) activity have been shown to be maximal at frontal compared to central and occipital EEG derivations. This analysis investigated the topography of <1Hz. oscillation, specifically between frontal, central and occipital electrode sites.
Methods: Five healthy young men (mean age = 25.2 $\pm$ 1.3yrs.) were studied on three non-consecutive nights. EEG was recorded from 12 scalp sites (Fp1, Fp2, F7, F3, Fz, F4, F8, C3, Cz, C4, O1, O2) referenced to linked ears. Data were recorded using Neuroscan Synamps amplifiers and software with a 1000Hz sample rate and DC-200Hz bandpass. Night 1 was for adaptation. On either the second or third (counterbalanced) night, tones (50msec, 80dBA) were presented with a random ISI (20-35sec) during sleep, irrespective of sleep stage, for examination of evoked K-complexes and sleep auditory evoked potentials. The remaining night served as a 'no-tone' control. After sleep staging the records, the center 20 sec (spline-fitted to 16384 data points) of each 30sec epoch were prepared for spectral analysis using FFT. EEG data were zero-phase shift filtered (3rd order Butterworth, 96dB(A) roll-offs) with a band pass from 0.1-4.5Hz. Average power spectra for SWS were calculated with a frequency resolution of 0.05Hz at three electrode sites (Fz, Cz & O2), and the maximum power value between 0.5 and 1.0Hz, and the mean delta power value (1-4.5Hz) were determined. Data from both nights were analyzed, after no between-night differences were noted, using a 3 (electrode site) by 2 (frequency, <1Hz peak: mean delta power)

repeated measures ANOVA.
Results: There were significant main effects of site F(2,8) = 11.2, p = 0.005, and frequency F(1,4) = 64.5, p = 0.001 and a significant site by frequency interaction F(2,8) = 9.9, p = 0.007. Peak power in the <1Hz. power spectra was largest at Cz (mean = 162.7 ± 47.0 mV2super) followed by Fz (mean = 143.5 ± 48.4 mV\super2) and O2 (mean = 82.0 ± 30.8mV2). Average power across the delta band was maximal at Fz (mean = 12.8 ± 8.4 mV2) decreasing at Cz (mean = 9.4 ± 4.0 mV2) and was smallest at O2 (mean = 3.2 ± 1.5 mV2). Four out of the five subjects demonstrated this pattern of results. Paired comparisons showed that the peak in the <1Hz. power spectra at Cz was significantly larger than at O2 t(4) =4.6, p = 0.01 but not significantly larger than at Fz t(4) = 0.83, p = 0.45.
Conclusions: Whilst the present results should be taken with caution, they suggest that the <1Hz peak may have different anterior-posterior power gradient than 1-4.5Hz delta activities, and probably different to the previously reported distribution of K-complex amplitude. While such a scalp difference does not negate the possibility that the very slow frequency activity is in some way responsible for delta and K-complex generation, it would indicate that the interrelationships are potentially complex.

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0180.B

Evoked K-complex Elicitation At Transitions From Stage 2 To Slow Wave Sleep And Stage 2 To REM Sleep
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Introduction: Recent studies have shown that there is a relationship between spontaneous K-complex production and slow wave sleep (SWS) in humans. The present abstract reports an analysis of the relationship between the K-complex and SWS in the human sleep electroencephalogram. Specifically it sort to extend, using an evoked K-complex paradigm, De Gennaro et. al.'s 2000 finding that increased spontaneous K-complex activity occurred during stage 2 non-REM sleep, prior to transition to SWS compared to transition to REM sleep. It was hypothesized that K-complexes should be easier to elicit during stage 2 non-REM sleep prior to transition to SWS compared to REM sleep.
Methods: Five healthy young men (mean age = 25.2 ± 1.3yrs.) were studied on three non-consecutive nights. EEG was recorded from 12 scalp sites (Fp1, Fp2, F7, F3, Fz, F4, F8, C3, Cz, C4, O1, O2) referenced to linked ears. Data were recorded using Neuroscan Synamps amplifiers and software with a 1000Hz sample rate and DC-200Hz bandpass. Night 1 was for adaptation. On either the second or third (counterbalanced) night, tones (50msec, 80dBA) were presented with a random ISI (20-35sec) during sleep irrespective of sleep stage for examination of evoked K-complexes and sleep auditory evoked potentials. The remaining night served as a 'no-tone' control. After sleep staging, responses to tones presented during stage 2 sleep were classified into two groups based on whether they elicited a K-complex or not. The probability of evoking a K-complex [p(KC)] during stage 2 sleep for the 10 minutes prior to the transition to SWS and REM sleep for each sleep cycle was calculated. Values from all sleep cycles were combined and compared using the Wilcoxon signed ranks test, due to low subject numbers. Data from the second sleep cycle were analyzed separately as it was the most comprehensive data set for an individual sleep cycle.
Results: In the second sleep cycle, the p(KC) in the 10 minutes prior to the transition to SWS was substantially higher than the p(KC) in the 10 minutes prior to the transition to REM sleep [p(KC) sST2-SWSs = 0.92 ± 0.07, p(KC) sST2-REMs = 0.70 ± 0.08], Wilcoxon Z(4) = -1.83, ps(1 tailed)s = 0.034. When data from all sleep cycles were combined, the p(KC) prior to the transition to SWS was again higher prior to the transition to REM sleep [p(KC) sST2-SWSs = 0.92 ± 0.05, p(KC) sST2-REMs = 0.61 ± 0.30]. Wilcoxon Z(5) = -2.23, ps(1 tailed)s = 0.022.
Conclusions: The present results elucidated using an evoked K-complex paradigm are consistent with those previously demonstrated when measuring spontaneous K-complex activity The present data support the hypothesis that whatever mechanisms underlie the development of sufficient delta activity to score SWS are also acting to increase the likelihood of K-complexes being seen in response to external stimuli. These data support the hypothesis first put forward by Loomis and colleagues in 1938 that K-complexes are a 'forerunner' of SWS.

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0181.B

Gastric Myoelectric Changes During REM and Non-REM Sleep in Healthy Volunteers
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Introduction: Previous studies suggest that the normal gastric myoelectric activity is disrupted during sleep. It is unclear which changes may be attributable to sleep as opposed to modulation by a normal circadian rhythm. We describe results of a study which examines gastric myoelectric activity during sleep and during waking in three phases of the circadian cycle.
Methods: 12 young healthy volunteers (6 males and 6 females) underwent surface electrogastrographic (EGG) tests during night time (from 9pm to an hour after awakening). The EGG test was administered 3 separate times on each volunteer, once at 10 pm, approximately 3 am and the final one thirty minutes after the subject awoke. Volume of water ingested was noted during each test. Each EGG recording included 10-15 minutes of baseline tracings on an empty stomach followed by repeat recordings for 30 minutes after a standard water meal. Another two sets of EGG analysis were done during REM and Non-REM sleep that were identified by simultaneous polysomnography. EGG parameters were computed via overall and running spectral analysis.
Results: The percentage of 2-4 cpm activity decreased significantly from Non-REM to REM sleep ($p<0.05$). There was a significant ($p<0.05$) decrease in normal 2-4 cpm activity from 10 pm to 3 am followed by a nearly significant ($p=0.06$) increase in normal 2-4 cpm activity from 3 am to awakening the following morning. Volume ingested declined significantly over the three test periods ($p<0.01$).
Conclusions: 1. Sleep is associated with significant alteration in gastric myoelectric activity which suggests that it is substantially altered by the CNS mechanisms which regulate sleep. 2. There is also an evidence of circadian modulation of gastric myoelectric activity which is independent of the sleep related changes. 3. Gastric visceral perception changes significantly over the circadian cycle.

0182.B

Effect Of Vagus Nerve Stimulation On Sleep Architecture
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Introduction: Vagus nerve stimulation is an innovative therapy for intractable epilepsy. This device appears to stimulate various brainstem nuclei and may alter the regulation of sleep. We previously found, in a small group of patients with epilepsy, a decrease in the number of REM periods during sleep.
Methods: To examine the effect of vagus nerve stimulation on sleep, we performed in laboratory polysomnography on twenty-five patients with

intractable epilepsy before implant and after three months of stimulation. All patients had high intensity, high frequency stimulation. Subjects were asked to reschedule if they had seizures on the day of the recording. The sleep studies were scored according to the Rechtschaffen and Kales criteria. Parameters were compared using a repeated measures analysis.

Results: Three subjects were excluded because of seizures occurring during one of the two nights of polysomnography. The total sleep time, sleep efficiency, sleep latency, REM latency, total time in Stage 1, 2, 3&4, REM sleep and number of REM periods did not significantly change. We found no consistent changes in sleep architecture.

Conclusions: This study failed to show any consistent change in sleep architecture from vagus nerve stimulation, and contradict our earlier findings. The greatest improvement in seizure frequency is seen after two years of stimulation. Future studies of vagus nerve stimulation may require a longer period of stimulation to see potential changes in sleep architecture and sleep parameters.

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0183.B

Effects of a Tryptophan Free Drink Challenge on Normal Human Sleep-A Preliminary Report

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Introduction: Rapid and transient depletion of tryptophan (RTD) may reduce serotonin levels in the brain and enhance rapid eye movement (REM) sleep in normal volunteers with shorter REM latency and greater REM percentage (REM%). In our previous studies, some normal subjects were responders, others non-responders. This study investigates the relationship between the RTD induced REM sleep change and the serotonin transporter gene.

Methods: Nineteen healthy male subjects (age 18 to 50) without personal or family history of Axis I disorder joined the study. They drank a tryptophan-free drink and a control drink containing tryptophan in double-blind, random orders on separate days. The effects were assessed with mood rating, plasma tryptophan concentrations, and an all-night sleep polysomnography.

Results: The ANOVA with repeated measures failed to demonstrate statistically significant effects on any REM sleep measures.

Conclusions: These results do not support our earlier paper by T. Bhatti et al that the RTD disinhibited REM sleep in normal controls. On contrast, however, RTD has consistently reduced REM latency and increased REM% in euthymic depressed patients treated with selective serotonin reuptake inhibitors (P.Moore et al), bupropion (L. Evans et al), the MAOI phenelzine (H. Landolt et al), and unmedicated euthymic patients with a history of mood disorder who were treated with group cognitive behavioral therapy (in preparation). Contrary to other RTD studies in euthymic medicated patient, RTD in our experience did not reverse antidepressant benefits.

0184.C

The Effects of Sodium Oxybate on Clinical Symptoms and Sleep Patterns in Fibromyalgia

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Introduction: Fibromyalgia is associated with the sleep phenomenon of alpha intrusion, and with low growth hormone secretion. Sodium oxybate has been shown to increase both slow-wave sleep and growth hormone levels. This double-blind, randomized, placebo-controlled, crossover trial was conducted to evaluate the effects of sodium oxybate on the subjective symptoms of pain, fatigue, and sleep quality and the objective polysomnographic (PSG) sleep parameters of alpha intrusion, slow-wave (Stage 3 & 4) sleep, and sleep efficiency in fibromyalgia patients.

Methods: Patients selection criteria included a history of fibromyalgia meeting ACR guidelines, a lack of clinically significant OSA or PLMS and the presence in at least 3 of NREM sleep epochs of alpha intrusion. Patients received either 6.0 g/d sodium oxybate or placebo for 1 month, with an intervening 2-week washout period. Efficacy measures included PSG evaluations, tender point index (TPI), and subjective measurements from daily diary entries. Safety measures included clinical laboratory values, vital signs, and adverse events.

Results: Twenty-four female patients were included in the study; 18 completed the trial. TPI was decreased from baseline by 8.5, compared with an increase of 0.4 for placebo ($p=0.0079$). Six of the 7 pain/fatigue scores (overall pain, pain at rest, pain during movement, end of day fatigue, overall fatigue, and morning fatigue) were relieved by 29% to 33% with sodium oxybate, compared with 6% to 10% relief with placebo ($p<0.005$). Alpha intrusion, sleep latency, and REM sleep were significantly decreased, while slow-wave (Stage 3 & 4) sleep was increased significantly, compared with placebo ($p<0.005$). Two of the 5 subjective sleep-related variables were significantly different from placebo – morning alertness (improved by 18% with sodium oxybate, compared with 2% for placebo; $p=0.0033$) and quality of sleep (improved by 33% and 10%, respectively; $p=0.0003$).

Conclusions: In this study, sodium oxybate effectively reduced the symptoms of pain and fatigue in fibromyalgia, and dramatically reduced the sleep abnormalities (alpha intrusion and decreased slow-wave sleep) associated with the non-restorative sleep characteristic of this disorder. Alpha intrusion was extremely stable across baseline nights and did not show a first night effect, suggesting a potential diagnostic value for sleep clinician.

0185.C

Treatment Of Severe Morning Sleep Inertia (SI) With Bedtime Sustained-Release (SR) Methylphenidate, Bupropion-SR, Or Other Activating Agents

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Introduction: SI is characterized by inarousability from sleep or by confusional arousals with inappropriate behavior. B. Roth et al. (Arch Gen Psychiatry, 1972) stated that SI "can be much alleviated by one tablet [of stimulant drugs] before going to bed." However, "some patients do not sleep well after administration of the drugs before retiring." (SR-stimulants were not available then). The treatment of SI has subsequently received scant attention in the medical literature.

Methods: Over 10 years, 22 clinical referrals presented with longstanding (usually life-long) severe morning SI, with major consequences at work, N=12; at school, N=4; interpersonally, N=3; and with child care, N=2, or personal medical care, N=1, responsi- bilites. Besides clinical exams, all pts (save one) had polysomnography & multiple sleep latency tests.

Results: Females, 63.6% (N=14), mean age, 33.4 $\pm$(SD) 14.1 yr (range, 18-62); males, 36.4% (N=8), mean age, 33.2 $\pm$ 12.7 yr (range, 17-50). Associated psychiatric disorders (usually in substantial remission), 68.2% (N=15: usually non-psychotic mood/anxiety disorders). Associated sleep disorders, 40.9% (N=9; 1 pt had 3 disorders): obstructive sleep apnea, n=3; narcolepsy, n=3; DSPS, n=2; parasomnia, n=2; periodic limb movement disorder (PLMD), n=1. The severe a.m. SI had long

antedated the onset of any associated disorder and its Rx, and had persisted despite control of any associated disorder. All pts with psychiatric disorders continued with their pharmaco- therapies. Most pts tended to be long sleepers. Rx data: 86.4% (19/22) of pts responded substantially/ completely to nightly hs stimulant Rx. Mean follow-up, 2.7 ± 2.6 yr (range, 0.5-10 yr): methylphenidate-SR, N=12 (20-40 mg; n=1 also took fluoxetine, 60 mg q hs, strictly as a stimulant; n=1 took 40 mg at 8 a.m. to induce a full awakening at 9:30 a.m.; hs use had caused >5 hr sleep latency); bupropion-SR, N=5 (100-300 mg; n=1 also took methylphenidate-SR q hs); methylphenidate, N=1 (10 mg in a 16 yr old with DSPS); modafinil, N=1 (200 mg); tranylcypromine [Parnate], a monoamine oxidase inhibitor, N=1 (60 mg). (The latter agent was used after all other stimulants were unsuccessful in this non-depressed pt). Stimulant abuse did not occur. Adverse effects, 15.8% (N=3): sleep disruption, N=1 (not severe); prolonged sleep latency, N=1 (described above); PLMD aggravation, N=1 (controlled with gabapentin).

Conclusions: Our findings confirm and extend those of Roth on the efficacy of hs stimulant Rx for severe a.m. SI, and are consistent with findings that SI can often be found with other hypersomnia disorders and psychiatric disorders (Ohayon et al., 1999;2000). Nevertheless, SI may require separate treatment.

0186.C

Effect of Mirtazapine on Genioglossus Activity In the Anesthetized Rat

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Introduction: Activity of the genioglossus (GG), a tongue protruder, is believed to be important for maintaining upper airway patency. This muscle is innervated by the hypoglossal nerve (CN XII). Hypoglossal augmentation of GG activity is believed to be mediated by the action of serotonin (5HT) at type 2 receptors (2a > 2c) on hypoglossal motornuclei. If so, then serotonin type 2 receptor antagonists would be expected to decrease GG activity. Mirtazapine, a widely used antidepressant, has 5HT2 receptor antagonist activity (should decrease GG activity). However, the medication also increases 5HT and blocks 5HT3 receptors (should increase GG activity). For example, systemic administration of ondansetron, a 5HT3 blocker, has been shown to increase hypoglossal activity. Therefore, mirtazapine has a number of actions with potentially opposite effects on GG activity. The net effect of mirtazpine on GG activity has not been determined.

Methods: Either saline or mirtazapine was administered to adult male Sprague-Dawley Rats 300-500 gm (N = 7 in each group). The rats were anesthetized with 1.2 gm/kg urethane IP followed by tracheostomy and placement of femoral arterial and venous lines. Fine wire hook electrodes were inserted into the GG and into the diaphragm (subcostal approach). The raw EMG signals were amplified, filtered (50-1000Hz), rectified, and integrated to obtain a moving time average (MTA). The rats were spontaneously breathing a hyperoxic mixture. The raw and MTA EMG of the GG and Diaphragm (Dia) and arterial blood pressure were digitally recorded. Bilateral vagotomy was performed below the insertion of the superior laryngeal nerves. Once blood pressure and respiration were stable (at least 15 minutes after vagotomy), a baseline period was recorded. Then either saline or 5mg/kg of mirtazapine was injected IP. Measurements were made of the peak MTA EMG activity for 10 breaths every 10 minutes for 3 hours. The data for each hour were averaged (means ± SEM) and expressed as a percentage of the baseline (pre-injection) period.

Results: In both the control (C) and mirtazapine (M) groups GG activity decreased from baseline values during the monitoring period whereas diaphragmatic activity remained fairly constant or increased slightly. Mirtazapine reduced the peak moving time average activity of the genioglossus over the 3 hour period compared to the saline control,P <0.05. Mean data as % of baseline are as follows: First hour: M: 30.3 ± 7.2 versus C: 64.3 ± 6.0%; Second hour: M: 43.4 ± 8.0 versus C: 62.4 ± 7.5%; Third hour: M: 46.5 ± 8.1 versus C: 60.0 ± 7.2%. Mirtazapine also decreased the diaphragm activity(P<0.05): First hour: M: 94.3± 0.9 versus C: 98.4 ± 1.9%; Second hour: M:100.4 ± 4.3 versus C: 105.8 ± 3.2%; Third hour: M: 98.8 ± 4.1 versus C: 109.5 ± 3.4%. Arterial blood pressure remained stable over the monitoring period.

Conclusions: Mirtazapine induced a decrease in both GG and diaphragm activity over 3 hours that was larger for the GG. We hypothesize that at least in this model, the effects of 5HT2 blockade appear to predominate over the other effects of mirtazapine. It is possible that either vagotomy or anesthesia may alter the net effect of mirtazapine on GG activity. Thus, the relevance of these findings with respect to mirtazapine induced changes in GG activity during sleep remain to be determined.

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0187.C

A Safety, Tolerance, and Pharmacokinetic Study of Five Single Doses of TAK-375 in Healthy Adults

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Introduction: TAK-375 is a novel, selective ML-1 receptor agonist being evaluated for treatment of insomnia and circadian rhythm sleep disorders. This study of TAK-375 was conducted in healthy adult volunteers to assess safety, tolerance, pharmacokinetic parameters, cognitive performance, and alertness.

Methods: Sixty subjects (age, 35-65 years) were randomly assigned to receive 1 of 5 doses of TAK-375 (4, 8, 16, 32, and 64 mg; n=8 per dose group) or placebo (n=20). Each subject received a single oral dose of drug or placebo. As this was an ascending dose study, the group receiving the lowest dose was treated first. Subsequent groups were treated in an ascending manner if no limiting adverse events were experienced at the lower doses. Subjects were monitored and confined to the clinic beginning the evening before drug administration and ending 24 hours after. Study drug was administered in the morning (following a 10-hour fast), and subjects were exposed to normal indoor light for 12 hours after drug administration. Blood samples were obtained at regular intervals for 16 hours post administration. Performance measures were the digit symbol substitution test (DSST) and a visual analog scale (VAS) of alertness (measured 1, 2, 3, 4, 6, and 8 hours postdose). Safety measures included recording of adverse events and vital signs, electrocardiograms, and standard laboratory tests.

Results: Mean AUC and Csmaxs values for TAK-375 increased with dose (AUCs0-infs = 1.7, 7.0, 9.9, 22.5, and 36.1 hr-ng/mL, respectively; Csmaxs = 1.1, 5.7, 6.9, 17.4, and 25.9 ng/mL, respectively). In contrast, mean Tsmaxs remained relatively constant with dose (Tsmaxs = 0.78, 0.75, 0.79, 0.88, 0.94 hr, respectively). The mean elimination half-life was short and somewhat dose dependent (Ts½s = 0.83, 1.36, 1.28, 1.59, and 1.90 hr, respectively). When AUC and Csmaxs were normalized according to dose, there were no significant differences across the 5 dose groups (P>0.2), suggesting that the pharmacokinetics were essentially proportional to dose. The parent compound (TAK-375) was extensively metabolized. AUC values indicated that the most prevalent metabolite was M-II, followed by M-IV, M-I, and M-III, respectively. Half-lives of each metabolite were comparable across dosing groups. Urinary excretion of unchanged drug was less than 2% of the dose. Mean DSST and VAS scores were similar across all dose groups and did not differ from placebo. All adverse events (AEs) were mild or moderate in intensity and resolved before study completion. The most common AEs were somnolence and nausea, each reported by 2 subjects.

Conclusions: At all doses studied, subjects administered TAK-375 exhibited AEs of only mild or moderate intensity, which subsequently

resolved. In addition, subjects exhibited no evidence of cognitive impairment. AUC and Csmaxs were approximately proportional to dose. Further clinical development of TAK-375 as a selective ML-1 receptor agonist is warranted based on the initial pharmacokinetic profile.

0188.C

Acute Bedtime Administration Of Zolpidem Does Not Induce Residual Daytime Driving Impairment Compared To Zopiclone In Primary Insomniac Subjects: Preliminary Results In 16 Patients

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FORENAP

Introduction: The therapeutic efficacy of hypnotic drugs must not only be considered by its ability to improve sleep but also by its possible residual effects the next morning, such as vigilance impairment or daytime sedation. Zolpidem (Stilnox) is a strong sedative, shown to be effective in inducing and maintaining sleep in insomniac subjects. The objective is to evaluate, in primary insomnia patients, the effects of acute and repeated administrations of zolpidem on daytime driving performances, wake electroencephalogram and neurocognitive functions by comparing with placebo, zopiclone or lormetazepam administration. Here are presented preliminary results obtained on driving performances.
Methods: Acute and repeated (7-day) doses of zolpidem (10 mg), zopiclone (7.5 mg), lormetazepam (1 mg) and placebo were administered at bedtime (10:30 p.m.) in a randomized double-blind, cross-over study to subjects with primary insomnia (men and women; aged from 18 to 65 years). Patients should 1) be healthy except for primary insomnia, 2) have had, during the month preceding the screening visit, at least two of the three following symptoms: sleep onset latency greater than 30 minutes for at least 4 nights each week and/or 60 minutes or more being awake after sleep onset for at least 4 nights per week and/or daytime impairment due to sleep disturbance, 3) have usual bedtime, 4) have a valid driving license. During each period, a driving simulator session was performed on day 2, at T+8h30 after the first administration and on day 8 at T+8h30 after the last administration. The task consisted on driving one hour on a motorway with no traffic. Driving performance was evaluated by the analysis of absolute speed and deviation from ideal route parameters. Treatments were statistically compared by use of a 3-way analysis of variance (sequence, period, and treatment) and contrasts between each treatment for each time measurement, and placebo were evaluated (MIXED of SAS procedure).
Results: Preliminary results were reported on sixteen patients [5 men and 11 women, age (mean $\pm$SEM): 34.6$\pm$2.4] (out of a total of 24). On Day 2 (i.e. 8h30 after the first dosing), absolute speed was significantly ($p<0.05$) decreased under zopiclone compared with zolpidem and placebo (mean $\pm$SEM: 119$\pm$3 km.h-1, 122$\pm$2 km.h-1 and 125$\pm$3 km.h-1, respectively). Similarly, deviation from the ideal route was impaired only after acute administration of zopiclone (mean $\pm$SEM: -0.7$\pm$0.4 meters vs -0.3$\pm$0.1 meters, and -0.2$\pm$0.1 meters, for zolpidem and placebo, respectively). By contrast, no significant residual effects were detected after repeated administration of zolpidem or zopiclone.
Conclusions: As preliminary conclusions, zopiclone, 7.5 mg impaired driving performances 8h30 after single administration, whereas zolpidem 10 mg did not induce residual effects the next morning when administered at bedtime. This absence of first night effect may suggest that zolpidem could be preferred to zopiclone for discontinuous use.

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0189.C

Long-Term Exposure To Zaleplon Is Safe And Effective In Younger-Elderly and Older-Elderly Patients With Primary Insomnia

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Introduction: Multiple studies have confirmed the safety and efficacy of zaleplon, an oral non-benzodiazepine sedative hypnotic agent, in the treatment of primary insomnia in the general adult population, and several studies have demonstrated the lack of cognitive and psychomotor residual effects in as few as two hours after administration. One published study specifically addressed the efficacy and safety of this agent in older individuals. This paper reports the results of the open-label extension phases of two randomized, double-blind trials.
Methods: Data were collected at 36 centers in the United States and 50 centers in Europe. 316 US patients and 170 European patients continued into the open-label-phase. The mean age was 73.3 years (range=65-86 years; SD=5.3) in the United States and 71.8 years (range=59-95 years; SD=6.8) in Europe. Patients self-administered zaleplon nightly from 6 to 12 months and were then followed through a 7-day single-blind placebo-controlled run-out period. Patients were assessed monthly by sleep diary and with physician visits with included sleep questionnaires and physical examinations. The data were aggregated and analyzed separately for patients 65-69 years (younger elderly patients) and patients 70+ (older elderly patients).
Results: Latency to persistent sleep, sleep duration and number of awakenings all improved significantly during open-label treatment relative to baseline ($p<0.001$ for each variable). Moreover, although statistically different changes were observed between open label and day 1 run out assessments, ($p<0.001$ for each variable), none of the sleep values obtained during the 7-day run out phase approached the original baseline levels ($p<0.001$ for each variable). No significant changes were observed between any of the days during the 7-day run out period. Finally, there were no differences between the younger-older and older-older patients. Treatment-emergent adverse events most frequently associated with discontinuation of drug were pain (n=29, 5%), somnolence or dizziness (n=23, 4%), gastrointestinal changes (n=11, 2%), cardiovascular changes (n=8, 1%).
Conclusions: The data indicate that long-term zaleplon therapy induces statistically significant improvement in time to persistent sleep onset, duration of sleep, and number of nocturnal awakenings without rebound insomnia upon discontinuation. The safety profile of zaleplon when administered in doses of 5 mg and 10 mg nightly at bedtime to community-dwelling adults aged 65 through 95 years was similar to that observed in a short-term trial of an equivalent population. There were no significant differences between the younger elderly and the older elderly. Within each variable, changes seen during open-label therapy and the placebo run-out phase never approached baseline levels.

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0190.C

Efficacy and Tolerability of Four Doses of Indiplon (NBI-34060) Modified-Release in Elderly Patients With Sleep Maintenance Insomnia

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Introduction: Indiplon is a non-benzodiazepine sedative-hypnotic that modulates activity of the GABA-A receptor. The parent compound has a mean T1/2 of ~1.5 hrs, and the modified release formulation has an extended duration of sedative activity. We report here results from a dose-response study with indiplon modified-release in elderly patients with chronic sleep maintenance insomnia.

Methods: : A randomized, double-blind, placebo-controlled, Latin-square design was used at 15 sites to investigate four indiplon modified-release doses (10/20/30/35 mg), and placebo (PBO). Three polysomnography (PSG) screening nights assured patients met entry criteria, including wake after sleep onset (WASO) >40 minutes; total sleep time (TST) 240-390 minutes on at least two nights; total wake time (TWT) >60 minutes on all nights. Seventy-nine patients with DSM-IV primary insomnia characterized by at least three-month history of sleep maintenance difficulty were randomized. Sixty patients completed all conditions and are included in this report (19m, 41f; mean age: 69.1+3.1 yrs). Six randomized patients discontinued with adverse effects (none serious); three had protocol violations or scheduling problems. Ten patients were excluded from analysis prior to unblinding because of deviations from entry criteria. Randomized patients received each dose of study drug before PSG on two consecutive nights. Time in bed was 8 hours. Residual effect measures administered approximately 30-minutes after PSG termination included digit symbol substitution test, symbol copying test and a visual analog scale for sleepiness. Repeated measures ANOVAs, followed by paired comparisons, were used to compare conditions.

Results: Mean sleep efficiency (SE) for the 0/10/20/30/35 mg doses was 74.0, 75.9, 80.0, 81.3 and 81.0% (three higher doses, p=<0.0001 vs. PBO). The change in SE was the result of significant reduction in a) latency to persistent sleep (LPS) for all indiplon doses and b) WASO at the three higher doses. Specifically, the mean LPS values in ascending dose order were: 26.0, 17.6, 11.2, 11.0, and 9.9 minutes (all p<0.01 or better vs PBO). WASO declined from 103.2 on PBO to 102.1, 87.3, 81.9, and 83.0 minutes (three higher doses p<0.01 or better vs PBO). The number of PSG awakenings during the night and all subjective measures of sleep showed significant differences from PBO for all four doses of indiplon. There was a modest effect on DSST at the highest doses (mean change from placebo was 2.5 substitutions). VAS and SCT showed no next-day residual effects compared to placebo.

Conclusions: Indiplon modified-release at the 20 mg to 35 mg doses significantly improved sleep maintenance and sleep onset PSG measures of DSM-IV diagnosed primary insomniacs. The 10 mg dose also showed efficacy in subjective endpoints.

Research supported by Neurocrine Biosciences.

0191.C

The Cognitive-Enhancing Properties of Modafinil are Limited in Non Sleep- Deprived Middle-Aged Volunteers

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Introduction: Modafinil is a selective wakefulness-promoting drug, licensed in the UK for EDS in narcolepsy and OSAHS. Whilst it has been shown to improve cognitive performance in conditions of sleep deprivation its effects in normal young volunteers have been equivocal. The present study investigated effects on mood and cognition in middle-aged volunteers who were not sleep-deprived.

Methods: Forty-five healthy volunteers (20 men and 25 women, aged 50-67 years) were randomly allocated to placebo, or modafinil (100 or 200 mg) and 3 h later completed visual analogue scales of mood and bodily symptoms before and after an extensive battery of cognitive tests, including several from the Cambridge Neuropsychological Test Automated Battery (CANTAB).

Results: There were no significant treatment-associated changes in mood or bodily symptoms. There were no significant differences between the three treatment groups on three tests of executive function (Stockings of Cambridge, Verbal Fluency, Trail Making Test B), episodic memory (e.g. Delayed Matching to Sample, Logical Memory), Category Fluency or attention (e.g. Trail Making Test A, Rapid Visual Information Processing). Modafinil significantly improved the time taken to complete the colour naming part of the Stroop test ($F(2,27) = 4.0$, $p<0.05$) and post-hoc tests showed that this was due to the 200 mg dose differing significantly from placebo ($p<0.02$). In the interference part of the Stroop test there was a significant treatment x IQ interaction ($F(2,33) = 4.0$, $p<0.05$). There was better performance in the subjects with lower IQ treated with the 200 mg dose. Modafinil also significantly improved constructional ability, with the 200 mg group obtaining a better score in Clock Drawing compared with the placebo group ($U = 51.5$, $p<0.05$). In one test, there was evidence that modafinil produced cognitive impairment. Subjects in the 200 mg group made significantly more total errors in the Intra/Extra Dimensional Set Shift (executive function) than the 100 mg and placebo groups ($U = 44$, $p<0.005$; $U = 59$, $p<0.05$ respectively) and also more errors at the extra-dimensional shift stage than the 100 mg group ($U = 60$, $p<0.05$). Analysing total errors adjusted for the number of stages successfully completed, there was a dose-related increased error rate, primarily affecting the lower IQ female volunteers (treatment x sex x IQ interaction, ($F(2,33) = 3.6$, $p<0.05$).

Conclusions: This study found limited evidence of cognitive-enhancing properties with 200 mg modafinil in middle-aged volunteers who were not sleep-deprived and the possibility that these effects could have arisen by chance cannot be excluded. There was some evidence that both the positive and negative cognitive effects of modafinil were IQ related. In contrast with the increased anxiety previously seen in young volunteers after 100 mg, modafinil (100 & 200 mg) had no effect on the mood or bodily symptoms of our middle-aged subjects.

0192.C

Low Cholinergic Tone During Slow-Wave Sleep Is Crucial For Sleep-Related Consolidation Of Declarative Memories

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Introduction: The neurotransmitter acetylcholine (ACh) is thought to be critical for proper memory functioning. Reduced central cholinergic tone is found under conditions of impaired memory, like Alzheimer's disease, and is the basis for pharmacological treatments of such memory deficits. While the cholinergic tone is high during wakefulness and REM sleep, it drops to a minimum during slow-wave sleep (SWS). However, SWS is a period of enhanced declarative memory consolidation. This study examines the effects of increased central cholinergic tone during SWS on hippocampus-dependent (declarative) and hippocampus-independent (non-declarative) memory.

Methods: 12 healthy, male subjects aged 18–35 years received an infusion of physostigmine (0.75 mg over 2 h) dissolved in 50 ml of saline solution beginning with sleep onset on one night, and 50 ml of saline solution (placebo) on another, according to a randomized, double-blind cross-over design. Before sleep, the subjects learned a declarative

paired-associate wordlist task and a non-declarative mirror tracing task. After 3 h of sleep, subjects were awakened and recall testing took place 30 min thereafter. Throughout the whole duration of the experiment, blood samples were taken half-hourly via long plastic tubes from an adjacent room without disturbing the subjects' sleep. Blood concentrations of ACTH, cortisol, and glucose were determined. In a second experiment, a group of 10 subjects received the same treatment and tasks at the same time of day as in the first experiment, but stayed awake between learning and recall.

Results: The central finding is that during sleep recall performance for hippocampus-dependent memory distinctly decreased after administration of physostigmine as compared to placebo (7.5±1.5% vs. 16.25±2.1% increase in word recall after sleep; $P<0.001$). Physostigmine thus reduced recall performance during sleep to a level comparable to that during wakefulness, eliminating the enhancing effect of sleep on declarative memory. During wakefulness recall performance did not change significantly after physostigmine administration (5.5±1.7% vs. 3.0±3.1%; n.s.). The hippocampus-independent mirror tracing task was not affected by physostigmine administration. Sleep parameters showed a slight decrease in sleep depth after physostigmine administration (Wake: 1.7±0.7% vs. 2.2±1.3%, n.s., physostigmine vs. placebo; S1: 10.1±2.3% vs. 6.5±2.3%, n.s.; S2: 49.1±3.1% vs. 44.3±3.1%, n.s.; SWS: 23.3±1.7% vs. 32.1±3.0%, $P<0.05$; REM: 14.5±1.7% vs. 13.4±2.2%, n.s.). Concentrations of cortisol, ACTH, and glucose did not differ between conditions.

Conclusions: The results show a specific effect of physostigmine on sleep-related consolidation of hippocampus-dependent memory. While during wakefulness a decrease of central acetylcholine is known to impair hippocampal memory encoding, during SWS an increase of acetylcholine impairs declarative memory consolidation. Hippocampus-independent memory is not affected by physostigmine during either wakefulness or sleep. This result is in accordance with theories supposing that during wakefulness, high cholinergic tone permits the encoding of new information into the hippocampus. During slow-wave sleep, the low cholinergic tone enables the transfer of that information to the neocortex and thus promotes memory consolidation.

0193.C

TAK-375 and Its Metabolites Are Selective Agonists at MLs1s Receptors

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Introduction: The MLs1s receptor is located in cells of the suprachiasmatic nucleus and is thought to mediate the circadian rhythm effects of endogenous melatonin in mammals. Exogenous melatonin, proposed as a treatment for some sleep disorders, has been associated with side effects, possibly related to its binding to other receptor subtypes in other brain regions. Initial studies have suggested that TAK-375 is a novel, highly selective agonist at MLs1s receptors, showing little affinity for numerous other receptors, including MLs2s. This receptor selectivity may result in the ability of TAK-375 to induce and maintain a physiologic sleep, with few side effects and no abuse potential. The purpose of this study was to examine the binding specificity of TAK-375 and its major metabolites for MLs1s and MLs2s receptor subtypes in vitro.

Methods: Binding affinities of TAK-375 and its metabolites were measured by conventional binding assays utilizing displacement of 2-[125I]-melatonin. MLs1s receptor assays were performed using tissue isolated from the chick forebrain, known to be rich in MLs1s receptors. MLs2s receptor assays were performed using hamster brain tissue, known to be rich in MLs2s receptors. Cyclic AMP production assays were performed using Chinese hamster ovary (CHO) cells expressing the human MTs1s (MLs1as) gene (hMel R7-58 cells).

Results: TAK-375 exhibited high affinity for the MLs1s receptor from chick brain (Ksis, 0.0254 nM) and low affinity for the MLs2s receptor from hamster brain (Ksis, 2600 nM). The selectivity of TAK-375 for MLs1s over MLs2s was more than 1000-fold greater than that of melatonin, as melatonin had a lower affinity for MLs1s receptors (Ksis, 0.399 nM) and substantially higher affinity for MLs2s receptors (Ksis, 27.6 nM). Of the TAK-375 metabolites, the most abundant in human serum is M-II, which also has the highest affinity for MLs1s receptors. Like its parent compound, the active metabolite M-II exhibited high selectivity for MLs1s receptors (Ksis, 0.675 nM) over MLs2s receptors (Ksis, >9000 nM). None of the tested metabolites exhibited substantial affinity for MLs2s receptors. Both TAK-375 and M-II inhibited forskolin-stimulated cAMP production in CHO cells expressing the human MTs1s gene, with ICs50s values of 10.8 and 159 pM, respectively.

Conclusions: TAK-375 is a novel, highly selective agonist at the MLs1s receptor, showing more than 1000-fold higher selectivity over the MLs2s receptor compared with melatonin. Although the major metabolites of TAK-375 bind to MLs1s receptors with lower affinity than the parent compound, they also are highly selective for the MLs1s receptor over the MLs2s receptor. Clinical trials are ongoing to assess the efficacy and safety of TAK-375 for treatment of insomnia and circadian rhythm sleep disorders.

0194.C

TAK-375 and Its Active Metabolite: Lack of Binding to Non-ML Receptor Binding Sites

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Introduction: Common therapies for insomnia or circadian rhythm sleep disorders (CRSDs) often have undesirable side effects related to activity at benzodiazepine or opiate receptors. TAK-375, a novel agent currently being evaluated in clinical trials for treatment of insomnia and CRSD, is a highly selective MLs1s receptor agonist, exhibiting only weak affinity for MLs2s receptors. In this study, we examined the binding affinities of TAK-375 and its active metabolite (M-II) to other potential active binding sites such as receptors for neurotransmitters, peptides, and cytokines, as well as ion channels and various enzymes. Specifically, we were interested in receptors known to affect cognitive function and abuse liability.

Methods: Conventional binding assays were used to measure the affinities of TAK-375 and M-II for a large number of binding sites from a variety of tissues. Agents were initially tested at a concentration of 10 mM to measure displacement of a radiolabeled high-affinity ligand at the binding site of interest. If any binding was detected at this concentration, then other concentrations were tested to determine an approximate binding affinity. In addition, the ability of TAK-375 and M-II to interfere with any of a large number of enzyme activities was studied using well-characterized substrate reactions.

Results: TAK-375 showed no measurable affinity for any of a large number of ligand binding sites, including benzodiazepine, dopamine, and opiate receptors. Although melatonin showed weak affinity for Ds1s and 5-HTs1As receptors, TAK-375 showed no evidence of such binding. M-II showed affinity for only one site, the 5-HTs2Bs receptor; however, the affinity was low (Ksis, 1.75 mM). Such low-affinity binding is unlikely to have clinical relevance owing to the low concentrations of parent compound required for activation of MLs1s receptors. Also, TAK-375 and M-II had no effect on any of various enzyme activities.

Conclusions: TAK-375 is a highly selective agonist for MLs1s receptors with no activity at any of a large number of other potential binding sites. These results are consistent with behavioral studies demonstrating that TAK-375 exerts sleep-promoting action without causing learning and memory impairment, motor dysfunction, and drug-abuse ability.

0195.C

Sleep in Freely Moving Monkeys: Comparison of TAK-375, Melatonin, and Zolpidem

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Introduction: TAK-375, a novel, selective high-affinity agonist at MLs1s receptors, is under investigation for the treatment of insomnia and circadian rhythm sleep disorders (CRSDs). We studied the effects of TAK-375, exogenous melatonin, and the non-benzodiazepine hypnotic agent zolpidem on nocturnal sleep in freely moving monkeys using recordings of behavior, eye movement, electromyograms, and electroencephalogram (EEG).
Methods: Twenty-two young adult female macaques were housed individually, kept on a 12-hour light/dark cycle, and fed once daily. Under anesthesia, electrodes were placed on the dura mater, in the superoexternal side of the orbit, and in the cervical back muscles. After a 1-month recovery, animals were habituated to the recording chamber. Electrodes were connected to recording equipment using a lightweight, flexible cable that allowed free movement. Recordings were initiated at 17:00, and study drug (suspended in 0.5% methylcellulose solution) was administered orally just before lights were turned off at 18:00. Each test session consisted of control (vehicle administered), active drug, then control again. Some animals participated in more than one session if they were in sufficient condition to record EEG.
Results: Treatment with TAK-375 (0.003, 0.03, and 0.3 mg/kg, p.o.) shortened the latency to sleep onset in a dose-dependent manner. Although melatonin (0.3, 1, and 3 mg/kg, p.o.) also decreased the latency to sleep onset, the effect was not dose-dependent. TAK-375 increased total duration of sleep; however, melatonin had no significant effects. Treatment with TAK-375 and melatonin had no observable effect on behavior. In this study, zolpidem (1, 3, 10, and 30 mg/kg) had no significant effect on latency to sleep onset. Although the highest dose of zolpidem tended to increase the duration of slow-wave sleep, it did not increase total duration of sleep. At the highest zolpidem dose, 3 of 4 animals exhibited sedation and muscle relaxation. EEG recordings during sleep were analyzed with fast-Fourier transform. TAK-375 and melatonin had no effect on the power spectrum; however, zolpidem increased high-frequency components (>14 Hz) during non-REM sleep.
Conclusions: TAK-375 significantly reduced latency to sleep onset in freely moving monkeys without altering the EEG waveform or causing observed behavioral changes. Clinical trials of TAK-375 for the treatment of insomnia and CRSDs are ongoing.

0196.C

Effect of the Centrally Acting Wake-Promoting Agent Modafinil on Blood Pressure and Heart Rate

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Introduction: Excessive sleepiness is common in patients with narcolepsy, obstructive sleep apnea (OSA) and shift work sleep disorder (SWSD). Although studies demonstrate that the centrally acting wake-promoting agent modafinil reduces sleepiness and improves quality of life in each of these conditions, the cardiovascular effects have not been reported. Because of a theoretical link of CNS stimulants to hypertension and tachycardia, we evaluated the effects of modafinil on blood pressure and heart rate from randomized, placebo-controlled trials.
Methods: In seven randomized placebo-controlled trials, patients had assessment of systolic and diastolic blood pressure (SBP and DBP) and heart rate (HR) (narcolepsy: 2 studies, 548 patients, OSA: 3 studies, 462 patients, and SWSD: 2 studies, 443 patients). All studies excluded patients with uncontrolled hypertension or tachycardia. Because of the high prevalence of hypertension in OSA (58% in these studies), these patients were grouped into quartiles based on their BP prior to therapy and grouped according to whether they were diagnosed with hypertension. For the entire population, and for the analysis of OSA patients by quartile, changes in SBP, DBP and HR were calculated as the difference between baseline value and last measured value (on therapy).
Results: Analysis across all studies revealed no significant changes during modafinil therapy compared to placebo in SBP (95% CI: -0.4, 2.4), DBP (95% CI: -0.4, 1.6) or HR (95% CI: –9.4, 1.3) during treatment of 4-12 weeks. Changes (mean±SD) from baseline to endpoint in SBP, DBP and HR were -0.3 ± 13.2, -0.4 ± 9.1 and 0.1 ± 11.1, respectively, in modafinil-treated patients (n=902) and -1.3 ± 12.8, -1.0 ± 9.0 and -0.1 ± 10.1 mm Hg, respectively, in placebo-treated patients (n=551). Similarly, neither blood pressure nor heart rate was affected significantly by modafinil compared to placebo therapy in OSA patients whose baseline blood pressure was in the higher quartiles. Modafinil did not adversely affect BP or HR in patients with a diagnosis of hypertension at baseline.
Conclusions: Modafinil therapy was not associated with clinically relevant changes in BP or HR in patients with excessive sleepiness associated with narcolepsy, OSA, or SWSD, even in patients with controlled hypertension. Therefore, despite central nervous system effects, modafinil is a rational therapy even in patients with cardiovascular diseases.

Research supported by Cephalon Pharmaceuticals, Inc.

0197.C

Effect of Age and Gender on the Pharmacodynamics of TAK-375: Tests of Sedation, Psychomotor Function, and Memory

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Introduction: TAK-375 is a selective ML-1 receptor agonist currently under evaluation for the treatment of insomnia and circadian rhythm sleep disorders. Because many individuals with insomnia are elderly, the issues of altered sensitivity to sleep-inducing drug effects and adverse reactions are of clinical concern. The present study evaluated the influence of age and gender on the pharmacodynamics of single doses of TAK-375.
Methods: A total of 48 healthy subjects participated, divided into 4 groups (n=12 per group): young male and female, aged 18-34 years, and elderly male and female, aged 63-79 years. In a randomized double-blind, single-dose, two-way crossover study, subjects received 16 mg of TAK-375 or placebo in the morning on two occasions, separated by at least one week. Self and observer ratings of sedation, and the digit-symbol substitution test (DSST), were done prior to dosing and at multiple time points during the next 24 hours. The word-list test of information acquisition and recall was done at 1.5 and 24 hours after dosing.
Results: Area under the 8-hour curve of pharmacodynamic effect (change over baseline) versus time was compared between TAK-375 and placebo conditions. There were no statistically significant differences between TAK-375 and placebo in young males, young females, or elderly males for measures of observer-rated sedation, self-rated sedation, or DSST scores. The same was true for elderly females on the observer-rated sedation measure. However, TAK-375 was significantly different from placebo ($p<0.05$) in elderly females for self-rated sedation (increase) and DSST score (decrease). There were no differences between TAK-375 and placebo on the test of information acquisition and recall in any of the subject groups. The incidence of adverse events was similar between age groups, and between males and females, with the most common adverse event being somnolence.
Conclusions: In young males, young females, and elderly males, TAK-375 16 mg and placebo were not significantly different for measures of observer-rated sedation, self-rated sedation, memory, or DSST scores. For elderly females, there were no significant differences in observer-

rated sedation or memory. There was a statistically significant effect of TAK-375 on self-rated sedation and DSST scores in elderly females; however, the differences from placebo were quantitatively small.

0198.C

Age and Gender Effects on the Pharmacokinetics of TAK-375

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Introduction: TAK-375 is a selective ML-1 receptor agonist currently under evaluation for the treatment of insomnia and circadian rhythm sleep disorders. Because many individuals with sleep disorders are elderly, the effects of age on the pharmacokinetics of TAK-375 were evaluated in a clinical study.
Methods: A total of 48 healthy subjects participated, divided into 4 groups (n=12 per group): young male and female, aged 18-34 years; and elderly male and female, aged 63-79 years. Subjects received a single 16-mg dose of TAK-375 in the morning 90 minutes after a light breakfast, followed by blood sampling during the next 24 hours. Plasma concentrations of TAK-375 and its principal metabolite (M-II) were analyzed by liquid chromatography-mass spectroscopy. Pharmacokinetic parameters for TAK-375 and M-II were determined by model-independent methods.
Results: In all subjects, TAK-375 had a half-life of less than 3.7 hours and high oral clearance. Comparisons of elderly males to young males showed that elderly males had higher mean area under the plasma concentration curve (AUC) (17.0 vs. 7.7 ng/mL x hr, $p<0.1$), lower clearance (381 vs. 757 mL/min/kg, $p<0.05$), longer half-life (1.6 vs. 1.2 hours, $p<0.1$), and no significant difference in peak plasma levels (Csmaxs) (12.0 vs. 5.9 ng/mL, NS). Findings were similar for comparisons of elderly females to young females for AUC (19.8 vs. 12.9 ng/mL x hr, $p<0.1$), clearance (387 vs. 1009 mL/min/kg, $p< 0.05$), half-life (2.2 vs. 1.3 hr, $p<0.05$) and Csmaxs (11.4 vs. 9.5 ng/mL, NS). AUCs for the M-II metabolite, which has about 1/50 the activity of the parent drug, greatly exceeded AUCs for TAK-375; age effects on M-II kinetics were similar. The incidence of adverse events was similar between age groups, and between males and females, with the most common adverse event being somnolence.
Conclusions: Regardless of gender, elderly subjects, on average, experienced higher systemic exposure of TAK-375 compared to young subjects, although individual variability was high.

0199.C

The Co-Administration of Indiplon (NBI-34060) and Alcohol Lacks Pharmacokinetic and Pharmacodynamic Interactions

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Introduction: Although not recommended, alcohol and sedative hypnotics are commonly taken in combination leading to changes in pharmacokinetics (PK) and additive impairment. This study examines the effect of alcohol on the pharmacodynamics (PD) and PK of indiplon. Indiplon is a novel non-benzodiazepine GABA-A modulator under development for sleep initiation and sleep maintenance insomnia in transient and chronic insomnia populations.
Methods: This randomized, placebo-controlled, double-blind, three-way crossover study was conducted in ten healthy males. Subjects were randomized to a treatment sequence using a Latin square design such that all subjects received indiplon (10mg), EtOH (0.7mg/mL), and a combination of the two. Indiplon (or placebo) was administered thirty minutes prior to alcohol (or placebo) ingestion. Blood samples were collected over eight hours and indiplon plasma levels were measured by a validated HPLC-MS-MS method. Pharmacodynamic assessments of performance (digital symbol substitution test (DSST) and symbol copying test (SCT)), subjective sedation (visual analog scale of sleepiness (VAS)), and reaction time (Psychomotor Vigilance Reaction Task (PVT)) were conducted at pre-dose and 1, 2, 4, 6, 8 hours post-dose.
Results: Indiplon PK was not affected by alcohol (peak plasma level=10ng/mL at one hour, half-life=1.3 hours; all p-values >0.05). Indiplon or alcohol alone produced comparable reductions in performance at maximal effects (DSST=-15.2 and -11.5, respectively, and SCT=-29.7 and -37.4, respectively). As expected, indiplon alone produced a greater increase than alcohol alone in measures of subjective sedation (VAS=+25.7 and +11.1, respectively) and reaction time (PVT=+53.7 and +20.9, respectively). There was a small non-additive reduction in performance when alcohol was added to indiplon (DSST=-20.0, and SCT=-34.7), however, sedation and reaction time remained unchanged (VAS=+17.1 and PVT=+51.8).
Conclusions: The absence of any significant PK interaction is not unexpected since different pathways metabolize the compounds: ethanol by alcohol dehydrogenase and CYP2E1, and indiplon by carboxyesterase and CYP 3A4. However, the finding of little or no additive interaction effects on accepted measures of performance, subjective sedation, or reaction time, and no additional side effects, is in contrast to other studies with alcohol and benzodiazepines or non-benzodiazepines. In conclusion this acute single dose study indicates that there is little or no interaction effect when alcohol is co-administered with indiplon (10 mg).

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0200.C

Significant Effects On Sleep Of Low Dose Mirtazapine In Patients With Primary Insomnia

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Introduction: The most prominent complaints in primary insomnia are difficulty falling asleep, difficulty maintaining sleep and unrefreshing sleep. Pharmacotherapeutic hypnotic treatment today is mainly targeted on gabaminergic transmission. Mirtazapine (15-45mg) showed sleep promoting effects in clinical studies both in healthy subjects and in depressed patients. The current study was a multi-center, multi-country, randomized, double-blind study to assess the hypnotic effects and safety of three low doses of mirtazapine as compared to temazepam and placebo in outpatients with primary insomnia.
Methods: Patients could be included if they were 18-65 years of age, with a diagnosis of primary insomnia (DSM-IV) and having at least two out of the following three characteristics: 1) sleep latency > 30 and < 90 min; 2) number of awakenings ≥ 3/night; 3) total sleep time £ 6.5 hours. After a single-blind placebo washout period of one week, eligible patients entered a double-blind treatment period of 14 days. They were treated once daily with an oral evening dose (30 min before lights-off) of either 0.5 mg, 1.5 mg or 4.5 mg mirtazapine, 20 mg temazepam, or placebo. During a single-blind placebo run-out period of one week possible rebound and withdrawal effects were recorded. Efficacy was assessed by means of an 8-hour nocturnal polysomnography (PSG) in the sleep lab. Main PSG variables were sleep efficiency , sleep latency, total waking time, total sleep time, and total slow wave sleep (stages 3+4).
Results: A total of 168 patients were treated with study medication of which 154completed the in-treatment period. Sleep efficiency

(TST/8hrs) was determined to be the primary efficacy criterion. Statistical procedures for the intent-to-treat population analysis included ANCOVA to control for the participating sleep centers. After 14 days of treatment, low dose mirtazapine showed a statistically significant increase of about 7% in sleep efficiency (change from baseline) as compared to placebo (p=0.013) and temazepam (p=0.02).
Conclusions: During a period of 14 days, the hypnotic efficacy of low dose mirtazapine given before bedtime is superior over placebo in primary insomniacs. Both mirtazapine and temazepam were well tolerated in this study.

0201.C

Modafinil Attenuates the Decline in Frontal Lobe Function During Simulated Night Shift

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Introduction: Reduced alertness during night shift and the associated risk of errors and impaired performance remains an intractable problem for many industries and occupations. Therefore, we studied the effects of the alerting drug modafinil (MOD) on executive function during usual night shift hours in a simulated shift work protocol.
Methods: 32 subjects (15 male, 17 female; mean age 31.5; range 18-55) participated in a parallel groups, double-blind, repeated measures design. Written informed consent was obtained. All subjects were free of medical and psychiatric disorders, kept a regular sleep schedule, habitually consumed < 10 alcoholic drinks/week and < 400mg caffeine/day, and did not take CNS active medications. A standard PSG adapted subjects to laboratory procedures and excluded those with sleep disorders. A daytime MSLT excluded individuals with a mean latency of < 5 minutes. Prior to randomization, subjects were trained on performance tests and maintained a regular sleep wake schedule. Either MOD 200mg or placebo (PBO) was given at 2200 hours each night during a 4-night/4-day simulated night shift schedule. From 2300 until approximately 0700 each night, subjects engaged in a variety of performance tests, alertness measures and a cognitive testing battery. This report includes results for the cognitive testing battery. Tests included were the Wisconsin Card Sorting Test (WCST), Torrance Tests of Creative Thinking-Verbal (TTCT-V) and Figural (TTCT-F), Category Test (CT), Optimal Telegram (OT), Anagrams, Thurstone Word Fluency (TWF), Sentence Completion (SC), and Letter Number Sequencing (LNS). MANOVAs on the difference scores between baseline and treatment were used to analyze TTCT-V and TTCT-F variables. MANOVAs were conducted on the WCST, OT, CT variables. T-tests were conducted on all other variables.
Results: Though performance on TTCT-V and TTCT-F was worse for both groups during the night shift compared to baseline, the MOD group performed less poorly during treatment than the PBO group on the TTCT-V. A main effect for group (p = .015) was significant as were univariate F tests for subscales of verbal flexibility and originality. The mean decline in flexibility standard scores were -2.62 and -16.38 for MOD and PBO, respectively, and for originality were -1.44 and -9.93 for MOD and PBO, respectively. On the WCST, fewer overall errors were made in MOD (106.1 standard score; p=.005) than PBO (90.9), as well as fewer errors of perseveration (MOD= 110.9, PBO = 93.5; p=.007). MOD made fewer perseverative responses (4.5; p=.043) on SC than PBO (7.5). No group differences were found for TTCT-F, OT, CT, TWF, or LNS.
Conclusions: These data suggest that modafinil 200mg reduces the decline in some executive functions during the night shift.

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0202.C

Sedative Effects of Codeine

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Introduction: Sedation is a frequently reported side effect of opiates. Studies of opiate effects have been done using subjective assessments and performance tests with inconclusive results. Further, many of the studies have not included a positive control whereby the extent of the sedative effects can be evaluated. Using the Multiple Sleep Latency Test (MSLT) studies have shown the sedative and performance disruptive effects of a reduced (2-6 hrs) bedtime the previous night. Thus, the present study, using the MSLT, assessed the sedative effects of low dose codeine in comparison to the effects of four and zero hours time in bed (TIB).
Methods: Six healthy, normal adults, 21-35 yrs old, participated. All were in good medical and psychiatric health with no history of alcoholism or drug abuse. All had sleep efficiencies >85% on a screening 8 hr NPSG with no evidence of primary sleep disorders and an average sleep latency of >8 min on a standard MSLT conducted on the following day. Each underwent four conditions presented in a Latin Square design: 8 hrs TIB + placebo, 8 hrs TIB + codeine 60 mg bid, 4 hrs TIB + placebo, and 0 hrs TIB + placebo. In the 8 hrs TIB conditions bedtime was set to 2300-0700 hrs, in the 4 hrs TIB 0300-0700 hrs, and in the 0 hrs TIB no sleep was allowed. The following day after arising at 0700 hrs and a breakfast (0800-0830 hrs) each participant received codeine 60 mg or placebo at 0900 and 1300 hrs. A standard MSLT was conducted at 1000, 1200, 1400, and 1600 hrs. Pain threshold for a radiant heat stimiulus was assessed at 1030 and 1430 hrs.
Results: Pain threshold on the am and pm testing was increased significantly by codeine 60 mg (bid) ($F_{1,5} = 7.28$, $p<.04$). The average daily sleep latency in the 8 hrs TIB + placebo condition was 12.4 ($\pm$ 3.3) min which was reduced to 6.8 ($\pm$ 2.1) in the 8 hrs TIB + codeine, 4.6 ($\pm$ 1.4) in the 4 hrs TIB + placebo, and 3.4 ($\pm$ 2.8) in the 0 hrs TIB + placebo conditions. The four conditions differed significantly ($F_{3,12} = 12.8$, $p<.001$) with each differing from the 8 hrs TIB + placebo condition in post hoc contrasts ($p<.01$).
Conclusions: The results of this study indicate that codeine 60 mg bid has a mildly sedative effect. It reduces average daily sleep latency on the MSLT from that found after 8 hrs of sleep the previous night, but not to that level found after 4 hrs of sleep. While 60 mg (bid) codeine produces mild sleepiness, higher doses and the interaction of codeine with disease related sleep loss and fragmentation needs further clarification.

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0203.C

Modafinil Treatment In Patients With Opiate-Induced Sedation

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Introduction: Opioids are among the most effective analgesics for the treatment of chronic pain. However, the use of opioids is often limited by side effects, particularly sedation, which may impair physical and cognitive functioning. The novel wake-promoting agent modafinil, which acts selectively through the sleep/wake centers of the brain, has been shown to improve cognitive functioning in several models of excessive sleepiness. This study was conducted to assess the effect of modafinil treatment in patients who experience sedation associated with opiate treatment for chronic pain.
Methods: This single-center, double-blind, placebo-controlled, random-

ized, parallel-group pilot study included 30 patients with chronic pain who had been receiving opioids for ³ 3 months. Patients were required to have at least moderate sedation on the Clinical Global Impression (CGI) of Severity scale that was associated with opioid use. Patients were randomized to modafinil (100-400 mg/day) or placebo treatment for 6 weeks. Efficacy assessments included the Trail Making Parts A and B for cognitive function and CGI of Change (CGI-C) for sedation, the Epworth Sleepiness Scale, and the Fatigue Severity Scale, and were performed at baseline and Weeks 1, 2, and 6.

Results: Of the 30 patients randomized, 25 patients (83.3%) completed the study (93.3% modafinil; 73.3% placebo). Modafinil improved cognitive function, as assessed by the Trail Making Parts A and B. Mean changes (±SD) from baseline at the last visit in the time to complete Trail Making Part A were –0.251 ± 0.32 and –0.004 ± 0.15 in the modafinil and placebo groups, respectively ($P < .01$). Modafinil significantly reduced time to completion on Part A compared with placebo at Weeks 2 and 6 ($P < .05$). Modafinil improved the mean (±SD) time to completion of Trail Making Part B compared with placebo (–0.5 ± 0.93 and –0.1 ± 0.27 for modafinil and placebo, respectively), although the difference was not statistically significant. ESS scores at endpoint were not significantly different between treatment groups. However, modafinil improved overall clinical condition with respect to sedation (demonstrated by CGI-C) in a higher proportion of patients than placebo, although the difference between treatment groups did not achieve statistical significance. At the last visit, 12 (80%) of the 15 patients in the modafinil group were at least improved on the CGI-C, compared with only 8 (53%) of the 15 patients in the placebo group. Modafinil was well tolerated; the most common adverse events reported were nausea (20% modafinil and 20% placebo) and nervousness (20% modafinil and 13% placebo).

Conclusions: Modafinil significantly improved cognitive function compared with placebo in chronic pain patients with opiate-induced sedation. Modafinil also improved overall clinical condition with respect to sedation in a greater proportion of patients than placebo. Modafinil was well tolerated. Further research is warranted to elucidate similarities and differences between symptoms of sedation and excessive sleepiness as well as the differential effects of modafinil in chronic pain patients.

0204.C

Methylphenidate Self Administration and Sampling State of Sleepiness

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Introduction: Our studies showed methylphenidate (ME) improved alertness and performance in sleepy [4 hrs time in bed (TIB)], but not alert (8 hrs TIB) people; normals chose ME (5 20 mg) 54-80% of days after a 4 hrs TIB, but only 28-35% of days after a 8 hrs TIB; and those rating themselves most sleepy were most likely to self administer ME. These results suggest ME is a reinforcer (i.e. chosen more than placebo) and its reinforcing function is restoring alertness to sleepy people. In these studies subjects experienced ME in both an alert (8 hrs TIB) and sleepy state (4 hrs TIB) during sampling. To further investigate the reinforcing function of ME, the present study was conducted to determine how the experience of ME in a sleepy vs alert state during the sampling period would alter subsequent ME choice.

Methods: Fourteen healthy, 21-45 yrs old, volunteers in good medical and psychiatric health with no history of alcoholism or drug abuse participated. All had sleep efficiencies >85% on a screening 8 hr NPSG with no evidence of primary sleep disorders and a MSLT > 8 min the following day. They were randomized to a 4 hrs or 8 hrs TIB sampling group in which they received placebo and ME 20 mg in color coded capsules on 4 consecutive sampling days (2 placebo and 2 ME) at 0900 hrs. After sampling each subject chose their preferred capsule by color code on 4 consecutive days after both a 4 hrs and a 8 hrs TIB. Color coding, placebo vs drug sampling days, and 4 hrs vs 8 hrs choice days were counterbalanced. The 3 study phases (sampling, choice 8 hrs and choice 4 hrs) were each separated by 3-7 recovery days.

Results: Overall the sleepy group choose ME 48% of days and the alert group 43% of days (NS). The only circumstance in which ME was preferred to placebo was in the sleepy group after the 4 hrs TIB (58%). That is, the group that experienced ME in a sleepy state choose ME on average 2.29 (± 1.80) of the 4 choice days of the 4 hrs TIB and 1.57 (± 1.27) days in the 8 hrs TIB ($t=2.28$, $p<.06$). The alert sampling group choose ME on 1.43 (± 1.62) of the 4 hrs TIB days and on 2.00 (± 1.40) of the 8 hrs TIB days (NS).

Conclusions: The results indicate sampling while sleepy and thus, experience of ME's alerting effects, alters its self administration pattern. For the sleepy group ME was a reinforcer after a 4 hrs TIB, but not a 8 hrs TIB, while for the alert group ME was never a reinforcer regardless of TIB. This further confirms that the reinforcing function of ME in normals without a drug abuse history is restoration of alertness and function in a sleepy state.

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0205.C

Is the Increase of the Amplitude of the Auditory N1-P2 an Specific Effect of the Hypnotic Zolpidem?

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Introduction: The zolpidem (Z), an imidazopyridine derivative, is a hypnotic with a distinct biochemical structure in relation to the benzodiazepines (BDZs), with relative selectivity for the type 1 receptor subtype or 1. Acute drug effects can be observed by neurophysiological measures such as event-related evoked potentials (ERPs) and electroencephalogram (EEG).The aim of the present study was to investigate the acute effects of clinical oral doses of the hypnotic zolpidem in young normal volunteers in neurophysiological measures (ERPs and EEG).

Methods: This was a double blind, independent group study of single oral doses of Z. Thirty-six subjects were randomly assigned to one of 3 treatments: placebo, 5mg and 10mg of Z and were tested before and after treatment (in two occasions: 45 and 105 minutes after). The ERP latencies and amplitudes were measured at Fz, Cz and Pz ("oddball paradigm"). The EEG was registered in 16 EEG epochs (1024 points, 250 samples/s intervals) and were recorded at Pz, which were referenced to the right earlobe (A2), and bandpass filtered from 0.5 to 100 Hz. The 16 power spectra were averaged resulting in the final power spectrum of the total EEG recording. Five specific frequency bands were chosen for analysis: 1.0-3.5 Hz (delta), 4.0-7.5 Hz (theta), 8-13Hz (alpha), 13.5-18 Hz (beta 1) and 18.5-40 Hz (beta 2).

Results: Zolpidem led to a progressive, dose-related increase in the latency of N200 and P300 at Fz, Cz and Pz. N200- P300 inter-peak amplitude decreased at Fz, Cz and Pz (for both doses), but, surprisingly, the N1-P2 inter-peak amplitude increase at Fz and Cz after the highest dose. EEG frequency band beta1 increased (for the highest dose), but not significant differences were noted in alpha, theta or delta bands.

Conclusions: The explanation of the finding of N1-P2 inter-peak amplitude is complex, and some hypothesis can be raised: a) this in an specific effect of Z, probably related to the differential binding profile to the benzodiazepine receptor. b) there was an opposition effect between the controlled versus automating processing of the auditory information. When the controlled influence decreases, there are an increase of the automatic ones. This is a fact also observed in neglect patients . c) this is a feature linked to the sleep onset; d) the enhanced N1 response could be reflecting a general increase in sensory sensitivity associated with the arousal factor of the orienting response.Overall, all the EEG and ERPs results were similar to those described with benzodiazepines, except the

N1-P2 amplitude. This finding with zolpidem suggest that it is a characteristic that maybe related to its selectivity receptor binding profile and warrants further investigation.

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0206.C

The Activity of Modified Release Indiplon (NBI-34060) in a Transient Nighttime Venipuncture Model

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Introduction: Transient insomnia models have been used to investigate the activity of sedative hypnotics in normal healthy subjects, using first night effect, phase advance (2-3 hours) or a combination of both. However, both induce difficulties in sleep initiation and are not designed to affect sleep maintenance. Indiplon is a novel non-benzodiazepine GABA-A receptor modulator currently under development as a hypnotic agent for the treatment of insomnia. As part of our development of modified release indiplon we used a "venipuncture" model of insomnia, impairing sleep initiation and sleep maintenance, as well as providing nighttime pharmacokinetics (PK).
Methods: Young healthy male volunteers (n=36) aged 19-42 years took part in this placebo- controlled, parallel, double-blind randomized study. Subjects were administered tablets of placebo (PBO) or 40mg of modified release indiplon at 10 pm. Blood samples (n=16) were withdrawn throughout the night. Plasma drug concentrations were measured using a validated HPLC-MS-MS method. On awakening eight hours after study drug administration, subjects completed a sleep diary to capture latency to sleep onset (LSO), total sleep time (TST), number of awakenings after sleep onset (NAASO), and sleep quality. Next day residual effects were assessed using Digit Symbol Substitution Test (DSST), Symbol Copying Test (SCT), and the Visual Analog Scale of sleepiness (VAS).
Results: Subjective assessments of sleep showed that this model significantly disrupts normal sleep patterns as compared to standards cited in the literature. Indiplon modified release significantly improved both sleep initiation (LSO: indiplon = 30.2 minutes, PBO = 72.2 minutes; $p<0.001$) and sleep duration (TST: indiplon = 315.6 minutes; PBO = 246.6 minutes; $p=0.02$). Not unexpectedly, the number of awakenings was reduced, but not significantly, due to the multiple blood sampling. Sleep quality was significantly improved with indiplon compared to placebo ($p=0.04$). Indiplon was rapidly absorbed, reaching therapeutic levels of 5 ng/mL in 30 minutes and remaining above this level for 6-7 hours. There were also no changes in any of the next day residual effects tests compared with baseline. There was no difference in the incidence or profile of adverse events between treatment groups.
Conclusions: Models of insomnia in healthy volunteers for sleep maintenance are not well described and have relied on sleep disruption by noise. The results presented here suggest that this venipuncture model is appropriate for the assessment of both sleep initiation and maintenance of a hypnotic drug, as well as providing relevant nighttime PK measurements. This study specifically shows that modified release indiplon, with its formulated characteristics of an initial rapid release followed by a slower all-night release component, can significantly improve sleep quality, sleep initiation, and sleep maintenance, without next day residual effects.

Research supported by Neurocrine Biosciences, Inc.

0207.C

REM Latency and Sleep Architecture in Recreational Marijuana Users

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Introduction: Marijuana has been proposed as a sleep aid for insomniacs and for persons whose sleep is disrupted by pain. Yet the acute and chronic effects of marijuana on sleep have not been empirically reported for over 25 years, and these data have been inconsistent. Some of these prior studies have reported acute THC-induced decreases in REM sleep and REM rebound during THC withdrawal. However, the extent to which recreational marijuana use in non-dependent adults alters sleep architecture is unknown.
Methods: Twenty-seven non-dependent marijuana users (7 F, 20 M, mean [SEM] age = 25 [1.1]; average self-reported use = 13 of past 30 days) and seven normal controls (2 F, 5 M; mean [SEM] age = 23 [0.5]) completed a single acclimation night in a sleep laboratory. Bed and wake times were individually assigned based on mean data from 1-3 weeks of sleep diaries. Marijuana users were instructed to abstain for approximately 35 hours before assigned bedtime. Sleep latency, sleep efficiency, total minutes and percent time in each sleep stage, arousal index and awakenings were measured by polysomnography. To quantify daytime sleepiness, the Epworth Sleepiness Scale, Stanford Sleepiness Scale, and MSLT procedures were completed 1.5 and 3.5 hours after awakening. Group means were compared with t tests. When the data were not normally distributed, Mann-Whitney Rank Sum Tests were used.
Results: Average [SEM] total sleep time (7.5 [0.1] hours for users, 7.6 [0.3] hours for controls) and sleep efficiency (93.8 [0.7]% for users, 94.0 [1.8]% for controls) did not significantly differ between groups. Sleep latency, sleep architecture, awakenings, arousal index, and measures of daytime sleepiness also did not significantly differ between groups. The median [interquartile range] REM latency for users (79.5 [64.3-118.3] minutes) was significantly longer than that for controls (60.0 [56.8-61] minutes; $p<0.04$).
Conclusions: Recreational marijuana use is associated with extended REM latency but not reduced REM sleep. Whether residual anticholinergic actions of THC are directly responsible for this phenomenon is worthy of future study.

Research supported by NIDA Grant 12137

0208.C

Modafinil Improves Symptoms Of Cocaine Withdrawal And Treatment Retention In Patients With Cocaine Dependence

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Introduction: Cocaine withdrawal is associated with severe sleepiness, fatigue, and psychomotor retardation. The wake-promoting agent modafinil has low abuse potential and been shown to reduce fatigue and improve wakefulness and psychomotor retardation in major depression patients with sleepiness and fatigue. Modafinil is hypothesized to improve outcome in cocaine dependence by normalizing cocaine-induced neuroadaptations, increasing activity in the frontal cortex, and reversing cocaine withdrawal symptoms such as cognitive dysfunction and sleepiness. We recently reported that modafinil also blunts cocaine-induced euphoria under controlled conditions. This pilot study evaluated modafinil for treatment of symptoms associated with cocaine withdrawal and as relapse prevention for cocaine dependence.
Methods: This open-label pilot study included a 1- to 2-week inpatient treatment phase and an 8-week outpatient treatment phase. The study included 13 cocaine-dependent subjects with severe cocaine withdraw-

al, as measured by the Cocaine Selective Severity Assessment (CSSA). Subjects were randomized to receive modafinil 200 mg/day (n = 8) or 400 mg/day (n = 5) given as a single morning dose. Subjects received twice-weekly cognitive behavioral therapy (CBT) and twice-weekly research evaluations to evaluate tolerability and clinical outcome. Cocaine use was measured twice weekly by urine testing for the cocaine metabolite, benzoylecgonine (BE). Abstinence was defined as the number of BE negative urines supplied, divided by the total possible urines that could be submitted (16), and treatment retention was defined as the percent of scheduled assessments attended. For benchmarking purposes, abstinence and retention rates were compared with those of 23 placebo-treated subjects with high CSSA scores who were enrolled in another cocaine study at our center.

Results: Baseline CSSA scores of patients in the modafinil (mean 46.7, SD 13.8) and placebo (mean 37.0, SD 14.4) groups were consistent with severe cocaine withdrawal (CSSA ³22). In the in-patient treatment phase, modafinil rapidly reversed symptoms of cocaine withdrawal. In the outpatient phase, modafinil-treated subjects had higher abstinence (48%) and retention (74%) rates when compared to benchmark placebo-treated subjects (6.5% and 43%, respectively). Five modafinil-treated subjects produced 100% negative urines throughout the study, and 7 produced 100% negative urines after the first 3 weeks. Three modafinil-treated subjects had perfect attendance at outpatient visits and 2 missed only one visit each. Modafinil was well tolerated; no serious adverse events occurred, and none of the 13 modafinil-treated subjects discontinued due to adverse effects.

Conclusions: Our results suggest that modafinil should be further evaluated as treatment for cocaine dependence under controlled conditions.

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0209.C

Safety and Efficacy of Immediate Release Indiplon (NBI-34060) in Elderly Patients with Insomnia

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Introduction: Indiplon is a novel non-benzodiazepine GABA-A receptor modulator currently under development as a sedative-hypnotic agent for the treatment of sleep initiation and sleep maintenance insomnia in transient and chronic insomnia patient populations. The pharmacokinetic (PK) profile of indiplon, in contrast to some other sedative-hypnotic agents, is not different between young adult and elderly patients. The objective of this study was to explore the efficacy, safety, and dose response of immediate release indiplon in elderly chronic insomnia patients.

Methods: This randomized, placebo-controlled, double blind, multi center, four-period crossover study assessed three dose levels of indiplon (5, 10, and 20 mg) relative to placebo in elderly patients with DSM-IV primary insomnia. All patients underwent three PSG screening nights to confirm the diagnosis of primary insomnia, and eligible patients were randomized to receive a sequence of all four treatments. Efficacy was assessed objectively via PSG parameters, and subjectively through questionnaires during four treatment periods. Each period consisted of two nighttime PSG sessions. Hypnotic efficacy was evaluated objectively via latency to persistent sleep (LPS) and total sleep time (TST), and subjectively via latency to sleep onset (LSO). Next-day residual effects were assessed using the Digit Symbol Substitution Test (DSST), Symbol Copy Test (SCT), and Visual Analog Scale of sleepiness (VAS).

Results: Data are reported on 42 elderly patients (mean age 70 years; range 65-82 years). Indiplon demonstrated a significant improvement in mean LPS, with values of 13.8, 10.4, and 9.8 minutes for 5mg, 10mg, and 20mg, respectively, versus 25.2 minutes for placebo (p ¡Ü 0.001). Significant improvements in mean TST were also demonstrated for the 10 mg ($p = 0.027$) and 20 mg ($p < 0.001$) groups, with values of 363.7, 372.1, and 385.6 minutes for 5mg, 10mg, and 20mg, respectively, versus 354.4 minutes for placebo. Subjective assessments of mean LSO were significantly improved, with values of 28.8, 24.7, and 20.2 minutes, respectively, versus 41.8 minutes for placebo ($p<0.004$). There was no difference at any indiplon dose level on DSST, SCT, and VAS compared to placebo, and indiplon was well tolerated at all dose levels with no serious adverse events or discontinuations related to adverse events.

Conclusions: The immediate release formulation of indiplon appears to be an effective treatment for elderly patients with sleep initiation difficulties and is well tolerated at doses up to 20 mg, with next day residual effects similar to placebo.

Financial support and study drug provided by Neurocrine Biosciences, Inc.

0210.C

Lack of Pharmacological and Pharmacokinetic Tolerance Following Repeat Dosing of Indiplon (NBI-34060)

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Introduction: Repeated dosing of the early generations of barbiturates and benzodiazepines results in pharmacokinetic and pharmacological tolerance. This reduced effect over time leads to the need for increasing doses for equivalent effect. This is due to a combination of drug enzyme induction (pharmacokinetic tolerance - PKT) and reduced activity (pharmacodynamic tolerance - PDT). Indiplon is a novel non-benzodiazepine GABA-A receptor modulator currently under development as a sedative-hypnotic for the treatment of sleep initiation and sleep maintenance insomnia in transient and chronic insomnia populations. In this study, the safety, PKT and PDT following repeat daily dosing of indiplon were investigated after 14 consecutive days of administration.

Methods: Young healthy male subjects (n=30), 22-41 years of age participated in this randomized, placebo-controlled, double-blind, parallel-group study. Subjects were administered matching capsules of placebo, or 10 mg, 30 mg or 45 mg of indiplon each morning (0800 h) for 14 days. Quantitative EEG (qEEG) and pharmacodynamic tests (PD) were administered. Blood samples were collected up to 12 hours post-dose, and indiplon plasma levels were measured using a validated HPLC-MS-MS method.

Results: Indiplon was rapidly absorbed within 1 to 2 hours and rapidly eliminated from 1 to 2.5 hours at the highest dose. PK parameters were comparable between Day 1 and Day 14 at all indiplon dose levels, suggesting no change in kinetics and metabolic clearance after repeated dosing. An examination of the qEEG measures revealed a consistent and dose-related decrease in the amplitude of both the occipital and cortical alpha 1 wave, and an increase in the amplitude of frontal cortical beta 1 waves. There was also a smaller reduction in amplitude of occipital theta waves. Collectively, this pattern of qEEG changes is often seen with all sedative-hypnotics. The changes seen on day 1 were similar on Day 14 of administration for all indiplon doses indicating no PD tolerance. There were also no dose-related changes in digit symbol substitution tests (DSST) or critical flicker fusion (CFF) tests with repeated dosing.

Conclusions: PK/PD analysis confirmed that 14 consecutive days of dosing with indiplon did not result in either PK or PD tolerance. This study has also demonstrated that low levels 5ng/mL and above can induce changes in qEEG indicative of sedative effects, which has formed the basis for the design of indiplon modified release formulations. Indiplon was well tolerated up to 45 mg, when administered for 14 consecutive days, with no serious adverse events or adverse event related

discontinuations.

Research supported by Neurocrine Biosciences, Inc.

0211.C

Evaluation of the Sleep-Activity Profile of Pregabalin Compared With Alprazolam in Normal Volunteers

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Introduction: Pregabalin is an alphas2s-delta (as2s-d) ligand that exhibits analgesic, anxiolytic, and anticonvulsant activity. The current study was designed to evaluate the effects on sleep and daytime activity levels of pregabalin (PGB) compared with placebo (PBO) and alprazolam (ALP).
Methods: 24 volunteers with normal and stageable sleep were randomized, double-blind, to a 3-way crossover study (including a 7-day washout). Wrist actigraphy (WA) and sleep EEG (after adaptation) were performed serially during each treatment condition.
Results: On actigraphy, PGB was associated with modest but significantly greater activation compared with ALP. Both PGB and ALP modestly but significantly reduced time-to-sleep-onset ($P<0.02$) and improved sleep efficiency compared with PBO (in a normal volunteer sample with no sleep complaints). But the most notable differences were that PGB was associated with significantly less increase in REM latency compared with ALP, while PGB significantly ($P<0.001$) increased slow wave sleep (stage 3/4: 23% increase) compared with both ALP and PBO.
Conclusions: Pregabalin appears to have an effect on sleep and sleep architecture that distinguishes it from benzodiazepines. Enhancement of slow wave sleep is intriguing, since reductions in slow wave sleep have frequently been reported in GAD.

Research supported by Pfizer, Inc

0212.C

The Sleep-Promoting Effects of Gamma-Hydroxybutyrate (GHB) are Partially Blocked by the GHB Receptor Antagonist NCS-382

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Introduction: Gamma-hydroxybutyrate (GHB) can induce slow wave sleep in humans and has been shown to have sleep-enhancing properties in rodents as well. However, despite the existence of specific GHB binding sites in the brain, the mechanism by which GHB induces sleep is not known. A number, but not all behavioral and electrophysiological effects of GHB in rats are blocked by the selective GHB receptor antagonist NCS-382, suggesting that either GHB may act directly through specific receptor sites or indirectly by modulating other neurotransmitter systems such as GABA and dopamine. The aim of the present study was to test the hypothesis that the sleep-promoting effects of GHB in rats are mediated through GHB receptors by applying GHB in the presence of the GHB receptor antagonist NCS-382.
Methods: Pharmacological treatments were performed in adult male Sprague-Dawley rats which were chronically implanted with EEG and EMG electrodes for standard polygraphic sleep monitoring. In a first experiment, the rats received different doses of NCS-382 (20, 30, 50, 100 or 250 mg/kg i.p., n=4-6 animals per dose) administered at the onset of the dark phase. In a second experiment, the rats were injected with NCS-382 (20 or 30 mg/kg, n=7 animals per dose) 30 min before dark onset, and then with GHB (200 mg/kg i.p.) at the onset of the dark phase. Sleep-wake and EEG power spectra (Fast Fourrier Transform) values were compared to those obtained in the same animals receiving the appropriate vehicle (saline) injections under the same conditions.
Results: Administration of NCS-382 produced a dose-dependent decrease in both NREM and REM sleep from the dose of 30 mg/kg onwards. Animals treated with 200 mg/kg GHB alone showed an initial decrease of NREM sleep time (-52%) in the first hour after the injection. This effect was followed by an increase in NREM sleep time during the second (+65 %) and third (+68%) hours after the injection (p=0.01), associated with an elevated NREM delta power (+23%, p=0.001). Pretreatment with NCS-382 at a dose which did not affect sleep (20 mg/kg) or at a dose which had minor effects on sleep by itself (30 mg/kg) partially prevented the NREM sleep-enhancing effects induced by GHB, but not the increase in NREM delta power.
Conclusions: The results indicate that the sleep-promoting effects of GHB may be at least partially mediated through GHB receptors. However, the mechanism(s) of action underlying the effects of GHB on EEG sleep needs to be further clarified, in particular by testing the hypothesis of a potential interaction with GABAA or GABAB receptor function.

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0213.C

Effect of Modafinil on Cardiac Repolarization

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Introduction: Many agents commonly used for the treatment of excessive sleepiness and attention deficit/hyperactivity disorder (ADHD) are associated with adverse cardiovascular effects. In order to determine the safety of modafinil for treatment of these patients, we investigated the effects on cardiac repolarization, a marker for proarrhythmic effects.
Methods: ECG interval data were collected in 7 studies: 4 in healthy subjects; 2 in adults with SWSD; and 1 in children/adolescents with ADHD (except for the healthy subjects studies, all were randomized, double-blind, placebo-controlled studies). In healthy subjects, ECG data were obtained during the time of the expected modafinil Cmax (1-4 hours post-administration). In the patient populations, ECG data were collected at baseline visits and at the end of double-blind treatment (12 weeks in SWSD, and 4 weeks in ADHD). ECG parameters analyzed included QT interval, QRS duration, and PR interval. QT interval was corrected using Fridericia's QT correction method (QTc). Using the criteria proposed by regulatory agencies, QTc increase of < 30ms reflects low arrhythmic risk.
Results: Modafinil doses evaluated in healthy subjects ranged from 200 to 800 mg/day (200 mg/day 1, n=93; 200 mg/day 2, n=18; 400 mg/day 2, n=18, 600 mg/day 3, n=18; and 800 mg/day 4, n=12). Modafinil was not associated with clinically meaningful changes in ECG intervals in healthy subjects, when recorded during the time of the expected modafinil Cmax. In particular, no evidence of prolonged ventricular repolarization was observed, as measured by QTc interval. Mean change in QTc interval ranged from -4.1 msec (modafinil 200 mg/day 1) to -14.2 msec (modafinil 400 mg/day 2). Of 111 ECGs recorded after 200 mg dose, 98% had < 30 ms increase in QTc and no patients had an increase > 60 ms. Repeated doses of 400 mg were not associated with increased QTc, but 1 of 18 patients given 600 mg on day 3 and 1 of 12 given 800 mg on day 4 had increase in QTc > 30 ms.Similarly, modafinil was not associated with clinically meaningful changes in ECG intervals in adult patients with SWSD (N=261; modafinil 200-300 mg/day) or in pediatric/adolescent patients with ADHD (N=197; modafinil 300-400 mg/day). In SWSD, mean changes in QTc from baseline to endpoint were 7.6 msec and 5.1 msec for patients receiving modafinil 200 mg and placebo, respectively. In ADHD, mean changes from baseline in QTc ranged from -1.1 to 4.2 msec for patients in 4 modafinil dosing groups compared with -1.2 for patients in the placebo group. None of these changes were statistically significant. In SWSD, 86% of modafinil patients had a change of QTc < 30 ms compared with 87% of placebo

treated patients while in ADHD, 89% of modafinil vs. 96% of placebo treated had increase in QTc of < 30 ms.
Conclusions: Modafinil does not adversely affect cardiac repolarization, as shown by lack of clinically relevant changes in ECG intervals in healthy subjects, adults with excessive sleepiness associated with SWSD, and children/adolescents with ADHD. Therefore, modafinil does not appear to pose a significant proarrhythmic risk in these populations of patients without significant cardiac disease.

Research supported by Cephalon, Inc., West Chester, PA

0214.C

Efficacy and Tolerability of Indiplon (NBI-34060) Solution in Healthy Adults in a Model of Transient Insomnia

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Introduction: Indiplon is a non-benzodiazepine GABA-A receptor modulator with sedative-hypnotic properties. This study explored the dose-related efficacy of indiplon solution in healthy adults subjected to a laboratory model of transient insomnia.
Methods: This was a multicenter, randomized, placebo-controlled, parallel-group, dose response study in 228 young healthy subjects, aged 18 – 59 years, with no history of insomnia. Transient insomnia was induced by a combination of first night effect and a two-hour phase advance of bedtime. Subjects were excluded if they had: previously slept in a sleep laboratory, an irregular sleep-wake schedule, frequent daytime naps, or a medical/psychiatric disorder. Subjects were randomized to indiplon solution 15 mg, 30mg, or placebo, and dosed 30 minutes before lights-out. Hypnotic efficacy was evaluated objectively via polysomnography, and subjective assessments of sleep were evaluated via sleep questionnaires. The Digit Symbol Substitution Test (DSST), Symbol Copying Test (SCT) and Visual Analog Scale (VAS) of alertness were conducted approximately 30 minutes after rise time to evaluate next-day residual effects.
Results: Latency to persistent sleep (LPS) was significantly reduced in both indiplon groups with mean values of 17.5 and 16.2 minutes for the 15 mg and 30 mg dose groups, versus 34.1 minutes for the placebo group ($p<0.001$). Subjective latency to sleep onset (LSO) was also significantly improved with mean values of 15.8 and 15.4 minutes for the 15 mg and 30 mg indiplon groups versus 31.1 minutes for placebo ($p<0.001$). There was no effect of indiplon on either PSG or subjective measures of total sleep time, and no relevant changes in sleep architecture. Adverse events for both treatment groups were similar to placebo, with no serious adverse events. DSST, SCT, and VAS were similar in the indiplon groups relative to baseline or placebo values.
Conclusions: Indiplon solution at doses of 15 and 30 mg induced a rapid onset to sleep by both PSG and subjective measures. No residual effects were detected nine hours after dosing. As there was no apparent dose response on LPS or LSO, these findings suggest that doses lower than 15 mg may be effective. Both doses of indiplon were well tolerated with no next-day residual effects in this single-night study in healthy adults.

Research supported by Neurocrine Biosciences, Inc.

0215.C

Modafinil Improves Psychomotor Vigilance Performance in Shift Work Sleep Disorder

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Introduction: Shift work sleep disorder (SWSD; 307.45-1) is characterized in The International Classification of Sleep Disorders (1997) as affecting a subgroup of shift workers who experience chronic difficulty sustaining daytime sleep and/or excessive sleepiness during nocturnal work hours. The sleepiness associated with SWSD may decrease behavioral alertness on the job, leading to performance risks due to slowed reaction times (RT) and lapses of attention. We report here the effects of the wake-promoting agent modafinil on psychomotor vigilance performance in patients diagnosed with SWSD.
Methods: A 12-week, multicenter, randomized, placebo-controlled, double-blind, parallel-group trial was conducted in 193 patients diagnosed with chronic SWSD. Eligible patients met the following criteria: (1) worked at least 5 night shifts per month (£ 12h/shift with at least 6h between 2200 and 0800), of which at least 3 were consecutive; (2) no primary sleep pathologies other than SWSD and no other uncontrolled illnesses; (3) mean MSLT (at 0200, 0400, 0600, 0800) of £ 6 minutes following the last of 3 or more consecutive night shifts; (4) £ 87.5% sleep efficiency daytime PSG (from approximately 1000 to 1800) following a nocturnal period of waking. Patients were randomized to modafinil 200 mg once daily or placebo, administered 30 to 60 minutes before the start of each night shift. A 20-minute psychomotor vigilance task (PVT) was administered four times (0100, 0300, 0500, 0700) at baseline, weeks 4, 8, and 12, during a simulated night shift following the last of 3 or more consecutive night shifts. PVT outcomes included the fastest 10% RT, median RT, 10% slowest RT, and the number of lapses (RT ³ 500 msec). Complete PVT data were available and change from baseline was analyzed using ANOVA for 124 patients (modafinil n = 60; placebo n = 64).
Results: Relative to placebo, modafinil significantly improved nocturnal PVT performance for the 10% fastest RT ($p = 0.0242$, effect size = -0.42 SD) and for the number of PVT lapses (mean at end of study: modafinil = 18.7 vs. placebo = 31.5, $p = 0.0087$, effect size = -0.53 SD). In the case of both median RT and slowest 10% RT, the placebo group had a standard deviation for change scores that was at least twice that of the modafinil group, prompting a Wilcoxon Test, which was significant for modafinil improving both median RT ($p = 0.0022$) and slowest 10% RT ($p = 0.0192$) relative to placebo.
Conclusions: In patients with chronic SWSD, modafinil significantly improved PVT performance parameters during scheduled nocturnal periods of wakefulness. It appears that behavioral alertness as assessed by PVT performance can be improved by modafinil in night shift workers suffering from SWSD.

Research supported by Cephalon, Inc.

0216.C

Decreased Body-Mass Index (BMI) in Narcoleptic Patients Treated with Sodium Oxybate

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Introduction: The purpose of this study was to determine BMI changes in narcoleptic patients treated with sodium oxybate (xyrem) in an open-label long-term treatment study.Recent discovery of the role of hypocretin deficiency in the pathophysiology of narcolepsy prompted interest in weight control/feeding behaviors of the narcoleptic patients. The exact mechanism of the effect of sodium oxybate that is responsible for the improvement of cataplexy, sleep consolidation and improvement of daytime sleepiness is unknown. An early animal study demonstrated increased food consumption in GHB-treated rats relative to controls. Altered energy homeostasis may accompany narcolepsy, based on reported higher BMI in narcoleptic patients than in population controls, increased incidence of NIDDM in Japanese narcoleptics, and contrary to

the expectations lower daily caloric intake due to reduced carbohydrate intake.Patients enrolled in this study were on stable or reduced daily dose of stimulants. An analysis of weight changes in this group of patients was expected to provide additional clues to the understanding of Xyrem's mechanism of action.

Methods: An analysis of the changes of patients' BMIs at baseline (N=184), 2 (N=156), 6(N=175) and 12 months(N=97) were performed. Changes from baseline were calculated as BMI at 2,6, and 12 months minus BMI at baseline visit. Change from baseline to 12 month was also calculated for a constant cohort of 97 patients.Changes from baseline to 2,6,and 12 month was analyzed using Wilcoxon signed-rank test after data exploration (using histograms and the Kolmogorov-Smirnov test for normality) detected deviations for normality in the data.

Results: Median BMI at baseline was 28 (overweight individuals). At 2 months median BMI remained 28, but there was a statistically significant BMI reduction (-0.20;p<0.002). With longer duration of treatment, at 6 months and at 12 months BMI reduction became steadily more pronounced (-0.425; p<0.00002 and -1.103;p<p,0.00001 respectively).BMI change at 12 month for constant cohort was -1.029(p<0.00001).

Conclusions: Our results confirm previously observed high BMI in narcoleptics compared to normatives from general population. As already reported for a smaller group of patients, a small but significant BMI reduction is confirmed in a much larger group of patients treated with sodium oxybate for 12 months, suggesting that the pharmacologically induced improvement of sleeping behavior is associated with changes of weight control/feeding behavior.

Statistical analysis supported by Orphan Medical Inc.

0217.D

Dream Imagery Becomes More Intense After 9/11/01

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Introduction: There is a general consensus, based on anecdotal and clinical reports, that stress and trauma have an effect on dreams, but this has been difficult to study systematically. We have presented evidence that the CI Intensity Score, measuring the intensity of the dream's central image, is significantly higher for students who report any abuse than those who do not. Also, CI Intensity was higher in subjects who had recently experienced trauma than in control groups.1, 2 A systematic study should ideally involve a study of dreams before and after trauma within individuals who have been routinely recording their dreams. It is not easy to find such dream recorders who also happen to experience an acute trauma and are willing to share their dreams. We have suggested that the events of 9/11/01 represented a traumatic event for everyone living in the USA. Thus, anyone who has regularly been recording dreams over the past years would be appropriate for the study of dreams before and after trauma.

Methods: We were able to obtain complete dream series—the last ten dreams recorded before 9/11/01 and the first ten dreams recorded after that date—from sixteen regular dream-recorders living in various parts of the USA. A total of 324 dreams from these sixteen dreamers were assigned random numbers and scored blind for CI intensity. Fifty dreams were scored by two experienced scorers, showing inter-rater r = .76. Each dream was also scored for what emotion might be pictured by the central image of the dream, dream length, and "dream-likeness." In addition, each dream was scored on three ad hoc scales (scored from 0 to 3) estimating dream content involving a) attacks of any kind, b) buildings resembling the World Trade Center or the Pentagon and c) airplanes.
After the code was broken, a pre-9/11 mean and a post-9/11 mean was obtained for each subject. The pre- and post-means were compared using a t-test for correlated means.

Results: Before After Difference t p CI Intensity 1.19 1.35 0.16 3.21 .003 (one-tailed)Length (text lines) 11.64 11.55 -0.09 0.09 NSDream-likeness 4.5 4.54 0.04 0.47 NSAttacks 0.048 0.135 0.087 1.74 NSBuildings 0.069 0.122 0.053 0.95 NSAirplanes 0.012 0 -0.012 1.46 NS

There was a clearly significant increase in CI intensity score after 9/11. There was no significant increase in dream length, "dream-likeness" or the three ad hoc content categories. Results on the emotion thought to be pictured showed a shift towards more "fear/terror" and "vulnerability/helplessness." However, these emotions are always frequent in all samples, and the shift did not reach statistical significance.

Conclusions: In this group of regular dream-recorders, the effect of 9/11/01 was to increase dream image intensity without altering other measured aspects of dreams. Since they were selected only on the basis that they regularly recorded their dreams, we could tentatively generalize to the entire US population and suggest that the dream image intensity probably increased for the population. (Our experience, based on interviews and questionnaires, is that dream-recorders are unusual only in "sensitivity" and in interest in dreams, daydreams and mental functioning in general.) The present results, consistent with past studies cited, suggest that the intensity of dream image may be considered a measure of the emotional arousal of the dreamer.

0218.D

Dream Recall After Night Awakenings from Tonic/Phasic REM Sleep

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Introduction: There is no clear distinction in dreams originating from tonic and phasic REM sleep, although physiological properties of those two states of REM sleep are apparently different in regard of activation pattern in brain.

Methods: Dream recall in 11 healthy young subjects, aged 21-23, was analyzed. All the subjects were polysomnographically recorded for one night and awakened every time when apparent tonic/phasic REM occurred. Immediately after awakening the subjects were asked standardized questions as follows: Were you dreaming (yes/no); How do you feel (good/bad/neutral); Something sexual (yes/no); Short dream content (free interpretation); Colorness (colorful/colorless); Words (yes/no). In the morning the subjects were asked again for dream recall from the previous night.

Results: A dream was reported in 79%, i.e. 77/97 of all REM awakenings, with no significant difference in tonic (73%, i.e. 30/41) and phasic (84%, i.e. 47/56) REM sleep. There was no significant difference in the mood (good/bad/neutral) and in the content of reported dreams (meaningful/meaningless/bizzare/couldn't recall) between tonic and phasic REM sleep as well as in colorness (colorful/colorless/couldn't recall). But, after awakening from phasic REM sleep a particular color in the dream was spontaneously reported more often, mostly orange, yellow, and green. Sexual arousal after REM awakening was reported very sporadically, unrelated to dream content and tonic/phasic. In all dreams, regardless of originating from tonic or phasic REM sleep, there were differences in the content of the reported dreams immediately after night awakening (meaningful/meaningless/bizzare/couldn't recall) across remembering words in the dreams (yes/no/couldn't recall) (Chi-Square=17.631, DF=6, p=0.007; Fisher Exact Test (2-tail) p=0.00498). Major contribution to the difference was the absence of meaningful dreams in the group where examinees couldn't remember if their dreams were with or without words. In the group of dreams with words there were no dreams where examinees couldn't recall the content of their dreams. The significant difference in distribution of all dream contents after night awakenings (meaningful/meaningless/bizzare/couldn't recall)

was found between different morning remembering of dreams (good remembering/remembering with difficulties/no remembering) (Chi-Square=27.851, DF=6, p=0.001; Fisher Exact Test (2-tail) p=0.0000464). The Odds Ratios in Logistic Regression Analysis indicate that better morning remembering of dreams reported after night awakenings from REM sleep was connected with meaningless content, but also good mood, colorful and dreams with words, as well as with phasic REM sleep.

Conclusions: Night dreaming was reported in 79% of all REM awakenings, with no significant difference as to tonic/phasic. Mood after all REM awakenings was mostly good or neutral, regardless of the dream content or phasic/tonic REM. Colors were present significantly more often than words in all REM dreams. Diversity of colors was more evident in phasic REM. REM dreams were more often meaningful than meaningless, but it is possible that meaningfulness is the consequence of "editing" the dream immediately after awakening: the predictor of dream morning rememberings is meaninglessness and not meaningfulness of the dream.

0219.D

Cognitive, Affective, and Sensory Characteristics of Events Sampled from REM Sleep, NREM Sleep, and Waking

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Introduction: A comprehensive theory of human cognition and consciousness must account for mental activity over the sleep/wake cycle. As such, systematic comparisons of waking and dreaming are critical to resolving the question of whether dreaming is continuous or discontinuous with waking experience.

Methods: Six event samples were obtained from each of 26 participants: two from Rapid Eye Movement (REM) sleep, two from non-REM (NREM) sleep, and two from waking. Participants were selected on the basis of a self-reported high level of dream recall (one or more dreams recalled per night). Subjects received individual instruction in the procedure used to sample sleeping and waking experiences. Waking event samples were obtained with the aid of a pre-programmed beeper worn by the subject. When the subject heard the beeper, he or she provided a one-page description of the event that occurred just prior to the signal. The subject then completed two questionnaires that assessed cognitive, affective, and sensory qualities of the experience just described. For sleeping samples, the subject used a "DreamLight" in their home setting. The DreamLight is a portable, computerized device that can be programmed to use information about eye and head movement (relayed from the mask) to predict REM, NREM, and waking states. For each experimental night, the subject entered a pre-determined code number into the DreamLight which dictated whether a sound cue ("alarm") was delivered during a REM period or during a NREM period, always in the second half of the night. Subjects and research assistants were blind to the sleep stage that particular code numbers corresponded to. Upon being awakened by the alarm, the subject completed the same measures as were obtained for waking event samples, then returned to sleep.

Results: Repeated measures analysis of covariance (using MANOVA) was used to compare the participants' average ratings of the cognitive, affective, and sensory characteristics of events sampled from REM, NREM, and waking. The word count associated with the narrative description of the event was entered as a covariate. Major findings were that: (1) cognition sampled from REM sleep was highly similar to waking cognition; (2) differences observed in the affective qualities of events sampled from REM, NREM, and waking were not as great as many dream theories would predict; and (3) waking events were associated with more sensory information than REM or NREM events.

Conclusions: The present data support the claim that cognition and affect during sleep are largely continuous with waking experience. As well, the differences that do exist across waking and sleep experiences may be more quantitative than qualitative. These results are consistent with prior research indicating that the same neurocognitive system is responsible for the generation of both waking and sleep cognition.

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0220.D

Temporal Relationships Between Daily Events And Their Incorporation Into Dreams: A Gender Difference

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Introduction: Two types of temporal delay in dream content incorporation have been identified: the day-residue effect, which corresponds to incorporation into dreams of events from the preceding day, and the dream-lag effect, which refers to a resurgence in incorporation of events that occurred several days prior to the dream. Previous studies demonstrating the dream-lag effect involved some methodological problems and did not consider gender differences. We replicate the phenomenon using controls for memory limitations, biases implied in repetitive tasks, and gender.

Methods: 470 Introductory Psychology students recorded dreams for seven days. After selecting the most recent dream that they could remember well they recalled source events that occurred on a specific, randomly determined, day prior to the dream. To minimize effects of poor memory on incorporation ratings, subjects who rated their recall of events as <5 (10-point scale) were excluded. Among 202 remaining subjects ($X=19.6 \pm 2.10$ years), 78.2% were female and 21.8% male. To maximize N for males, three groups were formed: Day-residue (Days 1-2; N=82), Control (Days 3-4; N=50) and Dream-lag (Days 5-7; N=70). To measure incorporation of events into dreams, students identified on 10-point scales the degree of correspondence between events from the specified day and the dream selected. Incorporation scores were entered into a 3 x 2 ANOVA with Temporal Group (Day-residue, Control, Dream-lag) and Sex (Male, Female) as independent factors.

Results: An interaction effect revealed different patterns of incorporation over Temporal Groups for females and males ($F(2,196)=5.265$; $p=0.006$). A quadratic trend ($F(1,196)=10.846$; $p=0.0012$) described the groups for females (means=5.02 ± 3.22 vs. 3.37 ± 2.87 vs. 5.44 ± 2.98) whereas a decreasing linear trend ($F(1,196)=8.328$; $p=0.004$) described the males (means=6.3 ± 2.27 vs. 4.8 ± 2.76, vs. 2.89 ± 2.52). Planned comparisons revealed that only for females, incorporations for Day-residue and Dream-lag groups were significantly higher than for the Control group ($p=0.014$ and 0.001). Further, only incorporations for the female Dream-lag group were higher than for the corresponding male group ($p=0.017$).

Conclusions: The U-shaped temporal pattern of incorporations into dreams found in at least four previous studies may apply only to females. However, assessment of more male subjects is clearly needed. The association of delayed incorporations with female gender may be related to findings that women recall dreaming more often than do men, are usually more sensitive than men to their dreaming states, and describe their dreams as being more vivid, meaningful and having a greater impact on their lifetime experiences. Further analyses of the correlates of this effect are reported in a companion abstract.

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0221.D

Temporal Delays In Dreaming About Daytime Events Vary With The Personal Impact Of Recalled Dreams

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Introduction: Incorporations of daytime events into dream content are influenced by one of two temporal effects: 1) the day-residue effect—correspondences between daytime events and dreams on the next night; and 2) the dream-lag effect—event/dream correspondences occurring about a week later. The two effects, which plotted together over time describe a U-shaped curve, have been replicated often, but never examined for psychological correlates.
Methods: For seven days, 470 Introductory Psychology students recorded their dreams and rated each (10-point scales) on a 4-item version of the Self-Perceptual Depth (SPD) Scale, a validated measure of an event's personal impact. Items were: 'made aware of aspects of self usually ignored,' 'affected mood,' 'reminded of past events,' and 'made to feel like changing the way one lives.' Subjects then selected the most recent dream that they could remember well and recalled source events from one of 7 randomly determined days prior to the dream. To minimize effects of memory on ratings, subjects whose confidence in recall of events was <5 (10-point scale) were excluded. Among the 212 remaining subjects (19.6 $\pm$ 2.10 yrs), 74.5% were female, 20.8% male and 4.7% unspecified. To rate incorporations, students evaluated (10-point scale) degree of correspondence between events from the specified day and the selected dream. To maximize N, three groups were formed: Day-residue (Days 1-2; N=85), Control (Days 3-4; N=50) and Dream-lag (Days 5-7; N=73). These were further subdivided into three levels based on per-week average SPD scores. Incorporation scores were evaluated in a 3 x 3 ANOVA with Temporal Group (Day-residue, Control, Dream-lag) and SPD score (Low, Middle, High) as between-groups factors.
Results: An interaction effect ($F(4,199)=8.1013$; $p=0.004$) revealed different incorporation patterns for Temporal Group over different levels of SPD. Only subjects with High SPD scores clearly demonstrated the familiar U-shaped curve (quadratic trend: $F(1,63)=18.021$; $p=0.00007$; means: 6.18 $\pm$ 2.89, 3.00 $\pm$ 2.77, 6.58 $\pm$ 2.22) in which incorporations for Day-residue and Dream-lag groups exceeded those for the Control group (both $p<0.001$). Low SPD subjects showed both mild quadratic ($F(1,65)=3.916$; $p=0.052$; means: 5.11 $\pm$ 3.08, 2.47 $\pm$ 2.39, 3.41 $\pm$ 3.48) and marginal linear ($F(1,65)=3.58$; $p=0.063$) trends, for which Day-residue incorporations exceeded those for the Control ($p=.006$) and Dream-lag ($p=.063$) groups. The latter two did not differ. Middle SPD subjects also did not differ by group (means: 5.19 $\pm$ 3.14, 5.23 $\pm$ 2.76, 4.4 $\pm$ 2.71).
Conclusions: Subjects who report dreams with high impact tend to display either the day residue effect (1-2 days), the dream lag effect (5-7 days), or both. By contrast, those reporting dreams with low impact tend to display only the day residue effect. These differences may reflect subject differences in the manner of processing and incorporating diurnal events into dreams, differences in how high vs. low impact events influence dreaming, or some combination of these factors.

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0222.D

Threat Simulation in Recurrent Dreams

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Introduction: Revonsuo (2000) recently put forth an intriguing and detailed evolutionary theory of dreams which stipulates that the biological function of dreaming is to simulate threatening events and to rehearse threat avoidance behaviors. In this theory, dreaming is viewed as both an organized and selective simulation of the world. A particularly well-organized form of dream content is the recurrent dream (RD) which is distinguished by its complete repetition as a remembered experience. The goal of the present study was to evaluate the extent to which the main postulates of the threat simulation theory apply to RDs.
Methods: The data presented are based on the content analyses of 212 RDs. They were obtained from 212 adults (187 females aged 30.1 $\pm$ 13.1; 25 males aged 37.2 $\pm$ 17.3) who had provided a written description of their RD on a sleep and dream questionnaire as part of an unrelated series of studies on personality and dream content. The RDs were selected from a larger pool of RDs and were all of the dream reports which met the following inclusion criteria: the RD must have occurred over a period of at least six months; its content had to be rated by the subject as being "always" or "almost always" identical; and it had to be described in sufficient detail to allow a content analyses of the dream's setting, its affective tone, and the characters present. All RDs were scored using a slightly modified version of the rating scale elaborated by Revonsuo specifically designed to identify and describe threatening events in dreams.
Results: 139 of 212 (66%) RDs were found to have had a threatening content but a sizable proportion of the threats were either unrealistic (47%) or unusual (34%). The dreamer was the target of the threat in 94% of the cases. The threats were life threatening or physically very dangerous in 64% of the RDs. Specific thematic subcategories included escapes/pursuits (26%), accidents/misfortunes (21%), physical/environmental anomalies (17%), aggressions (17%), emotional difficulties (8%), failures (7%), and disasters (3%). In a majority of cases (59%), subjects participated actively in the course of the threatening event and presented a fight or flight response. Nevertheless, threats were three times more likely to be actively experienced than successfully avoided or dealt with and the dreamer suffered important losses in 27% of the cases. The two most frequently observed types of losses were negative psychological consequences (e.g. guilt, loss of self-esteem, fear, sadness) and physical harm (e.g. serious injury).
Conclusions: The data indicate that many RDs do not depict situations critical for one's physical survival or reproductive success. Even in those RDs where they do, the threats are rarely realistic and the dream rarely contains successful avoidance responses.

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0223.D

Dream Reports Obtained From 20-min Nap Trials Repeated 78 Hours With An Interval Of 40-min Enforced Wakefulness

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Introduction: Most of previous dream experiments in laboratory settings have been conducted by asking the subjects awakened from REM/NREM sleep during all night polysomnographic recordings. With respect to limitation of this methodology, some researches have pointed out that this methodology may not correctly determine the time interval when the subject actually experienced the reported dream. Here we study dream reports obtained from 20-min nap trials repeated with an interval of 40-min enforced wakefulness (ultra-short sleep-wake sched-

ule), so that the reported dream would be experienced during the prior nap trial.
Methods: Eleven normal healthy men (20-26 years of age) participated in an ultra-short sleep-wake schedule in which 20-min nap trials followed by a 40-min enforced wakefulness was repeated for 78 hr under constant dark illumination (<8lux). During 20-min nap trials, we performed standard polysomnographic recording. A structured interview on formal aspects of dream was performed at the end of each nap trial. Quantity of dream was scored with a three-grade scale from 0 (none) to 3 (large amount). All procedures were carried out in the isolated laboratory at National Center of Neurology and Psychiatry.
Results: We obtained a total of 854 reports from 858 nap trials (4 missing sessions were eliminated). 172 reports were obtained from nap trials containing REM sleep (REM naps). 563 reports were obtained from nap trials containing only NREM sleep (NREM naps). 119 reports from nap trials containing no sleep were excluded from analysis. ANOVA revealed that dream score of REM naps was higher than that of NREM naps ($F(1,733)=105.89$, $p<.0001$). In REM naps, the amount of REM sleep in each nap trial was positively correlated with the dream score ($rs=0.24$, $p=0.0017$), while in NREM naps, the amount of NREM sleep was positively correlated with dream score ($rs=.232$, $p<.0001$). Detailed analysis revealed that dream score was positively correlated with amount of stage 2 ($rs=0.196$, $p<0.0001$) and stage 3+4 ($rs=0.191$, $p<0.0001$). In contrast, no significant correlation was found between the amount of stage 1 and dream score ($rs=-0.007$, $p=0.88$).
Conclusions: Using an ultra-short sleep-wake schedule in which the length of sleep prior to dream mentation was controlled, we first demonstrated that a quantitative relationship between REM/NREM sleep and dream. These indicate that amount of REM sleep contributes to amount of dream experience in nap trials. Dream amount in NREM sleep was suggested to be related to deeper NREM sleep not but shallow and drowsy state.

0224.D

Effects Of State And Trait Factors On Nightmare Frequency
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Introduction: Previous research has shown that trait factors such as neuroticism, thin boundaries as well as state factors such as current stressors are related to nightmare frequency. Studies comparing the effects of trait and state factors, however, have not yet been carried out. Based on the continuity hypothesis of dreaming, it was hypothesized that state factors mediate the effect of trait factors on nightmare frequency, i.e., nightmares reflect negative waking-life experiences.
Methods: The participants completed several questionnaires regarding day-time stressors, sleep behavior and personality (Big-five personality factors) and completed a dream diary over a two-week period. 444 persons whose mean age was 23.5 ± 5.7 years were included in the sample. Participants were recruited at the universities of Mannheim, Heidelberg and Landau and were paid for participation.
Results: Correlational analyses revealed that gender, trait factors such as neuroticism as well as state factors (current stress) are related to nightmare frequency. The first regression analysis including all trait factors (neuroticism, openness to experience, boundary thinness, absorption) in addition to gender (included in all analyses) explained 10.9% of the total variance (R2 adjusted). A similar analysis including the three stress measures (state factors) explained 17.5% of the total variance of nightmare frequency. The regression model including trait and state factors also explained 17.5% of the total variance, but the only the regression coefficients of two stress measures (state factor) were significant.
Conclusions: The findings indicate that state factors play a more important role in explaining interindividual differences of nightmare frequency in a non-clinical sample than trait factors and mediate the zero-order relationship between trait factors and nightmare frequency. The results, thus, support the general continuity hypothesis of dreaming. The investigated relationships may contribute to an etiological model of the nightmare disorder.

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0225.D

Continuity Between Waking and Dreaming
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Introduction: In order to test the so-called continuity hypothesis of dreaming mainly two paradigms has been applied: experimental manipulation of the pre-sleep situation and correlating interindividual differences in waking-life parameters with corresponding dream characteristics. A positive correlation, e.g., anxious persons dream more often about experience anxiety, would support the continuity hypothesis, whereas non-significant or negative coefficients are not in line with the hypothesis. Three studies correlating interindividual differences in waking-life parameters (activities, psychopathology, stress) with corresponding dream contents are presented.
Methods: In all three studies, the participants kept a dream diary over a two-week period and completed several questionnaires (study 1: daytime activities; study 2: Symptom Checklist SCL-90-R; study 3: stress questionnaires). Dream reports were typed out, randomized and scored by external judges along content analytic scales developed for the specific purpose of the study. Sample 1 included 133 persons whose mean age was 25.5 ± 10.9 yrs. Sample 2 consisted of 92 psychiatric inpatients (depression, eating disorders, schizophrenia etc.) whose mean age was 37.7 ± 17.3 yrs. Sample 3 included 444 persons whose mean age was 23.5 ± 5.7 yrs.
Results: In study 1, the amount of time spent with activities such as "Spending time with the partner", "Reading", "Driving a car" was significantly correlated to the occurrence of the respective activity within the dreams. In study 2, depressive mood was related to negative dream emotions in the total group as well as in the depressive group ($N = 36$) and the rest group including patients with other diagnosis. In addition, death themes and aggression in dreams were related to symptom severity in depressive patients. In study 3, the correlation between negative dream emotions and current stress was significant but not to the occurrence of problems within the dream.
Conclusions: The findings support the continuity hypothesis of dreaming but also stress the importance to specify the general formulation of the hypothesis, i.e., identifying factors which might affect the closeness of the waking-dreaming continuity and investigate whether different dream characteristics are affected in a different way by preceding waking-life experiences (e.g., dream emotions vs. dream content; see Study 3). A comprehensive mathematical model will be proposed.

0226.D

Dream Recall Frequency is Associated with Openness to Experience but not Sleep Length
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Introduction: Webb and Agnew (1970; Science 168: 146-147) found that people who sleep more than 8.5 hours per night have 50% more REM sleep than people who sleep less than 6.5 hours. Stickgold, Malia, Fosse, and Hobson (2001; Sleep 24: 171-179) found that 85% of awakenings from REM sleep and 67% of awakenings from NREM sleep result in dream reports with content, and that REM dream report length increases over the first 40 minutes of the REM period. It would thus be

expected that dream recall frequency and dream report length would be greater in individuals who sleep longer than in those who are short sleepers, a result found by Baekeland and Hartmann (1971; Comprehensive Psychiatry 12: 141-147) but not by Blagrove and Akehurst (2000, Dreaming, 10, 139-148). We investigate here the relationships of dream recall variables with sleep length and also with the personality measure openness to experience.
Methods: 671 participants (77% female, 23% male, mean age = 33.0 years, SD=17.3) answered a questionnaire assessing usual sleep length, dream recall frequency (DRF), frequency of telling dreams to others (DTF), and frequency of nightmares. Openness to experience was assessed by Saucier's (1994; Journal of Personality Assessment 63: 506-516) brief version of Goldberg's Big-Five personality factors. If participants could remember a recent dream they were asked to write it down: these dream reports were independently rated (0 – 3) for emotional intensity/presence of contextualizing image (CI: Hartmann, Kunzendorf, Rosen, & Grace, 2001; Dreaming 11: 97-104) and for bizarreness (0 - 2), and report length in words was counted.
Results: Sleep length had significant but small correlations with DRF ($r=.11$, $p<.005$) and DTF ($r=.18$, $p<.001$), but insignificant correlations with nightmare frequency, CI score, bizarreness, and dream report length. However, when age and sex were partialled out these correlations with DRF and DTF became insignificant ($r=.00$ and $r=.03$ respectively). Extreme sleep length groups (length <6.5 hours or > 8.5 hours) also did not differ in DRF and DTF when age and sex were controlled for. In contrast, with age and sex controlled for, the personality trait openness to experience was significantly correlated with DRF ($r=.16$, $p<.001$) and nightmare frequency ($r=.09$, $p<.05$), and marginally with DTF ($r=.08$, $p=.057$).
Conclusions: Large individual differences in sleep length (and thus presumably in REM sleep) do not result in differences in dream recall frequency or dream report length. However, it may be that the content of dreams from long sleepers may be different from short sleepers, although we did not find significant correlations of sleep length with emotional intensity/contextualized images (CI), bizarreness, or dream report length. Dream recall frequency is, however, related to openness to experience, which accords with previous work on DRF being related to individual differences in creativity.

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0227.D

Dream Recall Frequency and Attitude Towards Dreams: An Illusory Relation?
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Introduction: Numerous studies have found a positive relationship between people's favorable attitude towards dreams and dream recall frequency (DRF). However, most of these studies have relied on retrospective estimates of DRF. The goal of the present study was to test the idea that a positive attitude towards one's dreams might not be related to DRF per se but rather to an estimation bias.
Methods: Participants were 82 undergraduate students who were recruited as nonpaid volunteers in an undergraduate psychology class. Their estimated DRF and attitude towards dreams were evaluated via the McGill Sleep/Dream Questionnaire. Specifically, estimated DRF was measured with a single question (In general, how many dreams do you remember per week?) and Attitude was measured by three questions which were answered on a 7-point scale (How often do you discuss your dreams with family or friends? How much attention do you usually pay towards your dreams? How much significance do you usually attach to your dreams?). The scores from these three items were combined to obtain a single measure of Attitude. In addition, participants were required to keep a dream log for 2-3 consecutive weeks. Their actual DRF was calculated from the log data. The relationship between measures of actual DRF, Attitude towards dreams and Estimated DRF was assessed with Pearson's correlations and a linear regression.
Results: Attitude was positively correlated with Estimated DRF ($r=0.35$, $p<0.01$) but not with DRF ($r=0.00$, $p>0.10$) although DRF was positively correlated with Estimated DRF ($r=0.52$, $p<0.01$). The regression showed that the part of variance in Estimated DRF explained by Attitude (semi-partial corr.=0.35, $p<0.01$) was independent from the portion explained by DRF (semi-partial corr.=0.52, $p<0.01$). DRF and Attitude were consequently orthogonally related to Estimated DRF (total adjusted $r2=0.38$, $p<0.01$).
Conclusions: The data support the idea that a positive attitude towards dreams is not related to actual DRF but rather to an estimation bias. It is suggested that while Estimated DRF and DRF share common traits, Estimated DRF is also influenced by additional factors such as long-term memory. Consequently, using Estimated DRF scores to generalize to actual DRF rates may be unwarranted unless a direct measure of DRF is also used. Furthermore, the results show the usefulness of comparing correlates of DRF through regression analyses instead of simply calculating zero-order correlations to elucidate the relative importance of different factors related to DRF.

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0228.D

Limbic Activation During REM Sleep Influences Motivational Content of Mentation Report
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Introduction: Perhaps because of the salience of visual imagery reports from REM sleep, motivational features of REM dreaming have been largely ignored over the past 50 years. But recent Positron Emission Tomography (PET) studies of brain region activation during sleep and waking states indicate that paralimbic, and particularly amygdaloidal, structures, known to play a major role in the processing of motivation and emotions in the waking state, are quite active in REM sleep. Although brain stem inhibition in REM sleep may limit the expressive features of emotion that are characteristic of waking limbic activation, motivational features, which are the precursors of emotion, should modify, constrain, or "color," the visuo-spatial sequence of dreaming generated by the extra-striate cortex. On the other hand, low activation of the prefrontal cortex during REM sleep, which is associated in waking with goal-directed activity, suggests that the limbic contribution to motivation in REM sleep may not be realized by prefrontal processing. Therefore, we asked where motivational features might be "read into" the dream, or the dream report, as the sleeper awakens and the prefrontal cortex becomes increasingly active.We assessed motivational features by counting the number of words that describe implicit motivated behavior, such as trying and wanting, and explicit motivation by asking whether the "dreamer" was trying to do something. We measured the effect of waking activation on reported motivation in mentation reports by obtaining two consecutive reports: the traditional "Tell me everything that was going on in your mind just before I called you." (Q1), and 20 sec. later, "Please tell me one more time…" (Q2), followed by "Were you trying to do anything? (Q3).All reports were first scored by four judges for Word Information Count (logWIC) that excluded all words judged to be commentary, redundant, or corrections. All three questions were then scored for motivation (M). Reports were scored "blind" in subject sets of four (2 REM and 2 NREM), to help judges distinguish reporter's expressive style from true information.
Results: LogWIC was greater in REM than NREM WIC_Q1: $p = .07$;

Q2: p = .04). The effect sizes were .23 and .29 respectively. WIC_M, was higher in REM than NREM (WIC_Q1_M: p = .06, eta = .24), and WIC_Q2_M: p = .007, eta = .44. The REM-NREM difference was larger for WIC_Q1_M than WIC_Q2_M (F(1,13) = 7.58, p = .02, eta = .31. Explicit_M also showed more motivation in REM than NREM (p = .04). WIC_M was a better discriminator of REM-NREM than WIC itself, showing that the greater M values in REM sleep were not a function of the greater length of REM reports. Finally, the extent to which motivation in REM is more fully expressed in a 2nd report, 20 sec. after the first, is demonstrated by a significantly larger REM-NREM difference for Q2_M than Q1_M.

0229.D

Changes in Dreaming Induced by CPAP in Obstructive Sleep Apnea Patients

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Introduction: Dreaming is altered in obstructive sleep apnea (OSAS), but it is unclear whether patients dream less or more than usual or if their dreams have distinct characteristics. Dreaming has been related to duration and intensity of REM sleep. Patients with OSAS have disrupted and relatively decreased REM sleep that normalises with nasal continuous positive air pressure (CPAP) but it is unknown if these changes modify dream content.
Methods: Twenty patients (19 men; mean age 51 years) with severe OSAS were studied with four polysomnograms: two baseline nights, the CPAP titration night and one night three months after effective home treatment. Eleven of them with good long-term CPAP compliance were re-examined 2.5-3 years later. Patients were awakened during stage II and a mean of 9-10 minutes after the begining of the first and last REM periods. We measured dream recall (%), emotional content of the dream, word count, number of thematic units, sleep architecture, and REM density before each awakening. Seventeen healthy men of similar age were studied two nights and compared with the baseline nights of the patients.
Results: Sleep architecture in the baseline nights was characteristic of severe OSAS (mean Apnea/Hypopnea Index : 75.06 $\pm$ 26.85). Apneas disappeared after CPAP, with and increase in stages III-IV and REM the first CPAP night and a decrease thereafter. Dream recall in REM sleep the baseline nights was similar in patients and controls (51.5 % vs. 43.07% respectively; Chi-square (X2) 0.79; p:0.3755), but patients reported less dreams with neutral emotional content than controls (8/30 vs. 17/28; XX2: 6.85; p:0.0088). Dream recall decreased to 20% the first CPAP night or 24.3% the 3rd-month CPAP night, increasing to 39% 2-3 years later (XX2: 12.94; p:0.0047). Dreams with violent/highly anxious content were more frequent in patients at baseline than after CPAP (XX2: 10.17; p:0.0062) or than in controls (Fisher exact test p:0.0133). Word count and thematic units per dream were higher in patients than in controls (53.05 vs. 21.67 and 2 vs. 1.35 respectively) and decreased with CPAP. REM density was higher the first CPAP night than in any other night but this increase was not statistically significant. Dream recall in stage II was lower in the patients (7.3%) than in controls (21.87%; Fisher exact test: 0.043). Patients did not incorporate apneas or the CPAP mask into their dreams.
Conclusions: Patients with OSAS recall dreams in REM sleep as often as controls, but heir dreams have an increased emotional tone and more thematic units and words. After CPAP dream recall decreases –despite the transient increase in REM density-, at least for 3 months and recovers 2.5-3 years later, with disappearance of highly emotional dreams. Dreaming in REM sleep, particularly when its content is not emotionally neutral, may indicate a poor rather than a good night sleep and be unrelated to electrophysiological sleep measures.

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0230.D

Circadian Modulation and EEG Correlates of Dream Recall during a 75:150-min Sleep-Wake Cycle Paradigm

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Introduction: Dreaming is not limited to rapid eye movement (REM) sleep, but can be found to varying degrees in any stage of sleep. We investigated dream recall from REM and non-REM sleep (stages 2,3 and 4) prior to awakening from ten 75-min naps scheduled over the entire circadian cycle. Furthermore, we attempted to quantify spectral EEG correlates of dream recall during non-REM sleep.
Methods: Following two 8:16-h sleep-wake cycles with sleep at habitual times, 17 healthy volunteers (age range: 21-31 y) were scheduled to a 75:150-min sleep-wake cycle under constant posture conditions (light levels: < 8 lux). This paradigm started at habitual waketime and ended 40 hours later at habitual bedtime. EEGs were continuously recorded throughout the protocol and subjected to spectral analysis. Immediately after 'lights on' after each of the ten naps, a sleep mentation questionnaire was given to the volunteers to assess the number and content of dreams recalled (e.g. vividness, emotionality…). Non-REM sleep awakenings were defined as follows: the last 5-min interval preceding 'lights on' contained > 80% non-REM sleep and 0% REM sleep; REM sleep awakening: > 80% of REM sleep and 0% non-REM sleep. Five volunteers were excluded from the analysis because they did not report any dreams after any of the naps.
Results: The number of dreams recalled varied significantly across the circadian cycle (factor time: p<0.0001), showing a circadian modulation which was closely associated with the circadian rhythm of REM sleep occurrence during the naps. Peak values were observed in the late morning (10 am). The dream recall rate was 84% after awakenings from REM sleep and 57% after non-REM sleep awakenings. EEG power spectra from non-REM sleep awakenings with dream recall (57%) were compared with the 43% from non-REM sleep awakenings without dream recall. EEG power density (Cz) in the theta range (5-8.5 Hz) was significantly lower during non-REM sleep associated with dream recall compared with no dream recall (p<0.03). The amount of slow wave sleep and stage two sleep did not differ significantly between pre-awakening non-REM sleep with or without dream recall.
Conclusions: Our data indicate that the level of mental activity during sleep, as indexed by the number of dreams, shows a circadian modulation which is closely related to the occurrence of REM sleep. The association between dream reports and the reduction in theta activity during pre-awakening non-REM sleep may reflect a more "shallow" non-REM sleep state, allowing dream-like cognitive activity to occur during this state.

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0231.D

Affective Content and Intensity of Nightmares and Bad Dreams

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Introduction: Nightmares are usually defined as frightening dreams that awaken the sleeper. This definition emphasizes both an emotional (i.e., fear) and a behavioral (i.e., awakening) component. This definition presupposes that fear the only emotion in nightmares and that highly unpleasant dreams that do not awaken the sleeper (i.e., bad dreams) have

lower affective intensities than nightmares. Neither of these two assumptions, however, has been empirically tested.
Methods: Participants were 89 undergraduate students. They were given definitions of various types of dreams including a bad dream (very disturbing dreams which, though being unpleasant, do not cause you to awaken) and a nightmare (very disturbing dreams in which the unpleasant visual imagery and/or emotions wake you up). Participants kept a one-month dream diary and were instructed to report, for each remembered dream, the main emotions present (if any), their intensities on a 9-point scale, and to note whether the dream was a lucid dream, a nightmare, a bad dream, or a flying dream.
Results: Forty-two participants (47%) reported having had at least one nightmare in the four week log and 72 (81%) reported at least one bad dream. Thirty-six participants reported at least one nightmare in addition to one or more bad dreams. For these 36 participants, the mean emotional intensity of the nightmares and bad dreams was 7.95 $\pm$ 1.51 and 7.24 $\pm$ 1.15, respectively. A paired t-test showed that nightmares were rated as being significantly more intense than bad dreams ($p<0.001$). Six subjects reported mean emotional intensities for bad dreams that were greater than their mean nightmare intensities, and two had identical mean intensities. Eighty-four of the 180 bad dreams reported (47%) had an affective intensity equal to or greater than the average emotional intensity of the nightmares. An analysis of the principal emotions reported showed that 30% of all nightmares and 51% of all bad dreams contained primary emotions other than fear. In these dream reports, anger, sadness, and frustration were consistently cited as the most common main emotion. When compared to bad dreams, a significantly greater proportion of nightmares were reported to contain fear as a primary emotion ($p<0.01$). There was no evidence to suggest that nightmares and bad dreams which contain emotions other than fear are rated as being less intense than their fear containing counterparts.
Conclusions: Among individuals who report both nightmares and bad dreams, the average emotional intensities reported for nightmares is significantly higher than those reported for bad dreams. Almost half of the bad dreams, however, were rated as being as emotionally intense as nightmares. Therefore, dreams that do not awaken the sleeper can nevertheless be highly disturbing. A considerable proportion of individuals report intense nightmares in which the main emotion is one other than fear. The data thus support the awakening component of nightmares but not the fear criterion.

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0232.D

Age And Gender Differences In Dream Recall Estimated From A Web-Based Questionnaire

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Introduction: Studies examining retrospective dream recall frequency have reported age-related decreases in dream recall occurring in the thirties and more particularly after 50 years of age. Other studies indicate a net superiority in dream recall for females and decreases in recall starting much earlier for men than for women. We used results from a web-based questionnaire to examine relationships between age, gender and retrospective dream recall over the lifespan in more detail.
Methods: The sample was drawn from a collection of 5200 respondents who had completed a web-based questionnaire on typical dreams between January 1997 and November 2001. The target item was: 'How many dreams of any kind do you recall in an average month?'. Analyses were limited to subjects between 10 and 59 years old who responded to all demographic items and at least one typical dream item, who reported recalling not more than 100 dreams/month and whose internet address appeared no more than once in the database. The final sample consisted of 3589 women (M age: 25.92 ± 10.02) and 975 men (M age: 26.54 ± 10.56). Subjects were partitioned into ten-year age cohorts (10-19, 20-29, 30-39, 40-49, 50-59). For men, sample sizes were 309, 368, 164, 88, 46, respectively; for women, they were 1212, 1317, 619, 338 and 103. Responses were subjected to a 2 (Gender) x 5 (Age Cohort) mixed design ANOVA.
Results: An Age Cohort x Gender interaction ($F(4,4554)=2.39$, $p = .0487$) indicated different profiles for males and females. Male dream recall followed a linear trend ($p = .047$) with means for the 5 cohorts increasing with age: (10-19: $M=11.40 \pm 12.67$; 20-29: $M=11.80 \pm 11.17$; 30-39: $M = 13.21 \pm 15.08$; 40-49: $M=14.22 \pm 15.57$; 50-59: $M=14.61 \pm 17.92$). Female recall followed an inverted-U shaped quadratic trend ($p = .047$) (10-19: $M=14.10 \pm 13.39$; 20-29: $M=15.41 \pm 12.80$; 30-39: $M=15.57 \pm 13.49$; 40-49: $M=14.47 \pm 14.91$; 50-59: $M=11.59 \pm 11.42$). Females had significantly higher recall than males for cohorts 10-19, 20-29 and 30-39 (all $p < .05$) but not 40-49 and 50-59. When recall scores were log-transformed, essentially the same results were seen.
Conclusions: Results confirm the common finding (for ages 10-39 only) that females have higher recall than males as well as the finding that changes with age differ for the two sexes. Whereas the decrease among elderly women was expected, the continuing linear increase for males was not. Overall, this web-based questionnaire appears to provide retrospective recall estimates that are generally consistent with other methods of study but that may need to be improved to include control instruments that are sensitive to subject differences in internet usage habits with advancing age and other related demographic variables.

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0233.E

The Relationship Between Lifestyle Regularity and Subjective Sleep Quality

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Introduction: In previous work we have developed a diary instrument - the Social Rhythm Metric (SRM), which allows the assessment of lifestyle regularity, and a questionnaire instrument - the Pittsburgh Sleep Quality Index (PSQI) which allows the assessment of subjective sleep quality. The aim of the present study was to explore the relationship between lifestyle regularity and subjective sleep quality. We hypothesized that high lifestyle regularity would be conducive to better sleep.
Methods: Lifestyle regularity was assessed by both standard (SRM-17) and shortened (SRM-5) metrics; subjective sleep quality was assessed by the PSQI. Both instruments were given to a sample of 100 healthy subjects who were studied as part of a variety of different experiments spanning a 9yr time frame. Ages ranged from 19 to 49 yr (mean age: 31.2 yr, s.d.: 7.8 yr); there were 48 women and 52 men. SRM scores were derived from a two-week diary.
Results: The hypothesis was confirmed. There was a significant (rho=-0.4, $p<0.001$) correlation between SRM (both metrics) and PSQI , indicating that subjects with higher levels of lifestyle regularity reported fewer sleep problems. This relationship was also supported by a categorical analysis, where the proportion of "poor sleepers" was doubled in the "irregular types" group as compared to the "non-irregular types" group.
Conclusions: There appears to be a positive association between lifestyle regularity and good sleep, though the direction of causality remains to be tested. This finding may have clinical relevance in the development of behavioral strategies to facilitate or protect higher sleep

quality on a regular (predictable) basis especially when the ability to sleep is compromised either by increasing age with its attendant illnesses and possible depletion of psychosocial resources, or by physical and/or mental ill-health.

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0234.E

Do We Practice What We Preach? Shiftwork and Sleepiness in the Association of Polysomnographic Technologists (APT)

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Introduction: Shiftwork is known to contribute to increased sleepiness and reduced sleep quality and quantity. This study examined the prevalence of these problems in APT members working on the frontline of sleep research and medicine. We hypothesized that these problems would persist, despite specialized knowledge and the use of countermeasures.
Methods: A randomly started, systematic survey of the APT was conducted by mail. The response rate was 62%. For preliminary analysis, night shift responses from individuals who worked ³ 13 night shifts (N-group)(n=133) were compared with day shift responses from those who worked <13 night shifts (D-group)(n=95)for the past year.
Results: Results revealed no significant differences between groups in age, gender, weekly hours worked or existing sleep disorders. Ds were more likely to work in a supervisory role (N 38.5%; D 61.5%). Ns worked longer shifts (N mean=11.68 hours, SD=1.5; D mean=9.27, SD=1.39; $p<0.05$). Stanford sleepiness scores, modified for typical lowest level of alertness at work, were higher for Ns (N median=4, IQR=2-5; D median=2, IQR=2-3, $p<0.05$). Ns reported significantly more sleepiness driving to and from work, with several admitting to falling asleep driving in the past year (N 10.0%; D 5.0%). Epworth sleepiness scores were not significantly different, with both groups having a high percentage of scores >10 (N 34.8%, D 30.6%). Ns reported fewer hours of sleep between shifts (N mean=6.6, SD=1.5; D mean=7.4, SD=0.9; $p<0.05$). Ns scored higher on the sleep disturbance scale of the Standard Shiftwork Inventory (N mean=15.6, SD=3.9; D mean=12.5, SD=3.3; $p<0.05$). Countermeasures were quantified by frequency using a 5-point scale. Combined responses of 'sometimes, frequently, and almost always' are reported. The only countermeasure that differed significantly between groups was the use of bright light for synchronization to work schedule (N 48.1%; D 15.0%). Many used caffeine (N 64.3%; D 58.6%); while few used other stimulants (N 1.5%; D 1.1%), melatonin (N 8.6%; D 7.2%) or hypnotics (N 8.8%; D 7.2%).
Conclusions: These findings support our hypotheses and replicate those of existing studies, that night shiftwork was associated with less sleep between shifts, higher sleep disturbance and increased sleepiness. Regardless of work schedule, roughly 1/3 of APT members were excessively sleepy by conventional scoring standards, and several fell asleep while driving to and from work. While many APT members utilize bright light and caffeine to cope with shiftwork, nearly all work long night shifts, which are known to cause coping problems. Excessive sleepiness and other problems associated with shiftwork appear prevalent in the APT. We propose the inclusion of education and management policies to address these problems in accreditation standards for sleep laboratories.

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0235.E

How Well Do Fixed And Free Sleep Schedules Predict The Dim Light Melatonin Onset In Young Healthy Subjects?

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Introduction: The endogenous melatonin onset in dim light (DLMO) is a commonly used marker of circadian phase, and can be used to determine the time for the administration of light or exogenous melatonin in order to elicit desired circadian phase shifts. In some settings determining the DLMO is not feasible or is prohibitively costly and time-consuming. In this study we examined how accurately the DLMO could be estimated from subjects with free or fixed sleep schedules.
Methods: We analyzed baseline data from 100 young healthy subjects who participated in various studies in our lab. Some subjects slept at times of their own choosing ("free sleepers", N=60, mean age 27.3 y) and others slept on a fixed sleep schedule that closely matched their typical sleep schedule ("fixed sleepers", N=40, mean age 24.2 y). Subjects recorded bedtimes and wake times on sleep logs (verified with wrist actigraphy recordings). Each subject then participated in a phase assessment session, where they remained awake but reclined in dim light (<10 lux). Saliva samples were taken every 30 mins and were later assayed to determine the DLMO (20% of maximum method). We analyzed the sleep log data from the 6 days before the phase assessment session.
Results: The average (± SD) bedtime and wake times for the fixed and free groups were 23:05 ± 0.8 h, 6:38 ± 0.7 h and 00:44 ± 1.2 h, 9:13 ± 1.4 h respectively, and were significantly later in the free group (both $p<0.01$). As expected, the within subject variance in bed and wake times was significantly higher in the free sleepers than in the fixed sleepers ($p<0.05$). However, there was no difference between the groups in the interval from the DLMO to average bedtime (2.3 ± 1.3 h for fixed sleepers; 2.2 ± 1.1 for free sleepers). The correlations between bedtime and the DLMO and between wake time and the DLMO were stronger in the free group than the fixed group (free: r=0.65 and r=0.78; fixed: r=0.56 and r=0.47). We derived a regression equation from the relationship between the DLMO and wake time in the free sleepers: DLMO (dec. time) = 0.83 x wake time (dec. time) + 14.90. Using this equation we were able to predict the DLMO to within 1.5 h of when it actually occurred in 96% of subjects from an independent sample of free sleepers (n=26, Martin and Eastman, Chronobiol. Int., 2002).
Conclusions: Our results indicate that when measuring circadian phase is too costly or impractical, wake times (verified with wrist actigraphy) in young healthy subjects who sleep at times of their own choosing, can be used to the predict the DLMO. Requiring subjects to maintain a fixed baseline sleep schedule does not appear to improve the ability to predict the DLMO.

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0236.E

Comparing Bright Light, Dark Sunglasses, and Melatonin to Phase Delay Circadian Rhythms for Night Shift Work

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Introduction: Melatonin and various patterns of bright light and dark have been tested to help phase shift the circadian clock and promote adjustment to night work and day sleep schedules. This study tested various combinations of these interventions to determine their ability to produce phase delays.
Methods: Healthy young adults (32 males, 35 females, 23.9 ± 6.2 yrs) participated in the summer months of 3 years. They worked 5 consecutive simulated night shifts (23:00 to 07:00) followed by sleep at home

(08:30 to 15:30). Bedroom windows were darkened with black plastic. While traveling home, subjects wore sunglasses with normal or dark lenses (transmitted 15% or 2% of light respectively). Subjects took a placebo or melatonin (1.8 mg sustained release) pill before daytime sleep. During the night shifts, subjects were exposed to a moving pattern of intermittent bright light (~5000 lux, 20 min on, 40 minutes off, 4-5 light pulse/night) or remained in dim light (~200 lux). There were 6 intervention groups: 1) Dark/Sleep + Normal Sunglasses; 2) Dark/Sleep + Dark Sunglasses; 3) Dark/Sleep + Dark Sunglasses + Melatonin; 4) Dark/Sleep + Normal Sunglasses + Bright Light; 5) Dark/Sleep + Dark Sunglasses + Bright Light; 6) Dark/Sleep + Dark Sunglasses + Melatonin + Bright Light. There was a circadian phase assessment before (baseline) and after (final) the night shifts to determine the salivary dim light melatonin onset (DLMO). Sleep and night shift performance data are reported in an accompanying abstract (Lee et al).

Results: The final DLMO (mean clock time (SD in h)) in groups 1 through 6 was 2:29 (4.0), 4:19 (3.0), 4:42 (1.5), 6:08 (3.1), 6:57 (0.5), and 7:31 (0.6), respectively. Thus, the three bright light groups achieved complete re-entrainment to the daytime sleep schedule (DLMOs were 1-2.5 h before bedtime at 8:30). There was no difference among the three bright light groups and their DLMOs were significantly later than those of group 1. The difference between groups 1 and 2 (which differed only in type of sunglasses) did not reach statistical significance, showing that very dark sunglasses added little to the phase delay. There was no significant difference between groups 2 and 3 (which differed only in that one took melatonin and one took placebo), showing that melatonin does not increase the phase delay given very dark sunglasses.

Conclusions: Given appropriately timed bright light during the night shift and a regular daytime dark period, neither very dark sunglasses nor melatonin had any added benefit. The minimum combination of interventions that produced complete re-entrainment to the daytime sleep and night work schedule was bright light during the night shift, normal sunglasses during the commute home and a regular dark episode for daytime sleep.

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0237.E

Apparent Mechanism of the Afternoon "Nap Zone"

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Introduction: An afternoon period of transitory increase in sleep propensity is well documented for sleep latency; napping/siesta patterns, sleep in temporal isolation, and day sleep/sleepiness in medical sleep disorders. It is maximum about 180° out of phase from the mid-point of the major sleep period. We tested the hypothesis (Broughton, 1999; Webb, 1999)) that the phenomenon represents the period after morning awakening when accumulating process-S has increased to a sufficiently high level to facilitate sleep onset, while a more powerful SCN-dependent circadian arousal process has not yet risen high enough to reverse it. This was done by delaying and advancing the circadian arousal process using evening and morning bright light therapy and recording sensitive waking measures of sleep propensity (simple RT; motivation-free EEG spectral power, SP).

Methods: Eight normal male subjects, aged 20-30 years, balanced for morningness/eveningness (Horne-Osberg) were studied over two continuous 4-5 day periods under low ambient light (150 lux). Night sleep was restricted to 2300-0600h. 24-hr PSG included EEG (C3-A2, O2-A1), rightEOG-M1, leftEOG-M2 and submental EMG using 8-channel Oxford Medilog 9000 ambulatory recorders with concurrent q1min core body temperature recording using rectal probe and a Minilogger Series 2000 system. Each condition was preceded by a 24-hour baseline recording followed by two consecutive days of bright light stimulation (10,000 lux) either in the evening (2000-2200h) or morning (0600-0800h) in a cross-over design (half of Ss first had the evening and half the morning light treatment; then reversed). Daytime snacks were taken q1hr. No time cues were allowed. There was a 30 day re-adaptation period of regular sleep hours (actograph) between treatments. During wakefulness (other than during periods of bright light treatment) the level of waking arousal was assessed hourly by a 5 min sampling of artefact-free EEG for quantified SP analysis followed by a 10 min simple reaction time test for performance (P) vigilance level. QEEG-SP measures were averaged hourly. Stats were by ANOVA.

Results: Baseline prior to evening bright light treatment Ss had a Tmin at 0340h, Pmin (longest RT, most gaps) at 1346h and SPmax (all frequencies; theta) at 1400h. Evening light delayed these by about 1.5h to Tmin at 1540h (p .001), Pmin at 1452h and SPmax at 1600h (p .001). Baseline prior to morning bright light had the Tmin at 0348h, Pmin at 1452h, SPmax at 1500h. Morning bright light phase advanced the measures by about 1hr with Tmin at 0255h (p .01), Pmin at 1352 (.001), and SP max at 1600h (.001).

Conclusions: The phase delay of minimum daytime arousal measures by evening bright light treatment and their phase advance by morning bright light is consistent with the hypothesis.

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0238.E

Weekday DLMOs are Stable in Subjects Who Sleep One Hour Later on Weekends

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Introduction: The time of the dim light melatonin onset (DLMO), the offset (DLMOff), and the midpoint between the two are commonly used markers of circadian phase. This study examined the stability of these markers in subjects who maintained a fixed sleep schedule during the week but had later bed and wake times on weekends. We also wanted to see whether the process of collecting the melatonin profile (keeping subjects awake overnight in dim light followed by a midday nap) would itself shift circadian phase.

Methods: Healthy young adults (5 males, 6 females; 26.8±5.7 yrs) were required to be in bed with lights out from 23:00 to 7:00 on weekdays (regardless of their previous schedule) for 23 days. On weekends they were allowed to wake up and go to bed up to one hour later and were allowed to nap between 13:30 and 16:30 (i.e. 12 hours from nocturnal sleep). Every morning the subjects were required to go outside for a minimum of 15 minutes between 8:00 and 9:00 to receive natural light. To ensure compliance, all subjects wore wrist activity monitors, light sensors around the neck, and completed Daily Sleep Logs and Daily Light Logs. There were two overnight circadian phase assessments in dim light (<5 lux) beginning on Tuesdays (days 15 and 22) in which subjects gave saliva samples every 30 minutes. Following the first phase assessment, subjects napped from ~13:00 to 17:00. The DLMO and DLMOff threshold was 35% of the average of the three maximum levels.

Results: Analysis of the sleep log data in-between the two phase assessments showed that all subjects adhered to the weekday sleep schedule and went to bed and woke up about one hour later on weekends. Seven subjects took naps on weekends. The mean±SD time of the DLMO for the first and second phase assessment was 21:48±1.0h and 21:54±0.7h; the DLMOff was 6:30±1.1h and 6:48±1.0h. The absolute phase change (i.e., the phase shift giving both advances and delays a positive sign) was 0.5±0.2h for the DLMO, 0.7±0.6h for the DLMOff, and 0.4±0.3h for the midpoint.

Conclusions: In this study, all three phase markers remained very stable in phase assessments one week apart. The phase assessment and subsequent nap, and later weekend bed times, wake times, and naps did not

significantly alter phase. Hence, researchers could conduct a baseline phase assessment one week before an experimental manipulation to let subjects recover from the sleep deprivation of the phase assessment. Our results suggest that even if subjects sleep an hour later on weekends and nap 12 hours from the midpoint of their nocturnal sleep, their circadian phase will not change as long as they receive morning bright light and continue to follow a fixed weekday sleep schedule.

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0239.E

Alignment of Circadian Rhythms to Daytime Sleep Improves Performance and Alertness in Night Shift Workers

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Introduction: Impaired performance, reduced alertness, and fatigue are common complaints of night shift workers. These problems occur because their circadian clock is not aligned to a night work and daytime sleep schedule. In this study, bright light during the night shift, melatonin before daytime sleep, a regular dark/sleep opportunity, and sunglasses during the commute home were tested to determine their ability to delay the circadian clock. The phase delays produced by various combinations of these interventions are reported in an accompanying abstract (Crowley et al). Here, we report performance and alertness during the night shifts and daytime sleep duration.
Methods: During each of 5 consecutive simulated night shifts (23:00 to 07:00), subjects completed the Neurobehavioral Assessment Battery. Following each night shift, subjects had to stay in bed, in the dark, for a full seven hours (08:30 to 15:30). Subjects recorded bedtimes, sleep onset, and wake times on daily sleep logs (verified by wrist actigraphy). After the 5 night shifts, final circadian phase was assessed using salivary dim light melatonin onset (DLMO). The temperature minimum (Tmin) was estimated by adding 7 hours to the DLMO.
Results: Subjects were divided into 3 groups: those whose final DLMO was <1:30 (n=10), i.e. the Tmin did not occur during the time of the previous daytime dark/sleep period ("non-shifters"); those whose final DLMO was >1:30 and <5:00 (n=16), i.e. the Tmin occurred in the first half of dark/sleep (partial re-entrainment); and those whose final DMLO was >5:00 (n=41), i.e. the Tmin occurred in the second half of dark/sleep (complete re-entrainment). There was no difference among the 3 groups in daytime sleep duration (mean ± SD): 6.5 ± 0.6, 6.6 ± 0.3, and 6.7 ± 0.2h. There was no difference in performance or alertness between the group who showed partial and the group who showed complete re-entrainment. However, these two groups had significantly better performance and alertness than the non-shifters. For example, the average response time on the Psychomotor Vigilance Task during the last 3 night shifts for the non-shifters was twice as long (794 ± 857 versus 301 ± 40 and 311 ± 79ms) with twice as many lapses (7.1 ± 3.7 versus 3.5 ± 1.6 and 3.7 ± 2.2). They were also much sleepier (Stanford Sleepiness Scale: 5.1 ± 1.3 versus 3.7 ± 1.1 and 3.6 ± 1.3).
Conclusions: Even though all 3 groups slept almost all of the allotted 7 hours, there were differences during the night shift depending on the amount of phase delay. This shows that a reasonable amount of daytime sleep is not enough to reduce sleepiness or improve performance in night shift workers; some circadian alignment is needed. Furthermore, in young adults, complete re-entrainment is not necessary; partial re-entrainment is enough to increase performance and alertness during the night shift.

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0240.E

To Eastward Jet Lag Sufferers: Not So Fast!

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Introduction: Our previous study (Burgess et al, Sleep. 25: A182, 2002) tested a method to advance circadian rhythms during the 3 days before flight to reduce jet lag after eastward travel. The sleep schedule of the subjects was advanced by 1 h/day and they were exposed to one of three light conditions for 3.5 h upon waking (continuous bright light > 3000 lux, intermittent bright light: 4 pulses, 0.5 h on, 0.5 off, etc, and dim room light < 60 lux). The phase advances (mean ± SD) produced by the 3 treatments were 2.1 ± 0.5 h, 1.5 ± 0.8 h, and 0.6 ± 0.3 h respectively. There was no significant difference between the phase shifts produced by the continuous and intermittent treatments, and both were significantly greater than the dim light treatment. Since intermittent bright light is more convenient than continuous, the present study aimed to advance the circadian system further using the same intermittent bright light pattern, but coupled with a 2 h/day sleep schedule advance.
Methods: Healthy young adults received morning intermittent bright light with 2 h/day sleep schedule advances (n = 15, ages 22-35) and were compared to the intermittent bright light 1 h/day subjects run previously (n = 11, ages 22-36). Subjects sat at a desk facing one light box. Before and after the 3-day treatments, saliva samples were collected every 30 minutes in very dim light (< 10 lux) to determine the dim light melatonin onset (DLMO).
Results: There was no statistically significant difference between the phase advances produced by the two treatments (1.8 ± 0.5 h for 2 h/day and 1.5 ± 0.8 h for 1 h/day). We estimated the time of the temperature minima (Tmin) by adding 7 h to the DLMOs. There was no difference between groups in the interval from the baseline Tmin to the start of the bright light on the first treatment day (2.0 ± 1.2 h for 1 h/day and 1.7 ± 1.2 h for 2 h/day). The first light exposure started after the Tmin, i.e. on the advance portion of the PRC. On the third treatment day, the light started 1.5 ± 1.1 h after the final Tmin in the 1 h/day group, but 0.5 ± 1.5 h BEFORE the final Tmin in the 2 h/day group.
Conclusions: Increasing the amount of sleep schedule advance from 1 h/day to 2 h/day did not produce a significantly greater phase advance. Many of the 2 h/day subjects probably received some delaying bright light, especially on the third treatment day, possibly reducing their net phase advance. Thus, the 2 h/day sleep schedule advance was "too fast" for the circadian system in some people, even with morning bright light. More slowly advancing schedules (e.g. 1.5 h/day) and adding more days of treatment should be tested.

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0241.E

The Role of Cholinergic Projections from the Brainstem and Basal Forebrain to the Suprachiasmatic Nucleus: Implications for a Feedback Loop Between the Sleep-Wake and Circadian Systems

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Introduction: Mammalian circadian rhythms are regulated by the suprachiasmatic nucleus (SCN), a set of paired nuclei located in the hypothalamus, directly above the optic chiasm. The circadian clock can be reset by a variety of stimuli in a time-dependent manner. Carbachol, a cholinergic agonist, is capable of advancing the circadian clock of both rats and mice when applied during the night. Cholinergic projections to the SCN arise from both the basal forebrain and brainstem. To understand the behavioral context of cholinergic regulation, we are studying the effects of cholinergic stimulation in vivo on acetylcholine (ACh)

release at the SCN.
Methods: Rats were surgically implanted with a bipolar electrode aimed at the pedunculopontine tegmental nucleus (PPT) and with a microdialysis cannula aimed at the SCN. For continuous sampling of ACh levels, a microdialysis probe was inserted into the guide cannula 1 hr prior to lights out and rats were placed into a light-dark box. Artificial cerebralspinal fluid containing 500 nM neostigmine was perfused through the probe at a rate of 1 ul/min. Samples were collected hourly for 36 hr both in 12 hr light/dark (LD) and in constant darkness (DD). For stimulation experiments, animals were attached to fluid and electronic swivels 2 hr prior to stimulation, and allowed to equilibrate. Baseline samples were collected for 1 hr, and animals were then stimulated (20 min, 150 mA, 10 Hz, 2 msec pulse duration) at either circadian time (CT) 6, 14, or 18. Microdialysis samples were collected from the SCN for 100 min following stimulation and were analyzed by HPLC.
Results: ACh release profiles in both LD and DD show a peak in ACh during the first 5 hr of the 36 hr collection, followed by a sharp drop-off to barely detectable levels. This may be due to the presence of neostigmine in the perfusion fluid. Stimulation of the PPT results in an increase of ACh release in the SCN to 177% of baseline levels.
Conclusions: Basal release of ACh in the SCN, presumably arising from cholinergic projections in the brainstem and basal forebrain can be measured by microdialysis. However, the addition of neostigmine to the perfusion fluid may disrupt the normal release patterns. Additionally, stimulation of the cholinergic regions that project to the SCN results in an increase in ACh release at the SCN. Due to the role of these cholinergic regions in regulating both arousal and the sleep-wake cycle, and the fact that cholinergic agonists are capable of resetting the circadian clock, these results imply that these projections may be involved in a feedback loop between the sleep-wake cycle and circadian rhythms.

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0242.E

Daily 0.5 mg Melatonin Entrains the Free Running Circadian Rhythms of Blind Subjects in a Phase Dependent Manner

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Introduction: Exogenous melatonin (0.5-10 mg) has been shown to entrain the free running circadian rhythms of some blind subjects. The aim of the present study was to assess whether the entraining effects of a daily dose of 0.5 mg melatonin on the free running cortisol rhythm was phase dependent. Melatonin's effect on subjective sleep was also investigated.
Methods: Ten subjects (9 males, 1 female) with no conscious light perception, aged 32-65 years, with free running circadian rhythms (6-sulphatoxymelatonin (aMT6s) period () 24.27-24.95 h) were studied. In a placebo-controlled, single-blind design, subjects received 0.5 mg melatonin or placebo \italp.o.daily at 2100 h for at least one full circadian beat cycle (treatment duration 26-81 days). Subjective sleep was assessed from daily sleep and nap diaries. Urinary cortisol and aMT6s were assessed for 24-48 hours weekly and measured by radioimmunoassay.
Results: Seven subjects exhibited an entrained or shortened cortisol period during melatonin treatment. Of these, four subjects immediately entrained with a period indistinguishable from 24 h, two subjects continued to free run for up to 25 days during melatonin treatment before their cortisol rhythm became entrained, and one subject appeared to exhibit a shortened cortisol period throughout melatonin treatment. The subjects who entrained immediately did so when melatonin treatment commenced in the phase advance portion of the melatonin phase response curve (PRC) (CT6-18). When melatonin treatment ceased, all the subjects' cortisol and aMT6s rhythms free ran at a period similar to that seen before melatonin treatment. In the three remaining subjects melatonin treatment commenced in the phase delay region (CT18-6), and they failed to entrain. Compared to placebo, melatonin treatment significantly delayed sleep offset, decreased the duration of night awakenings and increased total sleep duration ($P<0.05$). Melatonin also had a marked effect on napping, significantly reducing the number and duration of naps compared to placebo ($P<0.05$).
Conclusions: These findings show that low dose (0.5 mg) melatonin is effective at entraining the free running circadian rhythms of blind subjects. Melatonin also had a positive effect on sleep, which may be due partly to its acute soporific properties. In agreement with our previous study with 5 mg melatonin, entrainment was more likely when melatonin was started in the phase advance portion of the melatonin PRC. However, in contrast to our previous findings, when 0.5 mg melatonin was started in the phase delay region, free running rhythms became entrained in some individuals part-way through treatment, when an appropriate circadian time for administration was reached. Thus if appropriately timed, melatonin is able to correct the underlying circadian disorder in addition to its acute beneficial effects on sleep.

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0243.E

Formal Similarity Between The Two Process Model And A Coupled Oscillator Model

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Introduction: The two process model provides a powerful framework for studying human circadian rhythms, which has been recognized as an alternative to the coupled oscillator models (Daan et al., 1984). On the other hand, we have proposed the coupled phase oscillator model which implements a photic and non-photic entrainment mechanisms of human circadian rhythms (Nakao et al., 2002). In this paper, the two process model and ours are shown to have similar mathematical structure in terms of a circle map, although these models are originated from different contexts.
Methods: The two process model consists of the two threshold oscillatory processes (C-process) and the rising and decaying exponential curve (S-process). Although this model may not look like an ordinary oscillator, it could be regarded as a limit cycle oscillator by constructing a circle map of the model, which maps a preceding wake-onset (or sleep-onset) phase to the next wake-onset (or sleep-onset) (Nakao et al., 1997). In contrast, our model consists of mutually coupled three phase oscillators, i.e., Osc I (an oscillator originated from suprachiasmatic nucleus (SCN)), Osc II (non-SCN oscillator), and Osc SW (overt sleep-wake rhythm) (Nakao et al., 2002). By ignoring the weaker couplings, the model could be regarded as a master-slave oscillator system which has a unidirectional coupling from Osc I to Osc II. This approximation enables us to construct a circle map for our model. Dynamics of the two process model and ours are compared in terms of the circle map structure.
Results: Characteristically, both of the circle maps (from a wake-onset to the next and from a sleep-onset to the next) of the two process model are shown to have a discontinuous jump, which is due to the discontinuity of a mapping from a wake-onset to the next sleep-onset (Nakao et al., 1997). Our analysis here shows that our phase oscillator model has similar discontinuous circle maps to the two process model, which are due to an implemented discontinuous coupling from Osc I to Osc II. In addition, the gap (between the thresholds)-dependency of the map structure in the two process model corresponds to the coupling-dependency in the phase oscillator model of ours.
Conclusions: Our study shows that the two process model and the coupled phase oscillator model of ours have similar mathematical structure

at an abstract level, although the different ideas are implemented in the different forms. The result suggests a possibility that dynamics underlying commonly found discontinuity in the circle map are essential in human circadian rhythms.

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0244.E

Increases In Evening- And Night-Time Melatonin Levels Following Brain Music Therapy For Anxiety-Associated Insomnia

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Introduction: A variety of studies reported psychophysiolocal effects of music. Different types of music may induce different neuroendocrine changes. For instance meditative music has been found to decrease levels of cortisol and adrenalin. Recently, acute increases in nocturnal melatonin production were reported following mindfulness meditation. Chronic insomniacs are known to have suppressed nocturnal outputs of melatonin. Stress and anxiety mediation is multifactorial and strongly influenced by GABAergic and dopaminergic neurotransmission. Melatonin as a CNS depressant with anxiolytic, mild hypnotic and anticonvulsant actions may also be involved in these effects. The purpose of this study was to investigate whether a specific type of music - "brain music therapy", a new non-pharmacological method for treatment of insomnia, could affect endogenous melatonin levels in patients with chronic insomnia and heightened anxiety traits.
Methods: Eleven volunteers (7 females and 4 males, aged 43.1±4.2) who had complained of long-term insomnia and who had scored above 50 on the Zung Self Rating Anxiety Scale were recruited for participation in the study. Their response to treatment with endogenously generated brain music was evaluated in an open pre- and post-treatment design. The duration of the treatment, which entailed listening to the music on a daily basis, was two weeks. Severity of sleep disruption was assessed using Athens Insomnia Scale. Dim Light Melatonin Onset test (DLMO) was performed on the nights before and after treatment. Saliva samples were collected every hour from 20:00h to 02:00h under dim light (less than 50 lux). In order to collect the saliva samples, the subjects had to chew on a cotton roll for approximately 2 minutes, then transfer the roll directly from mouth into the open end of the filter tube, avoiding touching the cotton roll with their fingers. Melatonin was assessed by Enzyme Linked Immunosorbent Assay (ELISA). Analysis of variance using the General Linear Model Procedure was employed to detect statistically significant differences in melatonin levels. Further analysis included Tukey post hoc paired comparisons and the non-parametric Mann-Whitney's U-test was used for the psychometric data.
Results: Brain music therapy reduced anxiety scores (62±5.2 vs. 42.5 ±4.3, $p<.01$). There was a significant improvement in sleep quality as judged by the Athens Insomnia Scale ($p<.001$). Eight out eleven insomniacs had extremely low absolute values of endogenous melatonin secretion in all samples (between 1.1 and 9.2 pg/ml) on a before treatment night. No discernible DLMO could be detected. Three patients had delayed DLMO occurred at 01:00h. The point-by-point comparisons between melatonin concentrations on the pre- and post-treatment occasions showed significant increases at 21:00 ($p<0.01$), 22:00h ($p<0.001$), 01:00 ($p<0.001$ and 02:00 ($p<0.002$).
Conclusions: In this study a two-week regimen of brain music therapy was shown to increase endogenous melatonin production. Whether brain music alters hepatic metabolism of melatonin or there is a direct involvement of pineal physiology remains to be clarified.

0245.E

Circadian and Wake-dependent Modulation of Fastest and Slowest Reaction Times in the Psychomotor Vigilance Task (PVT)

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Introduction: The PVT sensitively reflects a circadian modulation of neurobehavioral functions as well the effect of sleep pressure developing with duration of time awake, without being confounded by a learning curve. These two aspects of neurobehavioral functions can be well described by the two-process model of sleep regulation, with a homeostatic "process S" and a circadian "process C" driven by the biological clock in the SCN. Here we investigate how the fastest and the slowest reaction times (RTs) of the neurobehavioral functions measured by the PVT are influenced by the two processes "S" and "C".
Methods: Sixteen subjects (8 male, 8 female, age range 20-31y, mean: 25.1±3.4 SD) underwent a 40-h sleep deprivation (SD) or a 40-h multiple nap (NAP) protocol under constant posture conditions in a balanced crossover design. In the latter protocol sleep pressure was reduced by an alternating cycle of 150 min of wakefulness and 75 min of sleep, whereas it rose during the SD. The PVT was carried out every 225 min starting 75 min after lights on in the morning (75 min before and after each nap). The duration of a single PVT run comprised 5 minutes. The 5%(=fastest) and 95%(=slowest) percentile of the RTs were analysed by 3- and 2-way rANOVAS with the group factor NAP vs. SD and two repeated factors (5%/95% percentiles and time course).
Results: A three-way rANOVA showed a interaction of the factors 'percentiles' (5% vs.95%), 'sleep pressure' (NAP vs. SD) and 'elapsed time into the protocol' ($p=.009$). The fastest RTs remained remarkably stable under both high and low pressure conditions (interaction n.s.). A circadian modulation was evident for both percentiles under both SD and NAP conditions (p at least <0.002). In contrast, only the slowest RTs showed a significant deterioration under SD but not under NAP conditions (interaction: 'protocol' x 'time'; $p=0.0002$).
Conclusions: Differential responses of slowest and fastest RTs are seen only in a protocol where high sleep pressure dominates and the circadian modulation is of minor importance. Whereas both components of PVT performance undergo circadian modulation in both protocols, only the slowest RTs showed an influence of "process S", deteriorating progressively under increasing sleep pressure (SD). This can be interpreted as a consequence of brief moments of fluctuation in sustained attention, and fits into the concept of 'state instability'.

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0246.E

Phase Angle Between Melatonin Onset And Habitual Waketime In Morning-Type And Evening-Type Individuals Free Of Sleep Schedule Constraint

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Introduction: Studies have reported a shorter phase angle between circadian phase and habitual waketime in evening-type (E-type) compared to morning-type (M-type) individuals. However, this observation could have resulted from constraints imposed on the subjects' sleep schedules.
Methods: Two groups of subjects were selected according to their score on the Horne & Ostberg Morningness-Eveningness questionnaire (M/E score): 12 M-types (M/E scores 59 to 71, aged 19 to 34 y.) and 12 E-types(M/E scores 27 to 40, aged 21 to 30 y.), 6 women in each group. All had an habitual sleep duration of about 8 hours. The experiment was

scheduled in the summer, when the subjects had no work or school constraints. Each subject was free to set his/her own bedtime and waketime, with an 8-h sleep duration. This schedule was kept for the duration of the study, including the week prior to the admission (confirmed by actigraphy and sleep logs). Circadian phase was estimated by the dim light melatonin onset (DLMO), after a night of adaptation in the laboratory. Melatonin concentration was determined in 11 saliva samples collected every 30 minutes before bedtime, while subjects were reading or watching TV in dim light (<15 lux).

Results: M-types slept on average 2.7 h earlier than E-types (23:08 to 07:08 „b 37 min vs 01:45 to 09:45 „b 58 min, p< 0.001). DLMO was missing for one morning subject. DLMO was correlated with the chosen sleep schedule (r= 0.82, p< 0.0001), with an mean difference of 2.5 h between the two groups (M-types: 20:53 „b 88 min; E-types: 23:23 „b 86 min; p< 0.001). On average, phase angles between DLMO and waketime were similar in the two groups (M-types: 10.21 h „b 73 min, E-types: 10.37 h „b 61 min, p= 0.74). However, within each group, there was a significant negative correlation between DLMO and phase angle, showing that a later circadian phase was associated with a shorter phase angle (M-types: r= -0.90, p< 0.001; E-types: r= -0.73, p< 0.01).

Conclusions: On average, morning types and evening types showed the same phase angle between DLMO and waketime. In both chronotypes, the internal relationship between circadian phase and waketime appears to be the same when the subjects are free of sleep schedule constraint: a later circadian phase is associated with a shorter phase angle.

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0247.E

Ambient Illumination Among Older Brooklyn Residents: Influence of Ethnicity and Eye Diagnosis

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Introduction: Bright light exposure is an approved therapy for chronobiologic disorders, but it may have deleterious biologic effects. Population-based data suggest that sunlight (or more specifically UV-B radiation) is associated with cataracts and macular degeneration. Although previous studies have shed light on the effects of sunlight on eye diseases, most have used subjective measures or indirect light measurements. This study investigated 24-hour ambient illumination exposure in a Brooklyn-based sample.

Methods: Enrollment of Black (n = 41) and White (n = 29) volunteers (mean age = 68.27 $\pm$ 5.97 years and mean BMI = 27.68 $\pm$ 5.72 kg/m2) was balanced across the study period, ranging from February to July 2002. Of the sample, 73% were women and 27%, men. In the present analyses, we included sociodemographic data, daily ambient illumination and activity levels, sleep duration, and eye diagnosis. Eligible volunteers underwent an eye exam at SUNY Downstate, yielding data on visual acuity, visual field defects, intraocular pressure, cup-to-disk ratios, cup asymmetry, and nerve fiber layer thickness. Medical and ophthalmic data were used to formulate eye diagnoses. During the following week, volunteers wore an actigraph (Actiwatch-L) to monitor home ambient illumination and activity levels. Sleep was estimated with an algorithm provided by the manufacturer. Cosine analyses were performed on the raw activity data and on the logarithm of measured illumination, yielding average daily illumination and activity levels and acrophase timings. Internal Review Boards at UCSD and SUNY approved the study.

Results: Eighty-five percent of the volunteers reported good to excellent health. None was legally blind, but 27% were visually impaired. Of the sample, 5.8% were diagnosed with glaucoma; 7.2%, cataract; and 7.2%, ocular hypertension. Black volunteers received a median illumination exposure of 227 lux, and White volunteers received 1321 lux. For volunteers with an eye diagnosis, the median illumination level was 141 lux, and for those without, 641 lux. ANCOVA showed that both ethnicity and eye diagnosis had a significant main effect on daily illumination (Fs1,59s = 4.37, p < 0.05; Fs1,59s = 4.47, p < 0.05, respectively); covariates included age, sex, education, income, BMI, activity level, sleep duration, diabetes, and high blood pressure. No significant interaction was noted between ethnicity and diagnosis.

Conclusions: Our results suggest that older White volunteers in Brooklyn might be receiving adequate illumination. Thus, it may be unwise to encourage those receiving 1321 lux daily to increase daily sunlight exposure, as Whites are at greater risk for cataracts and age-related macular degeneration. Likewise, although older Blacks seem to experience lower daily illumination relative to their counterparts, it might be imprudent to advise those receiving greater than 227 lux daily to augment their sunlight exposure, unless greater ambient illumination is optimal for circadian entrainment or better health. In laboratory experiments, 150 lux exhibited phase-shifting properties and 250 lux showed melatonin-suppression effects. Moreover, epidemiologic data from different geographic areas suggest that Blacks may be predisposed to sunlight-induced glaucoma. The finding that individuals with an eye diagnosis, Black or White, received relatively less ambient illumination is very illuminating and might result from less time spent outdoors because of restriction imposed by diminished visual capacity. Future studies should investigate the amount of daily illumination exposure necessary for optimal health and well-being across different ethnic groups.

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0248.E

Age Associated Changes in the Circadian Regulation of Sleep: EEG Power Spectral Characteristics

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Introduction: Disturbed sleep in older adults is often characterized by nocturnal awakenings, unwanted early morning wakefulness, and frequent daytime napping. Evidence supports a role for age associated changes in circadian and homeostatic regulations of sleep as contributing to disturbed sleep in the elderly. The aim of the current experiment was to identify age-associated changes in circadian and homeostatic regulations of sleep in healthy elderly and young adults using EEG power spectral analysis during a 90-minute sleep-wake schedule.

Methods: Subjects were 15 healthy older adults (mean 76 $\pm$ 4yrs) and 19 healthy younger adults (mean 23 $\pm$3 yrs) who underwent psychiatric, medical, and sleep screening. Subjects followed a 90-minute sleep-wake schedule for 60 hours. Each cycle consisted of 30-minute sleep opportunities with continuous EEG monitoring, followed by 60 minutes of wakefulness. Core body temperature was measured by rectal thermistor. EEG sleep recordings were digitized at 256 Hz, filtered, and stored. Sleep episodes were visually scored in 20 second epochs. Following computerized artifact rejection, EEG signals were analyzed with power spectral analysis. EEG power density was determined for the following frequency bins: delta (0.25 – 4Hz), theta (4 – 8 Hz), alpha (8 – 13 Hz), sigma (13 - 16 Hz), and beta (16 – 32 Hz). Power density data for each bin were analyzed with mixed effects models using first-order autoregressive error structure and fixed 48-hour, 24-hour, 12-hour, 8-hour, 6-hour, and linear components. Only data from the middle 48-hours of the study were included. The linear component was interpreted to indicate increasing homeostatic sleep drive, whereas the 24-hour component indicated circadian regulation of sleep drive.

Results: Significant group differences were present in EEG delta power (p<.003, F=9.15), theta power (p<.003, F=8.90), and sigma power (p<.004, F=8.41) with the younger group having greater overall power.

Linear components were present in both delta (p<.002, F=12.19) and theta (p<.003, F=10.43) powers. Prominent 24-hour components were present in delta power (p<.0002, F=15.22) and beta power (p<.0001, F=53.29). Significant between-group interactions regarding linear components in delta power were also present (p<.024, F=5.15). Delta and beta power appeared to vary out of phase with one another.
Conclusions: During an ultradian sleep-wake cycle there were differences in EEG power in several frequencies between younger and older adults indicating age-associated decline in overall EEG power. Homeostatic regulatory influences were present in slower frequencies in both younger and older adults, but younger adults showed greater linear increase in slow wave sleep, suggesting a more robust homeostatic response than in older adults. While circadian regulatory influences were present in slow and fast EEG frequencies in both younger and older adults, clear age-associated differences in circadian regulation were not present. Age-related changes in sleep microstructure appear to be more strongly associated with changes in homeostatic regulation than changes in circadian regulation.

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0249.E

Circadian Modulation of Mood Under Differential Sleep Pressure Conditions

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Introduction: In healthy young subjects, forced desynchrony protocols have shown that subjective mood is modulated by a complex and non-additive interaction of circadian phase and duration of prior wakefulness. To further investigate this interaction, we analyzed the time course of mood ratings under differential sleep pressure conditions.
Methods: Following two scheduled days in the laboratory during which subjects slept at their habitual bedtime, 8 male and 8 female volunteers (age 20-31 years), underwent a 40-h sleep deprivation (SD) or a 40-h nap protocol (NAP) in a balanced cross-over design under constant posture conditions. In the NAP protocol, subjects were scheduled to an alternating cycle of 150 min of wakefulness and 75 min of sleep with ambient light levels of <8 lux during wakefulness and 0 lux during sleep. Subjective mood was assessed at 30-min intervals during wakefulness using a linear, nonnumeric, 100-mm bipolar visual analogue scale.
Results: Subjective mood displayed a highly significant circadian modulation during the NAP protocol (rANOVA, p<0.0001), whereas the rhythm was of low amplitude during SD (rAnova: interaction: [SD vs. NAP] x time; p<0.05). In the NAP protocol, mood began to decline after the nap scheduled during the wake maintenance zone, with lowest values after naps around the core body temperature minimum. Within each 150-min wake episode between naps, the time course of mood was such that, after low mood on awakening (sleep inertia), a gradual amelioration occurred, which was not influenced by the sleep structure of the preceding nap (rANOVA, NAP x time: n.s.). In both protocols, women tended to have lower mood ratings than men (ANOVA: p = 0.08). However, the interactions gender x sleep pressure or gender x time did not yield significance.
Conclusions: During the increasing sleep pressure condition in the SD protocol, mood remained remarkably constant, whereas under low sleep pressure condition (attained by multiple naps), mood declined during the subjective night, revealing a marked circadian rhythm. Interestingly, these variations in mood contrasted with those of subjective alertness, which deteriorated considerably during sustained wakefulness. It may be that high sleep pressure, even in healthy subjects, attenuates the deterioration of mood at the circadian trough. Could this be related to the well known mood-improving effects of SD in depressive patients?

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0250.E

Does Variable Circadian Adaptation In Night Workers Predict The Degree Of Growth Hormone Adaptation?

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Introduction: We previously reported that night workers show variable circadian adaptation, with their melatonin (MT) onset varying between 2200h and 0500h. The objective of this study was to determine whether the extent of the shift in MT onset could predict the degree of adaptation of the sleep-related growth hormone (GH) rhythm.
Methods: We established the 24-hr hormone profiles in ten day-active subjects and ten night workers during their usual sleep-wake schedule (sleep from 2300 to 700h and from 700 to 1500h respectively). Experiments were conducted under continuous nutrition, bed rest, dim light, in sound-proofed, air conditionned rooms. MT and GH were measured every 10 min over 24h (2300-2300h) by radioimmunoassay. The MT onset was defined as the time when the value of the best fit curve exceeded the mean of the 10 lowest consecutive MT values of the 24-hour profile + 2 standard deviations in at least 10 consecutive samples. GH secretory rates were calculated from plasma concentrations by a deconvolution procedure. The polygraphic sleep recordings were scored visually at 30-sec intervals.
Results: In day-active subjects, a major GH pulse occurred shortly after sleep onset in temporal association with the first slow wave sleep (SWS) episode. This pulse accounted for 52.8 ± 3.5% of the 24-hr GH production and the amount of GH secreted was correlated with the duration of SWS occurring during the pulse (r=0.65; p<0.05, spearman). In night workers, the temporal organisation of the GH pulses within 24-hours differed widely. Three of them presented well-adapted GH rhythms with a major pulse centered around sleep onset accounting for 44 to 77% of the daily production. In seven of the night workers, the sleep-related GH pulse accounted for only 16.5 ± 3.8% of the 24-hr secretion, showing no longer a correlation with SWS duration despite no differences in the duration of the first SWS episode. The amount of GH secreted during the sleep period was significantly lower in night workers (47.0 ± 9.1 vs 94.0 ± 15.0 µg; p<0.01). However, the amount GH secreted during the waking periods was increased so that the total amount of GH secreted during the 24 hours was similar in both groups (159.0 ± 28.2 vs 156.3 ± 18.6 µg; NS). One could not predict from the extent of the MT shift the degree of GH adaptation, i.e. whether the major GH pulse was centered around the first SWS episode and whether it accounted for the main quantity secreted during the 24h period.
Conclusions: These results indicate that whatever circadian adaptation in night workers, GH adapts on its own without any predictive rules. They corroborate previous findings in sleep-deprived subjects that a compensatory mechanism may occur during wakefulness to counteract the reduction of sleep-related GH secretion.

0251.E

Regional Differences in the Circadian Modulation of Human Sleep Spindle Characteristics

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Introduction: Transient EEG oscillations in the sleep spindle frequency range (12-16 Hz) are a hallmark of human non-REM sleep. Sleep spin-

dles originate in the thalamus and are considered to have a sleep protective function by reducing sensory transmission to the cortex. There is also growing evidence for an involvement of sleep spindles in memory mechanisms. Spindle frequency activity (SFA) in the low- and high frequency range shows circadian rhythms with opposite phase positions: low-frequency SFA (12.25-13 Hz) coincides with the peak and high-frequency SFA (14.25-15.5 Hz) with the nadir of the endogenous rhythm of melatonin secretion. It is not known whether this inverse circadian phase relationship in low- and high frequency spindle activity is based on a modulation of spindle frequency per se (i.e. a general slowing of spindle frequencies during the night), or a frequency-specific circadian modulation of spindle amplitude. Neither is it known whether circadian modulation of SFA characteristics varies across brain locations.

Methods: Sleep EEGs of 17 healthy volunteers (9 female, 8 male, age range 20-31 years), recorded in a 40-h multiple nap paradigm, were analyzed to compare SFA and sleep spindle characteristics during and outside the circadian phase of melatonin secretion along the anterior-posterior axis (Fz, Cz, Pz, Oz). Two different methodological approaches were used: classical spectral analysis (Fast Fourier Transform, FFT) and a new method for instantaneous spectral analysis (Fast Time Frequency Transform, FTFT) that yields high-resolution spindle parameters in the combined time-frequency-domain.

Results: FFT: EEG power spectra revealed a shift of SFA towards the lower end of the spindle frequency range during the phase of melatonin secretion ("biological night") compared to the phase with no melatonin ("biological day"). This shift depended significantly on brain topography, being maximal in the parietal derivation (Pz) and minimal in the frontal derivation (Fz).FTFT: the shift in the power spectra was based on a modulation of both spindle frequency and amplitude: during the biological night the incidence of low-frequency spindles increased, and the incidence of high-frequency spindles decreased (i.e. mean spindle frequency was reduced). Spindle amplitude during the night was enhanced in the lower spindle frequency range (<14.25 Hz) and reduced in the higher frequency range (>14.5 Hz). Furthermore, during the night, spindles were more stable in terms of reduced intra-spindle frequency variability.

Conclusions: Our data suggest that the circadian pacemaker promotes low-frequency, high-amplitude and homogenous sleep spindles during the biological night. This circadian rhythm of sleep spindle characteristics clearly depended on brain topography, providing further evidence for a brain-region-specific regulation of sleep spindles, which is modulated by the endogenous circadian pacemaker.

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0252.E

Effects of Chronic Caffeine Intake on Circadian Rhythms in the Rat

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Introduction: Recent studies have revealed anatomical and functional interactions between circadian and sleep-regulatory mechanisms. For example, direct and indirect projections arising from the suprachiasmatic nucleus (SCN) circadian pacemaker reach both sleep-active and wake-active neural systems in the forebrain and brainstem, and presumably mediate circadian influences on the sleep-wake cycle. Conversely, physiological correlates of sleep and arousal reciprocally influence the phase and period of the circadian pacemaker. While the mechanisms underlying these effects are not fully understood, serotonergic and possibly other monoamine neurotransmitter systems appear to play a role in transmitting behavioral state-related cues to the circadian pacemaker. The purine nucleoside, adenosine, is another endogenous neuromodulator that has been implicated in both sleep and circadian regulation, and that may therefore play a role in functional coupling of these two systems. While a role for adenosine in sleep-promotion has been relatively well-established, recent studies indicate that adenosine and adenosine receptors also modulate neuronal interactions in the SCN as well as the response of the SCN circadian pacemaker to both photic and state-related signals. The purpose of the present study is to further explore a possible role for adenosine in circadian regulation.

Methods: Male Long-Evans rats were maintained in individual cages equipped with drinkometers, under constant dim red light, allowing for continuous monitoring of free-running circadian drinking rhythms. Drinking rhythms were assessed for several weeks before, during and after chronic administration of the adenosine receptor antagonist and central stimulant, caffeine (1.0 or 3.0 mg/ml via the drinking water). Free-running period was evaluated for each phase of the experiment using both objective cosinor and periodogram measures and by visual inspection of activity records.

Results: Relative to baseline and post-caffeine water intake, daily fluid intake during caffeine treatment was reduced by about 10% in the lower-dose group and by about 30% in the higher-dose group. Rats in the lower-dose group achieved daily caffeine intakes of about 50-55 mg/kg/day, while rats in the higher-dose group consumed about 100-120 mg/kg/day (by comparison, these intakes are approximately 10-20 times those of typical human coffee drinkers). Fluid intake patterns were dramatically altered during caffeine intake, in that rats typically displayed many fewer (but generally larger) daily drinking bouts. Nevertheless, despite the high drug intake and disrupted drinking patterns, effects on free-running circadian period were modest. Free-running periods were slightly but significantly lengthened during caffeine treatment, and lengthened further after treatment termination. No differences in circadian period were seen between higher- and lower-dose groups.

Conclusions: Chronic caffeine intake resulted in small but reliable alterations in free-running circadian period. During baseline conditions, rats expressed free-running periods of less than 24.0 hours, suggesting that the dim red light employed in this experiment was functionally equivalent to constant darkness. Therefore, the effects of caffeine on free-running period observed in this experiment may be related to blockade of adenosine receptors intrinsic to the SCN circadian pacemaker. We are currently extending these results by examining the effects of chronic caffeine treatment on circadian rhythms under constant light conditions, in order to better understand the possible role of adenosine as a neuromodulator of the circadian system.

0253.E

Morningness And Eveningness In Adolescents

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Introduction: Many teenagers have difficulty with sleep and daytime alertness. It has been reported that at about the age of 13, the adolescents' time of day preference shifts to staying up later and feeling that they work better during the evening hours from an inclination of waking up early and performing their best in the morning. The aim of this study is to assess eveningness and morning tendencies and the impact of daytime sleepiness on school performance in a population of adolescents.

Methods: This study was conducted in 63 adolescents in Grade 8 at an elementary school in Hamilton, Ontario. A five-page questionnaire was administered containing questions about the adolescents' sleep pattern, their ability to wake up in the morning, how sleepy they are during the day and their general daytime performance. An 11-item Children's Morningness and Eveningness scale was included in the questionnaire battery.

Results: The average age of the students was 13 ± 0.3 of which 41% were males and 59% were females.Twenty-seven percent reported extreme problems awakening in the morning, 40% stated that they were sleepy during school and also were too sleepy to do homework, 33% admitted to being late for school on one or more occasions, and 19%

reported that their grades had dropped due to daytime sleepiness. On the Children's Morningness and Eveningness scale, the population average response for 9 out of the 11 questions ranged from 1.9 to 2.9 indicating a preference for the evening/night hours. On 2 of the 11 questions, the students had an average score of 3.3 indicating a neutral type of circadian preference.
Conclusions: The overwhelming majority of students in our study population had a preference for evening hours. Almost one-half of the adolescents were sleepy during school and around one-third of those questioned had difficulties awakening and getting to school on time. Disturbingly, one-fifth of the adolescents attributed their lower grades to daytime sleepiness.

0254.E

The Effects of Napping and Activity as Countermeasures for Mitigating Fatigue- Induced Decrements in Performance on the Night Shift

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Introduction: The effect of fatigue on performance is a safety-related concern across all modes of the Department of Transportation. Consequently, in 1999, the U.S. Congress appropriated funding for the Federal Aviation Administration (FAA) Civil Aerospace Medical Institute (CAMI) in 1999 to study shiftwork issues related to Air Traffic Control Specialists (ATCS). Three research activities were developed: 1) the administration of a nation-wide ATCS workforce survey, 2) field studies at a Tower/TRACON and an Air Route Traffic Control Center (ARTCC), and 3) a laboratory study to evaluate clockwise and counter-clockwise rapidly rotating (2-2-1) shift schedules. The results from these studies suggest that regardless of the type of shift worked, working at night and to a lesser extent, early in the morning results in fatigue-related performance decrements. Based upon these findings, the current investigation examined the effectiveness of two short-duration countermeasures on performance during the night shift: two 20-minute naps and two 20-minute periods of mild activity (i.e., pedaling a stationary bike at 20% of Vo2 max).
Methods: Two experiments were conducted (Experiment 1, n = 11; Experiment 2, n = 12). Both protocols included two training days followed by three rapid rotations from early morning (0600-1400) to midnight shifts with 48 hours off between shifts. Participants were not allowed to sleep between the morning and midnight shift, resulting in approximately 17.5 hours of prior wakefulness at the beginning of the midnight shift. In experiment 1, performance was assessed immediately following each treatment. In experiment 2, performance was assessed 40 minutes after each treatment to allow time for sleep-inertia recovery. Treatments (naps, activity, and control) were administered twice during the night shift, and each participant served in all three, randomly ordered treatment conditions. Performance was assessed using the Bakan Vigilance Task.
Results: For experiment 1, there was no effect for treatment condition. The analysis for experiment 2, however, revealed a significant main effect for treatment, $F(2, 10) = 5.4$, $p < .05$. Multiple comparisons indicated that participants performed significantly better in the napping condition ($M = 87.5$, $sd = 27.8$) than in the control condition ($M = 78.0$, $sd = 25.4$), $t(11) = 3.4$, $p < .05$.
Conclusions: Results of these experiments indicate a potential benefit for napping, but not for mild activity, when performance was measured 40 minutes after the nap to control for sleep inertia. These data represent a "worst case scenario" where a controller works a rapidly rotating shift schedule with no opportunity for rest prior to the midnight shift. Nevertheless, two 20-minute naps appear to have been effective at mitigating performance decrements on the night shift.

0255.E

Effect of Increasing Light Intensity vs. Increasing Light Duration on Phase Shifts of the Circadian Clock of Humans

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Introduction: Exposure to bright light is the primary synchronizing stimulus for the circadian clock and an established method for the treatment of circadian rhythm and sleep phase disorders. The magnitude of the response of the clock to light is a function of both the intensity and the duration of the stimulus. Duration and intensity response curves are well established in rodents, but have not been fully characterized in humans following exposure to a single short pulse of light. Here we compare the effect of increasing the intensity of the exposure with increasing the duration of exposure on the magnitude of light-induced phase shifts of the circadian clock.
Methods: 44 healthy young subjects (19 M and 25 F, 29.3 ± 5.2 yrs of age) were admitted to the Clinical Research Center on two occasions, each stay lasting 4 nights/3 days. Subjects remained under controlled conditions during waking hours (light <20 lux) with sleep for 8 hours in dark. Following a habituation and baseline night, subjects were exposed to either dim control (< 20 lux) or bright light (2,000 or 4,000 lux for 1, 2, or 3 h or 8,000 lux for 1 h), 3 hours before the core body temperature nadir. Melatonin levels in plasma were assessed throughout the baseline and post-treatment nights. Light-induced changes in the melatonin rhythm were assessed at the midpoint (50%) of the melatonin profile. The difference in the magnitude of phase shifts obtained following bright light and control treatments (± SEM) was compared by ANOVA.
Results: Exposure to bright light for 1 h delayed the circadian melatonin rhythm in an intensity dependent manner. The rank order of phase delays was 2000 lux (0.14 ± 0.18 h, n = 4) < 4000 lux (0.20 ± 0.28 h, n = 5) < 8,000 lux (0.42 ± 0.21 h, n = 8). However, increasing the intensity of exposure did not significantly increase the magnitude of phase delays, and exposure to bright light (8,000 lux) for 1 h resulted in smaller phase delays than exposure to lower intensity light (2 - 4,000 lux) for 2 h (0.65 ± 0.18 h, n = 10) or 3 h (0.75 ± 0.20 h, n = 11). The effect of increasing the duration of exposure approached significance (p = 0.11).
Conclusions: These results indicate that either increasing the intensity of a short light pulse or increasing the duration of exposure can increase the effect of light on the circadian clock of humans. However, increasing the intensity of light exposure above 2,000 lux is not as effective as increasing the duration of light exposure beyond 1 h. These results can provide practical guidelines for the light treatment of circadian rhythm and sleep phase disorders.

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0256.E

SAFe to Drive? Circadian Pattern of Microsleep Episodes & Attention Lapses vs. Subjective Ratings of Sleepiness, Alertness or Fatigue in Healthy Drivers Sleep

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Introduction: Sleepiness and alertness are known to exhibit a biphasic pattern with increased sleep propensity and decreased alertness in the early morning and late afternoon periods. It is unclear to what degree drivers' ratings of sleepiness, alertness or fatigue (SAF) are accurate reflections of physiological fluctuations of propensity to fall asleep. We observed circadian patterns in subjective SAF ratings versus EEG-veri-

fied occurrence of microsleep (MS) episodes or attention lapses (AL) in a group of healthy adults repeatedly undergoing a computerized driving simulation task.

Methods: Subjects were given a series of baseline questionnaires and underwent clinical screening to ensure eligibility. 16 healthy adult subjects were included in the study; all possessed a valid driver's license, had regular sleep schedules, had no significant medical, psychiatric or sleep disorder and did not use medications that affected alertness. Mean values for Epworth Sleepiness Scale, Fatigue Severity Scale and ZOGIM Alertness Scale all fell within normal ranges.Using the York Driving Simulator (York Computer Technologies), subjects performed four 30-minute driving sessions at two-hour intervals (i.e. at 10:00, 12:00, 14:00, and 16:00). Before each simulation subjects completed the Stanford Sleepiness Scale (SSS) and subjective visual analog scales of sleepiness, alertness, and fatigue. During each session, individuals were monitored for occurrence of MS (defined as occurrence of 15 to 30 seconds of any sleep stage by EEG/EMG/EOG criteria) and AL (defined as intrusion of alpha- or theta EEG activity lasting more than 3 seconds but less than 15 seconds). Mean values of each variable at every time of simulation were attained and analyzed using a general linear model and paired sample t testing.

Results: Individuals' subjective SAF ratings did not show significant diurnal variation across the four testing sessions. While the occurrence of AL failed to show a circadian variation of significance ($F=0.5$, $df=3$, $p=.58$), there was a significant within-group variation throughout the day of testing for the occurrence of MS episodes ($F=4.4$, $df=3$, $p=0.2$). Specifically, MS episodes were found to occur more often at 16:00 in comparison to all other times, which between them did not vary significantly [MS10:00 – MS16:00 ($p = 0.01$) / MS12:00 – MS16:00 ($p = 0.02$) / MS14:00 – MS16:00 ($p = 0.00$)].

Conclusions: While our sample of healthy adults failed to rate a subjective fluctuation in SAF throughout the day during the driving task, episodes of MS occurred most frequently in the late afternoon. This suggests that individuals' subjective rating of their fitness-to-drive with respect to SAF may underestimate their physiologically occurring sleep-proneness. This prospective study correlates with known statistics of circadian patterns in sleepiness-related accidents. By better understanding circadian fluctuations in driver sleepiness and alertness, it is hoped that health-care professionals may be in a position to better educate the public about cautionary measures to prevent vehicle accidents.

0257.E

Morningness/Eveningness, Sleep Patterns and Internet Addiction in College Students

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Introduction: Morning-types and Evening-types have been shown to differ in sleep-wake habits, endogenous circadian rhythms and behaviors. The circadian preference is also known to vary with age: phase delay in adolescents and phase advance in the aged. The present study evaluated the relationships among M/E types, sleep patterns and internet addiction tendency in college students.

Methods: 559 college students in Korea(mean age=20.6) completed a comprehensive survey which included items regarding sleep and internet use, a morningness/eveningness(M/E) scale (Smith, Reilly and Midkiff, 1989) and several questionnaires (regarding internet addiction, self-esteem, loneliness).

Results: The M/E scores from 599 students ranged from 13 to 53 (higher scores indicative of greater morningness), and the mean was 30.44(sd=6.28). M/E types were identified by the 10-90 percentile split of the scale: M-types(39-53: n=60: mean=41.2) and E-types(13-22: n=54: mean=19.46). Compared to M-types, E-types reported significantly later bedtimes on weekdays and weekends, as well as wake-up times, more evident on weekends (all p values were < .001). There was a clear difference in the sleepiest hours of the day : 1-3pm for 57% of M-types vs. 8-11am for 56% of E-types. However, no difference in TIB(time-in-bed: sleep duration) was found between M-types and E-types, either on weekdays or on weekends. For the two types, the # of days taking a nap during weekdays was not different either. In spite of the same amount of TIB, E-types' daily sleep debt (subjective ideal sleep need minus weekday TIB) was 1 hour 16min, compared to M-types'16min. While 43% of E-types reported problems of falling-asleep, only 10% of M-types did. However, the two types were not different in the level of daytime sleepiness during classes. With no significant difference in total # hours of internet use,E-types showed higher scores on the Internet Addiction Test (Young, 1999) and spent relatively more time on 'games', compared to M-types ($p<.001$). E-types were also lower on self-esteem scale (Rosenberg, 1965) ($p<.001$).

Conclusions: The finding of more sleep debt on weekdays in E-types (in spite of same Time-in-Bed as in M-types) can be explained, at least in part, in relation with the delayed phase of their circadian rhythm. By forcing to go to bed and get up earlier, in the light of their delayed circadian rhythm, E-types's sleep latency is longer and they feel less rested upon awakening. And, they feel sleepiest in the morning(in 8-11am), right after awakening. This may lead to their subjective feeling of more sleep debt. On the other hand, when E-types attuned their bedtime and wake-up time to their endogenously driven preference on weekends, they didn't sleep longer than M-types. And, E-types showed more tendency toward internet addiction and lower self-esteem. Present findings suggest that morningness/eveningness might be related not only to sleep patterns but also to many other psychological variables. How M/E types, sleep need, and other cognitive/behavioral/personality factors are related needs to be further explored.

0258.E

The Effects Of Sleep-Wake Pattern And Social Interactions On Mental Health Of University Students

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Introduction: Both the rise time and the bedtime of university students are delayed as their grade progresses (Fukuda & Ishihara, 2001). Several studies showed that disturbed sleep-wake pattern was related with mental malfunctioning (e.g., Totterdell et al., 1994; Wolfson & Carskadon, 1998). University students' mental health might be adversely affected by their delayed sleep pattern. For university freshmen who left their home and have begun to live alone, social interactions with peers may keep their mental health well, but, at the same time, they may delay the bedtime of the freshmen. The present study aimed at investigating the effects of sleep-wake pattern and social interactions on mental health of university students.

Methods: The questionnaire was consisted of a part for demographic data, a sleep log, an estimation of time spent alone per day, and GHQ: General Health Questionnaire, which estimate students' mental health. The freshmen participated in the survey in May and July, and the same survey was conducted in July with students in higher grade. Total number of participants was 180 (freshmen in May and July, n=53; students in higher than second grade in July, n=74). Japanese academic year begins in April.

Results: The amount of social interaction was estimated by subtracting time of alone from total time of wakefulness. The amplitude of autocorrelation coefficient was calculated with sleep log data as an index of regularity of sleep-wake pattern. The correlation coefficient between the amount of social interactions and the regularity of sleep-wake pattern was significant only with the data of freshmen in May ($r=-.338$, $p<.05$). The multiple regression analysis was conducted to estimate the effect of the regularity of sleep-wake pattern, the amount of social interactions, and the type of residence (living with their family or not) on the total score of GHQ. With the data of freshmen in May, students living with

their family were significantly in good mental health (beta=-.372, p<.05). With the data of students in higher grade, the total score of GHQ was significantly correlated with the regularity of sleep-wake pattern (beta=-.432, p<.01) and with the social interactions (beta=.280, p<.05). However, with the data of freshmen in July, the multiple correlation coefficient was not significant (R=0.278, n.s.).
Conclusions: These results suggest that social interactions with peer students probably disturb the sleep-wake regularity immediately after entering the university, and that the importance of sleep-wake regularity for mental health increase with grade progress of university students. However the results of the correlation between mental health and social interactions were different from what we predicted. It turned out that the amount of social interaction had no effects on freshmen's mental health, and in higher grade students, social interactions might have even negative impact on their mental conditions.

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0259.E

Circadian Variations in the Onset Time of Acute Ischemic Stroke in Korean Population

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Introduction: We investigated diurnal variations of stroke onset in a hospital-based stroke data bank (Hallym Stroke Registry Data Bank: HSRDB) and analyzed demographic and clinical factors related to the circadian rhythmicity of stroke.
Methods: Five hundred and twenty consecutive acute ischemic stroke patients were recruited between January 1999 and December 2000. The onset of stroke was identifiable in 365 patients (70%) and divided in quartiles (0:00 to 5:59, 6:00 to 11:59, 12:00 to 17:59, and 18:00 to 23:59). Age (below 45 years, between 45 and 75 years, above 75 years), gender, temporal profile (transient ischemic attack; TIA, complete stroke, stroke in evolution), lesion location (anterior or posterior circulation), risk factors (prior stroke history, hypertension, diabetes mellitus, hyperlipidemia, cardio-embolic source, smoking) and etiologic stroke subtypes (small-vessel-occlusion, large-artery-atherosclerosis, cardio-embolism, stroke of other and un-determined etiology) were analyzed.
Results: Among 365 patients, 93 strokes (25.4%) occurred during the first quartile, 98 strokes during the second quartile, 98 during the third quartile and 76 during the fourth quartile (Chi-Square test; p=0.310). Age, gender, lesion locations and risk factors were not significantly different among each quartile. Of temporal profile, TIA occurred more frequently during the third quartile and least frequently during the first quartile (Chi-Square test; p=0.034). In the etiologic stroke subtypes, only cardio-embolism showed significant diurnal variation and occurred frequently during the second quartile and least frequently during the fourth quartile (p=0.030).
Conclusions: Our data suggests that circadian variation of acute ischemic stroke, as a whole, is not significant in Korean population. However, TIA and cardio-embolic strokes seemed to have significant diurnal variation.

0260.E

Corticosterone Circadian Rhythm is Shifted by Restricted Access to Food in the Rat

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Introduction: In the rat, a nocturnal animal, the circadian peak of plasma corticosterone is located at the beginning of the dark period. Food intake also follows a circadian rhythm and is known to influence the secretion of corticosterone. Some studies have reported that feeding, when restricted to daytime, entrains the circadian rhythm of corticosterone. The procedure however was associated with weight loss indicating that animals have ingested less calories and were undernourished. In the present study, we measured the effect of a feeding schedule restricted to the first 8h of the light period on the rat corticosterone circadian rhythm in the absence of body weight loss.
Methods: Eleven adult male Wistar rats kept in standard housing conditions were fed ad lib during the first of a three-week protocol. On the following two weeks, access to food was restricted to the first eight hours of the light period, i.e., from 8h00 to 16h00. Starting at 8h00, blood was collected from tail veins every four hours for 24 hours on days 7, 15 and 21. Food and water intake as well as body weight were also measured daily. Plasma samples were analyzed for corticosterone in one assay using a [125I]CORT radioimmunoassay kit. The sensitivity of the CORT assay was 7.7ng/ml and intra-assay coefficient of variation was 4.5 %. Comparisons were performed using an one-way ANOVA for food intake, water intake, body weight and repeated measures ANOVA for plasmatic corticosterone. The data are expressed as Mean ± SEM.
Results: Restricting access to food gradually shifted the maximum circadian peak of corticosterone from 20h00 to 8h00 without affecting its amplitude. A secondary peak of lesser amplitude remained at the onset of the dark period. Weight increased normally (+16%) during the three weeks except for the first three days of restricted access to food. During the restricted feeding schedule, rats ingested 88% of the total food ingested over 24 hours in the ad lib feeding period. Body weight increased similarly in the ad lib and the daytime feeding period.
Conclusions: These results support the notion that food can be regarded as a synchronizer of the circadian rhythm of corticosterone. The persistence of a secondary peak at dark-onset supports previous demonstrations of the existence of a peripheral clock that can be uncoupled from the SCN pacemaker.

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0261.E

Effects of Sleep and Time of Day on Epileptic Seizures

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Introduction: Various factors can influence the occurrence of seizures. These include metabolic disturbances, fever, illness, stress, and sleep deprivation. In many patients with epilepsy, seizures are more likely to occur in sleep – particularly NREM sleep. However, the effect of the circadian rhythms on seizures has not been well studied. We analyzed the time of day and sleep/wake state in which seizures occurred in our inpatients with epilepsy.
Methods: Patients were observed by nursing staff throughout 3-9 days of continuous video-EEG recording, while anti-epileptic medications were partially or fully withdrawn. This long term monitoring was performed to help localize the epileptiform focus in patients being considered for surgical intervention. We retrospectively analyzed 28 consecutive long term recordings in well-characterized patients: 16 patients had temporal lobe epilepsy (TLE) and 12 had extra-temporal focus or multiple foci (XTLE). Each seizure was classified according to subject group (TLE vs. XTLE); sleep/wake state, and the time of day of seizure occurrence (grouped into 6 x 4 hour 'bins').
Results: 93 seizures were recorded in the 28 patients: 42 seizures in the 16 TLE patients and 51 in the 12 XTLE patients. If seizures were evenly distributed across the day and night, we would expect approximately

17% of seizures to occur in each of the 6 x 4 hour bins. However, there were clear day/night patterns of seizure frequency in the two groups, with differences in the patterns between groups. In the TLE group, there was a clear peak in the time of occurrence of seizures, with 46% occurring between the hours of 15:00 and 19:00. The frequency ranged from 7% to 19% in the other 5 x 4 hour bins. In the XTLE group, there were two smaller peaks: between the hours of 7:00 and 11:00 (28% of seizures) and between 19:00 and 23:00 (30% of seizures). To ensure that no single subject contributed disproportionally to these observations of day/night patterns of seizures, we analyzed each individual's data. Of the 16 patients with TLE, 8 had most or all seizures between 14:00 and 19:30. In contrast, the 12 patients with XTLE had seizures occurring at various times with no definite 'preferred' time period.In the TLE group, only 17% of seizures started from sleep, with more than half of these (4/7) being associated with an arousal. In contrast, in the XTLE group, 43% of seizures started during sleep and only 4/22 were associated with an arousal. This difference between groups was significant (p=0.007, Fisher's Exact Test for proportion of seizures occurring from sleep in TLE vs. XTLE).

Conclusions: There are clear day/night patterns of seizure frequency in epilepsy, with differences in the patterns between temporal lobe and extra-temporal lobe epilepsy. There is an additional interaction with sleep/wake state, with relatively few seizures occurring from sleep in temporal lobe epilepsy (17%) compared to extra-temporal lobe epilepsy (43%). Thus, it appears that both sleep/wake state and circadian rhythms may affect seizure proclivity, with different effects depending upon the seizure focus.

0262.E

Temperature and Activity in Bilateral Olfactory Bulbectomy

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Introduction: Bilateral olfactory bulbectomy (OBX) syndrome has been proposed as a rat model of depression. In addition to biochemical and behavioral evidence, published literature has described REM sleep abnormities compatible with such a possibility. Previous reports on motor activity and temperature have been contradictory, some authors reporting changes in OBX rats, others not. Methodological issues possibly contribute to these apparently contradictory observations. Indeed, some of the previous reports surprisingly did not segregate between the light-dark phase. In other cases, measurements were taken for only two weeks. In the present study we recorded locomotor activity and central temperature for three weeks following OBX using the light-dark period as an analysis factor.

Methods: Thirty-six adult Sprague Dawley male rats were equally distributed into four groups: a control sham operated group and three groups according to time elapsed after OBX: one, two and three weeks. OBX was performed according to the method of Van Riezen et al. (1990) and radio-frequency emitters were installed in the abdominal cavity. Rats were then individually housed under standard conditions: 12:12 light-dark cycle with lights on at 8h00 AM, room temperature at 22°C and controlled humidity. Food and water were available ad libitum. Recordings started two weeks after surgery. Central temperature and activity of each OBX group rats were independently compared to sham controls using ANOVAs and LSD post hoc tests.

Results: We found a significant groups effect for temperature ($F(3;116) = 3,70$; $p < .05$). LSD post hoc analyses showed that temperature of OBX rats was higher than that of controls at one week following surgery, only during the dark period. We found a significant groups effect for activity ($F(3;38) = 3,10$; $p < .05$). LSD post hoc analysis revealed that all three OBX groups showed increased activity compared to controls, an effect restricted again to the dark period.

Conclusions: The temperature and activity disorders we observed in OBX rats support the contention that OBX syndrome is a valid animal model of depression. The fact that differences with sham operated animals were restricted to the dark period warrants further investigation in that respect.

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0263.E

Stability of Circadian Phase Markers Under Regular Sleep Schedules

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Introduction: Rhythms of core body temperature and melatonin are regulated by the circadian clock, and are commonly used as measures of the timing, or phase, of circadian rhythms. Comparison of these two measures under constant routine conditions indicates that the timing of melatonin is a more stable marker of circadian phase. However, little is known about the variability of these phase markers under less controlled conditions. In addition, there is little consensus about the method of analysis. The objective of this study was to assess the stability of various circadian melatonin and temperature phase markers in subjects with regular sleep schedules.

Methods: Baseline data was analyzed from 45 healthy young subjects (18 M, 27 F, 29.4 ± 5.4 years) who were admitted to the Clinical Research Center on at least two occasions, separated by at least 3 weeks. Subjects were instructed to maintain a regular sleep schedule, which was monitored for 1 week before admission by sleep logs and actigraphy. Subjects spent one habituation night under controlled conditions (< 20 lux, semi-recumbent, snacks/2 h, with 8 h sleep in dark) prior to collecting baseline temperature and melatonin measurements. Blood was sampled every 20-30 min throughout the night and analyzed by RIA. The phase of the melatonin rhythm was assessed by 8 different methods. The temperature nadir (Tmin) was estimated using both Cleveland and Cosine curve fitting procedures. Correlation analysis was performed to assess stability between repeated admissions and between the phase markers.

Results: Melatonin phase markers were significantly correlated between the first and second assessments, with r2 values ranging from 0.54 to 0.69 ($p < 0.001$). Markers of melatonin offset between the two admissions were more highly correlated than markers of melatonin onset (e.g., 20% onset: $r2 = 0.55$, 20% offset: $r2 = 0.69$). In contrast, Tmin for the two baseline assessments was not correlated if analyzed by the Cleveland procedure and modestly correlated if fit by a simple cosine curve ($r2 = 0.27$, $p < 0.01$). In addition, Tmin was more highly correlated with melatonin offset (20%, $r2 = 0.31$), than with melatonin onset (20%, $r2 = 0.11$).

Conclusions: These results indicate that in subjects with a regular sleep schedule, melatonin phase markers are stable over at least a 3 week period. There is, however, a tendency for the declining phase of the melatonin profile to be more consistent than markers of melatonin onset. In contrast, phase estimates of the circadian temperature nadir show little consistency between admissions. Of the two methods for estimating Tmin, simple cosine analysis appears to be more reliable. Further research is needed to determine the most reliable and appropriate analytic methods for determining the phase of circadian rhythms.

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0264.E

Circadian Rhythm Of Salivary Cortisol In Night Shift Workers With And Without Light/Darkness Intervention

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Introduction: We have previously described a light/darkness intervention designed to promote adaptive phase shifts in night shift workers, as evaluated using core body temperature and salivary melatonin collected during constant routines in the laboratory. In this report, we present preliminary analyses of the change in the salivary cortisol rhythm in this combined field and laboratory study.
Methods: Subjects were night shift workers scheduled to work 12 shifts over a 20-day ambulatory investigation period. Saliva samples, destined for the assay of cortisol concentration were collected hourly during 36-hour constant routines (<7 lux) preceding and following the work period. To date, samples have been analyzed for 10 subjects. Treatment group workers (n=5; mean age ± SD: 34.8 ± 6.3 years) received a light/darkness intervention (including 6-hours of bright light in the workplace and tinted goggles for use during the morning commute), designed to promote adaptive shifts of the circadian pacemaker. Control group workers (n=5; mean age: 41.15 ± 9.9 years) remained in their habitual work environments. All workers maintained regular sleep/darkness schedules following night shifts. Hormonal assays were performed using commercially available kits (Diagnostic Systems Laboratories). The fitted maximum and minimum of the curve of cortisol concentration during constant routines were determined for each subject using a dual-harmonic regression model. One subject significantly contributed to the variability observed in our control group results at the initial constant routine, but his results have been retained within the analyses. ANOVA and student t-tests and were used to compare means between groups.
Results: At the time of the initial constant routine mean (± SEM) fitted minima and maxima of the cortisol rhythm occurred at 03:15 ± 03:10 and 07:11 ± 1:20 and in the control group and 00:23 ± 0:14 and 07:10 ± 0:18 and in the treatment group. Following the work period, mean fitted minima and maxima of the cortisol rhythm occurred at 6:12 ± 3:07 and 10:14 ± 2:06 and in the control group and 8:10 ± 2:01 and 15:08 ± 3:03 and in the treatment group. For the cortisol maximum, a significant effect of time was detected where the time of the fitted maximum differed significantly between constant routines in the treatment group (F s1,8s=7.43, p=0.03).
Conclusions: Pending the analysis of results from all night shift workers in this study, these preliminary results suggest that the rhythm of salivary cortisol remained maladapted in the control group despite a small shift in the rhythm. This is in line with our previous observations of the melatonin and core body temperature rhythms. Our results may also indicate a distortion in the temporal relationship in the quiescent period and the peak of cortisol secretion in maladapted workers. This, too, is in line with previous reports and may be further investigated with forthcoming results from the rest of the experimental group.

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0265.E

Spindle Frequency Activity Following Simulated Jetlag in Young Adults

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Introduction: Recent evidence indicates that sleep spindles and spindle frequency activity display a circadian pattern. The temporal distribution of spindle frequency activity during the night should thus be sensitive to the circadian phase at which sleep is scheduled. The aim of the present study is to test the effect of a 5-hour advance of the sleep schedule on spindle frequency activity during sleep in healthy young subjects.
Methods: Seventeen healthy participants (mean age ± SD: 25.20 ± 3.29 years, 4 females) maintained a regular sleep schedule for at least 3 weeks prior to admission. After 3 baseline days, subjects underwent a 35-hour constant routine. They then lived for one week on a schedule that was advanced by 5 hours relative to baseline and were exposed to a daily 6-hour light stimulus of 380 lux administered in a background of 4 lux followed by a 45-hour constant routine. In one group (**late light**; n=7), phototherapy was planned prior to bedtime to prevent circadian adaptation. In the other (**early light**; n=10), phototherapy was started at the original time of awakening and was advanced by one hour daily until the stimulus start was at the shifted time of awakening. This schedule was designed to achieve circadian adaptation to the shifted sleep schedule. Sleep was polysomnographically recorded in total darkness. Sleep episodes of the last baseline day and of the last shifted day were analyzed. Spectral analysis of frequency ranges consistent with sleep spindles were performed using low (12.25–13.00 Hz), middle (13.00–14.00 Hz), high (14.25–15.00 Hz) and all sigma activity (12.25–15.00 Hz). Data was analyzed by hourly bins for each sleep episode and the bin of peak activity was determined.
Results: A phase advance of +5.32 ± 0.76 hours and +1.38 ± 2.64 hours was observed in the early light and late light groups, respectively. This shift was significant in the early light group only (Wilcoxon signed ranks: p=0.023) and indicated a circadian adaptation to the shifted schedule. A circadian misalignment thus persisted in the late light group in that subjects were going to bed at a circadian phase that was 3.5-hours earlier than on their original schedule. In this group, the peak of low sigma activity was delayed by -1.57 ± 1.51 hours compared to baseline (p=0.033). No significant differences were observed in peak hour of other sigma activity. No within group differences were observed in the early light group.
Conclusions: The present study indicates that circadian phase at which sleep is scheduled can significantly affect the time course of low sigma activity. As in previous reports, the low range sigma activity was the most sensitive to circadian phase. These results also indicate that the temporal distribution of spindle frequency activity is sensitive to light-induced phase shifts.

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0266.E

Subjective And Objective Evaluation Of Sleep And Performance In Daytime Versus Nighttime Sleep In Extended Hours Shift-Workers At An Underground Mine

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Introduction: There is a trend towards "compressing" the workweek, i.e. extending the workday from the traditional 8-hour rotating shift-work schedule to a 10- or 12-hour rotating shift-work schedule. However, the 10 or 12-hour workday has the potential for adverse consequences for workers particularly during the night shift such as poorer sleep quality, increased worker fatigue and fatigue-related accidents and decreased work performance.
Methods: The study was set out to examine subjective and objective measurements of sleep and performance in a group of randomly selected underground miners one-year after the change from backward rotating 8-hour to a forward-rotating 10-hour shift schedule. The purpose of

the study was to evaluate the impact of the 10-hour shift schedule on daytime versus nighttime sleep measurements and performance. Out of approximately 500 total subject pool, 182 workers (36%) responded to a questionnaire survey one month before, one month after and one year after the shift schedule change implementation. The subjects were almost exclusively male (95.7%), 41.9±7.0 years mean age, married (84.2%), working at the mine for 17.6±5.7 years and working shift-work at the mine for 15.2 ±6.6 years. 40 miners were randomly selected to participate in computerised performance testing (Mackworth Clock Test) only and a second group of 20 randomly selected miners were selected to participate in both computerised performance testing and sleep study (Polysomnography) on three consecutive days and then three consecutive nights.

Results: Polysomnography results showed 10-hour night-shift workers (day-time sleep) stayed less time in bed ($p<.0001$) but took shorter time to fall asleep ($p<.005$) and maintained sleep efficiency equivalent to 10-hour day shift workers (night-time sleep). Objective performance test findings suggested improved task vigilance as measured by mean reaction time ($p<.001$) for workers on the 10-hour night shift as compared with 10-hour day shift schedule. Subjectively, 10-hour night-shift workers reported fewer problems with job performance, more refreshing sleep and fewer driving difficulties than 8-hour night shift workers. 10-hour day-shift workers reported greater performance impairment (in terms of alertness, memory and attention) and less sleep than 8-hour day shift workers.

Conclusions: These are some of the first data to suggest that a night shift that does not encompass the entire night period may have significant benefits to shift-workers. We suggest that these benefits are due to the timing of the new night shift start and finish times rather than their longer duration. The improved sleep and performance that the workers reported on the new 10-hour night shifts schedule may be due to the earlier finish time (3:00 a.m.) compared with the 8:00 a.m. finish time of the 8-hour night shift.

0267.E

The Effect of Staying Up Late on Circadian Phase: Biomathematical Predictions versus Experimental Findings

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Introduction: Even at relatively low levels, light exposure has been shown to be a dominant zeitgeber for humans in laboratory experiments. The common practice of delaying bedtime by staying up late at night exposes individuals to light across a greater part of the delay portion of their phase response curve for light. The potential for circadian phase delay from delaying bedtime was investigated with an experiment and with biomathematical modeling.

Methods: As part of a larger experiment, n=11 subjects (ages 28.4 $\pm$ 4.8; 6 females) each underwent two 36-hour sleep deprivation periods in a laboratory. Prior to sleep deprivation, subjects were scheduled to go to bed either at 22:00 or at 04:00 for 7 consecutive days at home (rising time was fixed at 10:00). Only one of the sleep deprivation periods (in randomized order) was preceded by the 04:00 bedtime condition. Subjects were monitored by means of actigraphy to assess their sleep times and light exposure (30-second bins) during the 7 days scheduled at home. The last night of the 7 scheduled sleep periods was spent inside the laboratory and recorded polysomnographically. During the subsequent 36-hour sleep deprivation periods, core body temperature was recorded (6-minute bins) with a rectal probe to assess circadian phase. Posture and activity were controlled and meals were standardized, and ambient light levels in the laboratory were maintained below 50 lux. Biomathematical simulations using the state-of-the-art Kronauer-Jewett model equations (CPSS software version 1.2-beta) were also run, to assess the predicted differential effect for the 7 days of scheduled bedtimes (22:00–10:00 versus 04:00–10:00) on circadian phase during the subsequent 36-hour sleep deprivation period.

Results: Using mixed-effect harmonic regression models with a fixed 24-hour period, the phase difference between the body temperature curves recorded during laboratory sleep deprivation after the two different bedtime schedules was assessed. Circadian phase was significantly delayed by 14.3 $\pm$ 5.2 minutes (mean $\pm$ s.e.) after subjects went to bed at 04:00 compared to when they went to bed at 22:00 for 7 days ($t=2.77$, $p=0.022$). Biomathematical simulations using the population-mean observed sleep times (actigraphy and polysomnography estimates) and day-average light exposure levels yielded a circadian phase delay of 153.6 minutes for the 04:00 bedtime condition, which was significantly greater than the experimentally observed phase delay ($t=1781.5$, $p<0.001$). Further simulations showed that this modeling result was robust to error variance in sleep times and light levels.

Conclusions: Delaying bedtimes by 6 hours for 7 days did not result in the circadian phase delay we had expected. It is unclear what role the chronic loss of sleep may have played in stabilizing circadian phase. Light exposure may not have been the only entraining factor that acted on the circadian system in this study.

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0268.E

Relationship Between Circadian Phase, Sleep, and Diurnal Preference In Patients With ASPS and DSPS

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Introduction: Two of the most common sleep disorders in humans thought to be due to alterations in circadian timing are Delayed Sleep Phase Syndrome (DSPS) and Advanced Sleep Phase Disorder (ASPS). DSPS is characterized by a persistent inability to initiate sleep before 2-6am and difficulty waking up until 10am, whereas ASPS is characterized by habitual and involuntary sleep times that are several hours earlier than societal means. The most common complaints are sleepiness in the late afternoon or evening, and early morning awakening of 2-5am. The goal of this analysis is to determine if patients diagnosed with ASPS or DSPS also exhibit differences in objective measures of sleep times, physiological markers of circadian phase, and diurnal preference.

Methods: This retrospective study involves the clinical diagnosis and phenotypic characterization of 80 subjects (8 ASPS, 32 DSPS patients, and 40 phase-normal controls). ASPS and DSPS patients were diagnosed by sleep clinicians according to current diagnostic criteria based on self-reported sleep times and exclusion of possible confounding conditions. Extended evaluation of the phenotype included subjective and objective measures of sleep patterns and circadian rhythms. Sleep measures consisted of bedtime, wake time, sleep onset and offset, and sleep duration estimated from wrist activity recording. Circadian measures included the physiological monitoring of core body temperature and melatonin rhythm, and the subjective assessment of diurnal (time-of-day) preference.

Results: One-way analysis of variance showed significant differences between groups for sleep and circadian measures. DSPS patients were on average going to bed and waking up later than ASPS patients by 2.87 hrs and 3.14 hrs, respectively, and than control subjects by 2.22 hrs and 2.64 hrs ($p<.05$). Compared to controls, ASPS subjects had an earlier body temperature nadir by 2.95 hrs and dim-light melatonin onset (DLMO) by 2.72 hrs ($p<.05$), whereas DSPS subjects had a later temperature nadir and DLMO by 2.85 hrs and 2.94 hrs ($p<.05$), respectively. There was a strong correlation between circadian phase and sleep onset and offset in both ASPS and DSPS subjects. Interestingly, there was a different phase relationship seen as a longer interval between temperature nadir and sleep offset in the ASPS group compared to controls. All groups were different in diurnal preference, ASPS subjects scoring

as larks and DSPS subjects scored as owls (p=.0001).
Conclusions: Present results show significant differences in the means of these groups for sleep and circadian measures, however there is overlap of these measures in all groups. Inclusion of subjective and objective measures of habitual sleep time, circadian phase, and diurnal preference may greatly facilitate accurate diagnosis of ASPS and DSPS and lead to an improved understanding of the underlying pathopysiology of these disorders which will be important in the development of better treatment strategies.

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0269.E

A Length Polymorphism In The Circadian Clock Gene Per3 Is Linked To Delayed Sleep Phase Syndrome And Extreme Diurnal Preference

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Introduction: Circadian rhythms are generated by interacting clock genes, the concerted coexpression of which determines time-dependent aspects of physiology and behaviour, including sleep. Diurnal preference, as determined by the Horne-Östberg (HO) questionnaire, has been shown to correlate with circadian period (). The pathological diurnal extremes advanced and delayed sleep phase syndrome (ASPS and DSPS) are likely to be linked to extreme . We studied the correlation between a length polymorphism in the clock gene *Per3* and diurnal preference, both within the normal population and amongst patients suffering from DSPS. The two alleles defined by this polymorphism encode either four or five units of an 18-amino-acid repeat region.
Methods: Out of 484 volunteers who completed the HO questionnaire and donated buccal DNA samples, 7% of subjects with the highest (morning preference) and lowest (evening preference) scores, were selected, together with a control group of equal size with an intermediate score. Blood samples were also collected from 16 unrelated patients (8 males, 8 females, aged 27±16 years) suffering from intrinsic DSPS. Informed consent was obtained from all subjects. PCR and agarose gel electrophoresis were used to identify whether individuals were heterozygous or homozygous for either of the *Per3* repeat alleles.
Results: A significant trend was observed between the frequency of the two *Per3* alleles and the groups with extreme evening and morning preference (squared test for trend, P=0.030), with the frequency of the 5-repeat allele significantly higher in the morning-preference group (5-repeat: 0.42, 4-repeat: 0.58) than in the evening-preference group (5-repeat: 0.24, 4-repeat: 0.76; Fisher's Exact Test, P=0.047, odds ratio=2.205). Amongst DSPS patients, the frequency of the 4-repeat allele was significantly higher (5-repeat: 0.12, 4-repeat: 0.88) compared to the total control population (all 105 selected individuals; 5-repeat: 0.32, 4-repeat: 0.68) (Fisher's Exact Test, P=0.022, odds ratio=3.352). No 5/5 homozygotes were found in the DSPS group and 75% were homozygous for the 4-repeat.
Conclusions: This is the first reported correlation between a polymorphism in a clock gene coding region and extreme diurnal preference in humans, including DSPS, a pathological form of extreme eveningness. We speculate that this could be created by the varying number of phosphorylation target sites between the protein products of the two alleles. The identification of a robust link between this polymorphism and extreme diurnal preference in humans indicates a precise way in which differential PER3 phosphorylation may contribute to the phenotypic difference. This finding also identifies a potential genetic marker for extreme diurnal preference, which may prove clinically useful in the differential diagnosis of DSPS.

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0270.E

Sleep Length Skews Distribution of Morningness/Eveningness Scale Scores in a College Population

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Introduction: College-age individuals show clear evening preferences in their activities. However, recent morningness/eveningness (M/E) self-rating scale-score distributions show unusual increases in proportion of eveningness scores, with concomitantly reduced morningness scores. One explanation might be general decreasing sleep length and difficulties in wakening that would encourage individuals to answer scale items in an ¡°eveningness-oriented¡± manner despite their underlying biological M/E disposition. This could skew M/E score distributions of the 19-item MEQ scale (Horne-Östberg) and 13-item BALM scale (Brown). Distribution changes related to sleep length were investigated.
Methods: MEQ and BALM scales were completed by 1,079 university students (ages 18-22; 35% male, 65 % female), plus open-ended questions about bedtimes and awakening times for typical and non-typical days, and usual sleep duration. Correlation between the two M/E scale scores reached .875 (Pearson *r*); inter-scale correlation for chronotype classifications (Morning-, Evening-, or Neither-type) was .60 (Spearman Rho), with the MEQ classifying slightly more Evening-types than the BALM. Self-reported average hours of nightly sleep categorized subjects into three nearly equal sleep-length groups (short sleep (shortS) £¡Ü6.5 hours (n=358), medium sleep (mediumS) 6.6-7.4 hours (n=361), long sleep (longS) ³¡Ý7.5 hours (n=360)). ANOVA was used to compare M/E mean scores by sleep-length group. Kolmogorov-Smirnov (K-S) one-sample tests evaluated overall MEQ and BALM score distributions against the normal distribution. K-S two-sample tests evaluated distribution differences between sleep length groups on the two scales.
Results: The MEQ scores (mean=40.6) were approximately normally distributed (K-S p=.143) while the BALM scores (mean=29.5) differed from a normal distribution (K-S p=.003). Distribution kurtosis and skewness were somewhat larger for the BALM (-.309 and .230, respectively) than for the MEQ (-.271 and .152, respectively). Shorter sleep length was associated with greater eveningness scores on both scales: MEQ (shortS mean=39.4, mediumS mean=40.3, longS mean=42.1; p<.001) and BALM (shortS mean=29.1, mediumS mean=29.3, longS mean=30.2; p=.021). Further analysis by K-S tests showed significant differences between MEQ score distribution attributes for all sleep length groups (shortS vs. longS p<.001, shortS vs. mediumS p=.044, mediumS vs. longS p=.025). The BALM score distributions for sleep length groups differed only for shortS and longS groups (p=.011). The shortS group had the largest positive skew for both MEQ and BALM (.407 and .378, respectively) as compared with the mediumS group (-.007 and .278, respectively) and longS group (.086 and .043, respectively).
Conclusions: Shorter sleep is associated with increased evening-oriented M/E scale scores.Furthermore, shifts in M/E scores with changes in sleep length also result in changes in score distribution attributes, such as positive skew toward eveningness. This suggests differential rates of changes to various areas within the distribution, particularly on the morning-oriented end. Changes in sleep length appear to change the distribution more for the MEQ than for the BALM.

0271.E

Dissimilar Circadian Regulation Of Thyrotropin And Free Thyroid Hormone Between Short Sleepers And Long Sleepers

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Introduction: Thyrotropic function in humans is influenced by circadian and sleep dependent processes. Previously we reported reduced thyrotropin (TSH) secretion in habitual short sleepers (sleep duration < 6 h) compared to long sleepers (> 9 h). Here we sought to determine (1) whether this disparity can be attributed to a smaller circadian amplitude in TSH secretion in short sleepers than long sleepers, and (2) whether a potential difference in the TSH rhythm translates into corresponding changes in free thyroid hormone, the metabolically active component of the hypothalamo-pituitary-thyroid (HPT) axis.

Methods: Young (20-34 years) healthy short sleepers (8 males, 5 females) and long sleepers (5 males, 4 females) were recruited in the Washington DC metropolitan area on the basis of questionnaires, 2-4 week sleep logs and wrist motor activity recordings. After sleeping according to their habitual schedule subjects underwent a -h constant routine protocol during which they stayed awake in bed in dim light (<10 lux), without having access to clocks. Blood samples were collected half-hourly for 24 h (14:00-14:00) and plasma concentrations of TSH, free thyroxine (T4), and free triiodothyronine (T3) were measured.

Results: The amplitude of the educed circadian rhythm in TSH (non-linear regression model with 24-h and 12-h cosine components, plus linear component) was smaller ($p<0.001$, t-test) in short sleepers (0.69 ± 0.11 (SEM) mU/ml) than long sleepers (1.52 ± 0.21 mU/ml). This difference was accompanied by a difference ($p<0.008$) in the amplitude of the educed circadian rhythm in free T3 (short sleepers: 0.13 ± 0.02 pg/ml; long sleepers 0.24 ± 0.04 pg/ml). The amplitudes of TSH and free T3 correlated across subjects ($r=0.57$, $p<0.006$, $N=22$). In both groups the two circadian rhythms showed a close temporal association, with free T3 lagging TSH by approximately 1 h (median lag of individual cross correlation analysis). In addition, the smaller nocturnal TSH surge in short sleepers tended to be accompanied by a smaller nocturnal free T4 increase compared to long sleepers ($p=0.062$, Group x Time, rANOVA).

Conclusions: A short habitual sleep duration is associated with a dampened circadian rhythm in TSH secretion. In addition, and in contrast to previous reports that have focused on total thyroid hormone and found no circadian rhythm, the present results show that the circadian signal in plasma TSH translates into corresponding changes in free thyroid hormone. Previously we showed that short sleepers live under higher homeostatic sleep pressure than long sleepers. It is concluded that HPT axis function is governed by a complex interaction of homeostatic sleep pressure with the output of the circadian pacemaker. Furthermore, the present results identified a physiological pathway through which habitual sleep duration may affect metabolic function.

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0272.E

Sleepiness on the Night Shift in Shift Work Sleep Disorder

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Introduction: Despite years of working night shift the endogenous circadian rhythms of most individuals fail to adapt to the imposed work-sleep schedule. Therefore, many night workers experience circadian misalignment, and an unknown proportion of workers are at risk for developing Shift Work Sleep Disorder (SWSD; International Classification of Sleep Disorders). This disorder is characterized by excessive sleepiness during work and leisure time and/or insomnia when sleep is attempted. The combination of circadian misalignment and cumulative sleep loss can lead to lapses of attention and unintended sleep episodes that contribute to occupational and vehicular accidents. We report here objectively measured sleepiness, during typical night shift hours, for a large sample of patients meeting criteria for SWSD.

Methods: Patients meeting the criteria for SWSD for at least 3 months were identified for participation in a clilnical trial. Eligible patients worked „d5 night shifts/month („T12 hour/shift with at least 6 hours between 2200 and 0800), of which „d3 were consecutive. Sleep pathologies other than SWSD and uncontrolled illnesses were excluded by history, physical examination, and polysomnography (PSG). The PSG and a multiple sleep latency test (MSLT) were conducted following the last of three or more consecutive night shifts at their place of work. The MSLT was conducted on the first night (at 0200, 0400, 0600 and 0800) after the last night shift, and the PSG followed the next day at approximately1000-1800h. A 20-minute psychomotor vigilance test (PVT) was also performed on the night of the MSLT at 0100, 0300, 0500, and 0700.

Results: MSLT and PSG were completed for 372 patients. Nine patients were excluded for technical reasons. Thus, 363 patients (18 to 62 yrs) comprise the sample for this descriptive analysis. Approximately 90% worked steady night shift. The mean sleep latency on the MSLT for all 363 patients was 2.75 + 3.24 minutes. Mean latencies for each time of night, across all patients, were: 4.27, 2.68, 1.98, and 2.05. Of the 363 night workers screened, 327 (90.1%) met the MSLT criterion for pathological sleepiness (< 6 minutes). Analysis of the baseline PVT for a subgroup of patients yielded approximately a mean of 22.65 performance lapses per 20 minute testing period (greater than 1 performanc lapse per minute).

Conclusions: Patients meeting the diagnostic criteria for Shift Work Sleep Disorder had severe sleepiness during typical night shift hours. The level of sleepiness is comparable to patients with untreated narcolepsy or obstructive sleep apnea. The PVT data further suggest that the sleepiness is likely to have consequences in performance and accident risk. Identification of SWSD patients who place themselves and others at risk because of their occupational responsibilities should become a priority for the medical community.

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0273.E

Null Allele Mice for the MOP-3 Gene have Increased Sleep Time and Altered Sleep Consolidation

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Introduction: The regulation of sleep and wakefulness has been modeled as a two-process system, in which homeostatic and circadian components determine the propensity and timing of sleep, respectively. While homeostatic sleep drive cam be modulated by the circadian cycle, it is not clear whether these two processes are independent or interconnected at a cellular or systems level. Mice with mutations of the circadian gene, Clock, have attenuated sleep-wake rhythms, generate less total sleep and have an attenuated homeostatic response to sleep deprivation. In mammals, Clock heterodimerizes with MOP-3 (BMAL-1) to form an important translational-transcriptional feedback loop for the molecular control of circadian rhythms. In this study, we have recorded sleep in

mice with a null allele for the MOP-3 gene.
Methods: The generation of C57Bl/6J mice carrying a null allele for the MOP-3 gene has been described in detail previously (Bradfield et al., 1998). Mice (3-4 months old) were anesthetized and surgically implanted with EEG and EMG electrodes. Ten homozygous (-/-), 10 heterozygous (-/+) and 9 wild-type (+/+) mice were entrained to a 12 hr light/dark (LD 12:12) cycle with lights on at 6:00 AM and lights off at 6:00 PM. In a second experiment, baseline data was collected on 8 -/-, 8 -/+ and 7 +/+ mice in constant darkness (DD). Food and water were available to all animals ad libitum. Data were analyzed using ANOVA and Scheffe post-hoc tests.
Results: *Entrained conditions* : In -/- mice, amounts of sleep and wakefulness were evenly distributed across the 24-hrs, as evidenced by a light:dark ratio of nearly 1.0 for wake (.945±.02), NREM (.945±.02)and REM (.99±.25) sleep. Light:dark ratios were similar between +/+ and -/+ mice for wake (.54±.02; .51±.02), NREM (2.03±.14; 2.15±.14) and REM (2.84±.23; 3.03±.23) sleep. NREM delta power, locomotor activity and body temperature rhythms were similarly attenuated in -/- mice. In +/+ and -/+ mice, NREM delta power increased throughout the dark period and decreased across the light period, indications of a normal homeostatic pattern. Over 24 hours, -/- mice slept a total of 90.1 minutes more than +/+ (p £ .01) mice and 71.5 minutes more than -/+ (p £ .01) mice. This was attributable to increases in both NREM (-/-, 672.37 ± 19.35 min vs. +/+, 598.53 ± 18.36, p £ .01; -/+, 616.58 ± 18.36, p £ .05) and REM (-/-, 91.0 ± 3.12 min vs. +/+, 74.76 ± 2.96, p £ .01; -/+, 75.10 ± 2.96, p £ .01) sleep. Null allele mice had notably more fragmented sleep, indicated by an increase in stage shifts, brief arousals, NREM bouts and REM bouts compared to -/+ and +/+ mice (p<.01 in all comparisons). These differences were accounted for by increases during the dark phase (group x time interactions). The duration of NREM bouts was decreased for -/- mice compared with +/+ (p £ .01) and -/+ (p £ .01) as was the duration of REM bouts (+/+, p £ .05; -/+, p £ .05).*Constant darkness*: In DD, -/- mice exhibited an arrhythmic distribution of sleep/wake, NREM delta power, locomotor activity and body temperature, whereas +/+ and -/+ mice maintained free-running rhythms. NREM and REM sleep times and sleep fragmentation were increased in -/- mice, similar to results obtained under entrained conditions.
Conclusions: Mice lacking the circadian gene, MOP-3, show alterations in both sleep/wake consolidation and in the amount of sleep. These data indicate that perturbation to a key molecular component of the circadian system not only alters the rhythmicity of sleep and wakefulness, but also has additional effects on the amount of sleep that is generated. Therefore, the circadian system may have direct interactions with sleep generating processes.

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0274.E

Role of the Noradrenergic Locus Coeruleus System in Sleep and Waking Circadian Factors

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Introduction: Previous evidence indicates that the LC plays a role in regulation of the sleep-waking cycle (SWC). A recent study showed circadian variations in LC impulse activity that depended on a circuit involving the suprachiasmatic nucleus (SCN) and dorsomedial hypothalamus (DMH). To study the role of the SCN-DMH-LC circuit in sleep and waking, we analyzed the effect of DSP-4 lesion of the LC system on the SWC under 12h/12h light/dark (LD), or in constant darkness (DD).
Methods: Telemetry transmitters were implanted in adult male Sprague Dawley rats for recording ECoG, EMG and body temperature. One group of animals (n=7) was submitted to a LD cycle (light on 0600h, 200 lux), and another group (n=7) was kept in DD. Food and water were provided ad libitum. The animals were adapted to the environmental conditions for at least 3 weeks after surgery.
Results: LD Group: 18-21 days after DSP-4 injection, the amplitude of the circadian waking (W) and paradoxical sleep (PS) rhythms decreased (-26% and -22%, respectively, p0.05%). The total W duration decreased during the night (-11%, p0.05) due to an increase in the episode number (+58%) and a decrease in the episode duration (-48%, p0.05). Both slow-wave sleep (SWS) and PS were increased (+27% and +45%, p0.05) mainly due to an increase in the number of episodes (+52%, +40%, respectively, p0.05). During the day, the W amount was increased by +24%, while SWS and PS were decreased (-7% and -8%, respectively). These changes were not significant. DD Group: the lesion of the noradrenergic LC system did not significantly affect the sleep-waking mechanism during the active or rest period.
Conclusions: These results are consistent with the possibility that the LC provides a circadian waking signal.

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0275.E

Sleep-Wake Cycle Disorders in Autism with Mental Retardation: Effects of Melatonin

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Introduction: Autism and mental retardation (MR), taken separately or found in a same individual, are associated with circadian rhythm disorders. There are anecdotal reports of therapeutic success using melatonin. The purpose of this study was to characterize the rest-activity cycle in institutionalized patients with MR and to evaluate the therapeutic effect of melatonin in mentally retarded autistic patients suffering from sleep-wake cycle disorders, using adapted dependant variables.
Methods: The daytime rest-activity rhythm of 13 institutionalized patients with MR (8 men, 5 women, mean age = 43.2 /pm 4.6) was evaluated with a 3-point scale: lying (score=3), sitting (score=2), standing up (score=1). Measures were taken each 15 minutes, 24 hours a day, for seven days. An additional patient (SCR), a 17-year old autistic and mentally retarded male with violent behaviour patterns, was studied more extensively as he was referred to us for sleep-wake cycle disorders. The observational grid in SCR was extended by adding the following variables: sleeping, resting, and occurrence of violent behaviors. After 2 months of observation, SCR was treated with melatonin 2 mg, 30 minutes before bedtime. The three month follow-up data were compared to baseline.
Results: Patients with MR showed a regular rest-activity cycle, including a spontaneous early afternoon daytime peak occurrence of rest at 13h00-14h00. SCR showed signs of vigilance fragmentation where sleep and wake fragmented the morning period and naps were frequent in the afternoon (i.e., alternation of lying and lying/sleeping positions). Violent behaviors in SCR showed a bimodal peak of occurrence in mid afternoon (around 15h15) and late evening (between 21h30 and 23h00). Melatonin was associated with a a 28.3% decrease in sleep bouts between breakfast and lunch and 50.0% increase sitting with others. In the period between lunch and supper, sleep bouts decreased by 80.2% and sitting with others increased by 53.5%. In the evening, sleep bouts decreased by 100%. There was also a significant 79.1% decrease in the total amount of violent behaviour (from 96 to 20) and the disappearance of their semi-circadian pattern of occurrence.
Conclusions: Persons with MR show definite signs of chronobiological synchronization in an institutional, structured environment. The thera-

peutic results obtained with melatonin both on sleep-wake schedule and violent behaviors in a patient with autism and MR characterized by rest-activity cycle irregularities points toward a promising treatment strategy. Indeed, this patient could reintegrate his regular schedule and achieve optimal social interactions.

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0276.E

Morningness-Eveningness Assessed In Commercial Aviators

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Introduction: Similar to people exposed to night shift work, commercial airline pilots—especially those transiting time zones—often engage in high-level work at hours that conflict with their entrained circadian rhythms and non-work sleep-wake cycles (Gander et al., 1993). This can adversely affect pilot performance and potentially decrease the safety margin of flights. One way to determine the extent to which flight schedules are out of synchrony with pilots' endogenous circadian rhythms is to assess circadian phase preference using morningness-eveningness scales (extreme M-E has been demonstrated to reflect a genetic predisposition). As part of a program of work on pilot fatigue, morningness-eveningness (M-E) was assessed in a cohort of domestic and international commercial airline pilots using two M-E scales.
Methods: Morningness-eveningness data were collected from n = 20 commercial airline pilots (9 domestic, 11 international; 19 men, 1 woman; 10 captains, 10 first officers), with ages ranging from 28-59 years (M = 42.35, SD = 10.04). Types of aircraft flown varied from Boeing 737 to 777 and Embraer 135/145. Average caffeine consumption was 2.57 cups/day. M-E was measured with two scales, each yielding a total score that was categorized in a M-E type. The Horne-Ostberg Morningness-Eveningness Questionnaire (MEQ) (Horne & Ostberg, 1976) consists of possible scores ranging from 16-86 and 5 M-E type categories ranging from Definitely Morning Type to Definitely Evening Type. The Basic Language Morningness (BALM) Scale (Brown, 1993) consists of possible scores ranging from 13-55 and 9 M-E type categories ranging from Extreme Morning Type to Extreme Evening Type.
Results: Pearson product-moment correlations were performed for scores between MEQ (M = 59.25, SD = 8.68) and BALM (M = 42.35, SD = 6.00) yielding r = .93, p <.001. Spearman rank order correlations were performed for M-E types between MEQ (M = 1.40, SD = 0.75) and BALM (M = 2.90, SD = 1.21) yielding $r$sss = .93, p < .001.
Conclusions: Results to date show that both the MEQ and the BALM are similar in measuring morningness-eveningness in commercial aviators. Although this sample size is small, its results indicate that pilots are more likely to be morning-type. This issue suggests further research to understand which variable, age or profession, is the contributing factor for diurnal preferences in commercial aviation.

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0277.E

Reduced Sleep Time in Old Clock/Clock Mice is Exacerbated in Free Running Conditions

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Introduction: The regulation of sleep and wakefulness is under circadian and homeostatic control, however, it is unclear whether these two processes are independent or are interconnected at a cellular or systems level. Adult mice with mutations of the circadian clock gene, *Clock*, have significant reductions in total sleep time compared to wild-type controls. In this study, we hypothesized that sleep time would similarly be reduced in old clock/clock mice and that this deficit would be exacerbated under free-running conditions when animals are oftern arrhythmic.
Methods: Seven male wild-type (C57Bl-6J) and seven male homozygous *Clock/Clock* mice (18-20 months old) were anesthetized and surgically implanted with EEG and EMG electrodes. At least 2 weeks were allowed to recover from surgery followed by 5 days of adaptation to the sleep chamber. Under entrained conditions (12L:12D, lights on 06:00), data were collected for 48-hours of baseline sleep, for 6-hours during sleep deprivation by gentle handling in the second half of the light period (ZT6-ZT12) and during 18 hours of recovery sleep. Next, locomotor activity rhythms were recorded by infrared sensors for 2 weeks in 12L:12D and for 3 weeks in constant darkness (DD) to determine the free-running period and times of circadian rest (CT0) and activity (CT12) onset. Animals were re-adapted to the sleep chambers and the baseline-sleep deprivation protocol was repeated in DD. Food and water were available to all animals *ad libitum*. Data were analyzed using ANOVA and LSD post-hoc tests. Initial results for sleep stage percentages and sleep fragmentation during baseline recordings are presented below.
Results: Entrained conditions: In L:D conditions, *Clock/Clock* mice were awake significantly more than WT (57.64 ± 1.5 % vs. 51.49 ± 1.5 %, p £ .03) and had significantly less NREM sleep (38.17 ± 1.2 % vs. 44.75 ± 1.2 %, p £ .01). REM sleep was similar between the two genotypes. *Clock/Clock* mice had a significant reduction in brief arousals from sleep (108.3 ± 6.8 vs. 189.1 ± 6.8, p £ .001) and a tendency for decreased stage shifts (713.1 ± 33.96 vs. 835.9 ± 33.96, p £ .06) compared to WT mice. Constant darkness: In WT mice, tau = 23.87 ± .05 hours, whereas *Clock/Clock* mice were arrhythmic. WT mice had similar amounts of wake and NREM sleep in L:D and D:D conditions, however REM % increased in D:D (4.25 ± 0.34 % vs. 3.39 ± 0.22 %, p £ .01). In D:D, clock/clock mice had a significant increase in wake time (65.87 ± 2.27 % vs. 57.64 ± 1.5 %, p /leq .001) and decreases in NREM (30.40 /pm 1.56 % vs. 38.17 /pm 1.2 %, p /leq .001) and REM (3.13 ± 0.34 % vs. 4.06 ± 0.22 %, p /leq .001) sleep compared to entrained conditions. In both genotypes, the number of brief arousals (p £ .001) and stage shifts (p £ .001) decreased in D:D.
Conclusions: Old *Clock/Clock* mice generate significantly less NREM sleep under entrained conditions compared to old WT mice, and this difference is exacerbated when animals are placed in constant darkness. Therefore, L:D may mask the magnitude of the effects of the *Clock* mutation on sleep. These data indicate that alterations to circadian processes may have direct effects on sleep generating mechanisms in addition to regulating the time of sleep.

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0278.E

Modafinil Improves Quality of Life and is Well Tolerated in Shift Work Sleep Disorder

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Introduction: Shift work sleep disorder (SWSD) is a disease primarily of circadian misalignment associated with excessive sleepiness during waking hours and insomnia. Excessive sleepiness is usually present during workshifts and may result in the propensity to fall asleep and subsequent impairments in cognitive performance, physical function, and quality of life. SWSD is also associated with difficulty in sustaining daytime sleep, resulting in cumulative sleep loss that further impairs nighttime alertness and performance. Because of the circadian misalignment

and sleep loss, SWSD patients may experience lapses of attention and unintended sleep episodes, contributing to high rates of occupational/vehicular accidents among night workers. Previous studies in simulated night shift work demonstrated that modafinil improved objective and subjective measures of wakefulness without affecting daytime sleep. This multicenter, randomized, double-blind, placebo-controlled study evaluated modafinil for effect on quality of life and tolerability in SWSD patients.

Methods: A total of 278 patients (aged 21-60 years) with SWSD for ³3 months who worked ³5 night shifts per month received double-blind treatment over a 12-week period with either modafinil 200 mg/d, modafinil 300 mg/d, or placebo, taken 30 to 60 minutes before each night shift. Quality of life was assessed by changes from baseline at Weeks 4 and 12 (or final visit) in the Functional Outcomes of Sleep Questionnaire (FOSQ) and 36-item Short Form Health Survey (SF-36). Adverse events and changes from baseline in clinical laboratory tests, vital signs, electrocardiograms, and physical examinations were assessed.

Results: Modafinil improved quality of life at all time points compared with placebo, as assessed by the FOSQ and SF-36. Modafinil 300 mg/day significantly improved FOSQ mean total score compared with placebo at Week 12 ($P < .05$). Modafinil also significantly improved FOSQ domain scores at week 12 (or final visit) for activity level (200 and 300 mg/d doses) and vigilance and general productivity (300 mg/d dose). Both doses of modafinil significantly improved the SF-36 mental component compared with placebo at Week 12 ($P < .05$). Modafinil was well tolerated and had no adverse effect on daytime sleep. Among 263 patients evaluated for safety, the most common adverse events in the modafinil 300 and 200 mg/day treatment groups compared with the placebo treatment group were headache (26%, 17%, and 16%, respectively), nausea (19%, 6%, and 5%, respectively), and nervousness (10%, 3%, and 2%, respectively). Adverse events were mild or moderate in severity. Modafinil had no effect on laboratory values, vital signs, electrocardiograms, or physical exam assessments compared with placebo.

Conclusions: Modafinil significantly improved quality of life in patients with chronic SWSD who experienced excessive sleepiness. Modafinil was well tolerated.

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0279.E

A Diurnal Rhythm Exists in Circulating Levels of Lipopolysaccharide Binding Protein (LBP) in Healthy Young Volunteers

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Introduction: The clearance of endotoxin involves the action of specialized blood borne binding proteins including soluble CD14, LPS binding protein and bactericidal/permeability-increasing proteins. White blood cells and some inflammatory mediators produced by these cells are known to exhibit a diurnal rhythm (IL-6 for example), and a diurnal rhythm in LBP may in fact influence the host's response to bacterial challenge. We therefore present here for the first time, a descriptive study of the 24 hour rhythm of LBP in plasma sampled from healthy human subjects throughout normal wake and sleep.

Methods: We are conducting a study of 45 normal healthy volunteers participating in a 15 night protocol in the Clinical Research Center of the Beth Israel Deaconess Medical Center. As part of an ongoing study looking at the role of sleep restriction in host response to endotoxin in healthy humans, subjects slept between 23:00-07:00 on the first two nights in the study, before being randomly assigned to an 8 or 4 hour/night sleep condition. On the second baseline day, we performed hourly blood draws using a through-the-wall blood draw system. We have analyzed 6 samples per subject on this baseline day, in 23 subjects, for LBP (Chemiluminescent Immunoassay System, Diagnostic Products), sampled at 10:35, 14:35, 18:35, 22:35, 02:35 and 06:35am, for the purpose of this study. Data were subjected to a repeated measures analysis of variance [SAS Systems].

Results: There was a diurnal pattern in circulating LBP, evident in a significant time effect on repeated measures analysis of variance ($F(5,22)=23.29$, $p<0.0001$). The pattern was in keeping with the diurnal rhythm of cortisol, with lowest determinations in the night and higher during the day. Values (ug/ml) obtained were 4.8 (±0.30) at 10:35, 4.6 (±0.23) at 14:35, 4.7 (±0.25) at 18:35, 4.1 (±0.22) at 22:35, 3.9 (±0.20) at 02:35, and 3.9 (±0.24) at 06:35. Pairwise t-tests showed that samples of circulating plasma taken at 10:35, 14:35, and 18:35 were significantly higher than those taken at 22:35, 02:35 and 06:35 ($p<0.001$).

Conclusions: Elevated binding protein was seen during the daytime hours, which is adaptive, as this is the time of greatest likelihood of encountering bacterial pathogens. The specialized endotoxin receptor, CD14 is known to mediate the stimulation of non-myeloid cells by endotoxin in its soluble form. We are proceeding to analyze soluble CD14 in these subjects to further characterize the diurnal rhythm of proteins involved in endotoxin clearance. These data may have relevance for infection prevention and treatment strategies in post-operative recovery.

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0280.E

Dim Light Salivary Melatonin Profiles during Constant Routines: Amplitude and Development

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Introduction: Previous studies show decreased melatonin concentrations after childhood; age, pubertal stage, and body mass index (BMI) are suggested mediators of this developmental change. Furthermore, morningness/eveningness (M/E) preference in young adults is associated with amplitude differences in melatonin profiles. We examined salivary melatonin profiles obtained during constant routines to assess contributions of sex, age, BMI, M/E, and pubertal stage to measures of melatonin amplitude.

Methods: Sixty-nine children and adolescents ages 9.6 to 17.8 years (M=12.7, SD=1.5) participated. Pubertal status was determined with consensus Tanner staging by 3 clinicians: 15 were Tanner 1 (7 girls), 15 Tanner 2 (3 girls), 10 Tanner 3 (5 girls), 17 Tanner 4 (9 girls), and 12 Tanner 5 (6 girls). BMI ranged from 14.7 to 32.6 (M=20.6, SD=4). M/E was assessed with the Smith et al. 1989 scale (range=22-53; M=38, SD=7). Participants kept a fixed schedule (lights on 0800 h, lights off 2200 h; eyeshades at night) for at least 10 days at home, confirmed by actigraphy. The in-lab session included a constant routine in dim light (<15-20 lux), sitting semi-recumbant (45 degrees), and eating frequent small meals. Saliva (approximately 2 ml) was collected at 30-min intervals from 1750 until 1220 the next day. Melatonin levels were determined by radioimmunoassay (Alpco). Two amplitude measures were derived from data over the 38 samples: maximum value (MAX) and area under the curve (AUC, integrated value of melatonin computed by the trapezoid method). Data were analyzed using manova, pearson correlations, and multiple regression.

Results: MAX (M=30.6, SD=18.4) and AUC (M=224, SD=130) were strongly correlated (r=.96). Sex differences were not significant for either measure. One participant (Tanner 1 male) manifested a secretory pattern exceeding the sample means by about 4 SD units (MAX=116, AUC=728). Results were similar with and without his data; we present results with his data excluded. Significant effects for Tanner stage were evident for melatonin AUC ($F(4,63)=2.9$, $p<.03$). Mean (SD) melatonin AUC for Tanner 1 to 5: 275 (147), 252 (95), 216 (128), 189 (83), and 145 (90). MAX melatonin showed a trend for Tanner stage ($F(4,63)=2.4$,

p<.06). Mean (SD) MAX melatonin for Tanner 1 to 5: 36.6 (18.1), 33.9 (13.1), 28.1 (13.7), 25.6 (13.1), and 21.2 (15.3). Regression analyses included age, BMI, M/E, and Tanner stage as independent variables. Only Tanner stage contributed significantly to the model for melatonin AUC (partial r=-.44, p=.0005) and MAX (partial r=-.36, p=.005).
Conclusions: Although individual differences in salivary melatonin secretion were large, a clear developmental decline of amplitude and area under the curve was apparent. Our analyses highlight the importance of puberty (Tanner stage) relative to age, body size, or morningness/eveningness preference as possible mediators of the childhood-to-adolescent decrease in nocturnal melatonin secretion. On the other hand, our results cannot exclude gating of pubertal progression by melatonin levels.

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0281.E

Modafinil for the Treatment of Excessive Sleepiness in Chronic Shift Work Sleep Disorder

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Introduction: Shift Work Sleep Disorder (SWSD) is characterized by excessive sleepiness during nighttime wakefulness and/or insomnia during daytime sleep. The combination of circadian misalignment and cumulative sleep loss due to insomnia during daytime sleep can lead to lapses of attention and/or unintended sleep episodes at work. The wake-promoting agent modafinil has been found to improve objective and subjective measures of wakefulness on simulated night shifts. We report the results of treatment with modafinil in a large–scale clinical trial in SWSD patients treated while on the job.
Methods: Patients who met the ICSD criteria for SWSD for ³3 months were enrolled in a 12-week, multi-center, randomized, double-blind, parallel-group clinical trial. Eligible patients must have also worked ³5 night shifts/month, of which ³3 were consecutive; had mean sleep latency £6 minutes on a Multiple Sleep Latency Test (MSLT) conducted during night shift hours; and had £87.5% sleep efficiency on daytime polysomnography. Patients were randomized to modafinil 200 mg or placebo once daily administered 30 to 60 minutes before the start of each night shift. Efficacy measures included mean MSLT latency, and the Karolinska Sleepiness Scale (KSS), both completed during the simulated night shift, and the Clinical Global Impression of Change (CGI-C) completed at weeks 4, 8, and 12.
Results: Of 209 patients randomized, 153 (73%) completed the study. Modafinil significantly increased mean MSLT scores, compared with placebo at week 4 (1.24±3.29 vs 0.23±2.16, respectively; P<.05) and Week 12 (1.67±3.70 vs 0.40±2.83; P<.05). Mean change from baseline KSS values also indicated significantly improved alertness in the modafinil group at both time points (P<.001), relative to placebo. Modafinil also improved CGI-C scores in a significantly greater proportion of patients than did placebo (P<.05). At the final visit, 66 (74%) of the 89 patients in the modafinil group were improved on the CGI-C, compared with 37 (36%) of the 104 patients in the placebo group (P<.05). Modafinil did not adversely affect polysomnographically recorded daytime sleep (see companion abstract). Adverse events occurring in >5% of patients and more frequently in modafinil-treated patients than placebo were headache, nausea, abdominal pain, insomnia, nervousness, dry mouth, and tooth disorder.
Conclusions: Modafinil significantly reduced nighttime sleepiness on objective and subjective measures in patients with SWSD. These reductions were sustained for 3 months, while the patients were employed at their regular jobs. Modafinil also improved overall clinical condition with respect to sleepiness in a greater proportion of patients than placebo, and was well tolerated. These results indicate that modafinil may prove to be effective in the treatment of SWSD.

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0282.E

Changes in REM Sleep Following Immobilization Stress are Under Circadian Control

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Introduction: Sleep and wake patterns can be altered by a variety of behavioral and physiological perturbations. Acute immobilization is an animal model of stress that induces large increases in REM sleep in rats. Under entrained (light:dark) conditions, the increase in REM occurs during the dark phase, regardless of the time of day that stress is applied. In order to determine whether this response is under direct photic or circadian control, we performed immobilization stress in mice at different times of day under entrained (12L:12D) and free-running (constant darkness) conditions.
Methods: Male mice (C57Bl/6J, 3-4 months old) were anesthetized and surgically implanted with EEG and EMG electrodes. In the first experiment, mice were entrained to a 12L:12D cycle, adapted to the sleep recording chamber for at least 5 days and recorded for 24-hours of baseline sleep starting either at ZT0 or ZT12. The following day animals were kept awake at either ZT0 (N=9) or ZT12 (N=9) for 1 hour by gentle handling and sleep was recorded for the next 23 hours. On the third day, restraint stress was performed by immobilizing mice in a syringe tube for 1 hour at the respective ZT time, followed by 23 hours of sleep recording. In the second experiment, mice were maintained in constant darkness (DD), activity records were collected to determine the onset of rest (CT0) and activity (CT12) periods, and the handling and restraint stress procedure was performed at either CT0 (N=5) or CT12 (N=6). Different animals were used for each time (ZT 0 and 12, CT 0 and 12) point. REM and NREM percentages of total recording time were determined for light:dark or rest:activity periods. A separate 2 x 2 ANOVA was performed for each of the 4 time conditions. Tukey post-hoc tests were run to follow-up significant Trial (handling vs. stress) by Time (light vs. dark or rest vs. activity) interactions.
Results: Entrained Conditions: ZT0: When restraint stress was performed at light onset (ZT0), REM% significantly increased during the dark phase compared to the handling condition (3.94 ± 0.51 % vs. 2.2 ± 0.38 % vs. p £ .02). ZT12: When restraint was performed at dark onset (ZT12), REM% significantly increased during the immediate dark period compared to handling (3.66 ± 0.35 % vs. 1.79 ± 0.25 %, p £ .04) and was no different than handling during the subsequent light period. Constant Darkness: CT0: Following restraint stress at rest onset (CT0), REM% decreased during the initial rest phase (4.75 ± 0.52 % vs. 7.02 ± 0.34 %, p £ .01) and increased during the subsequent active phase (4.75 ± 0.44 % vs. 2.43 ± 0.35 %, p £ .01) compared to the handling condition. CT12: Restraint stress at activity onset (CT12) increased REM% during the immediate active phase (4.07 ± 0.39 % vs. 2.29 ± 0.19 %, p £ .03), but had no effect on REM% during the following rest period.
Conclusions: During entrained conditions, the increase in REM sleep in response to restraint stress was isolated to the dark phase, regardless of when restraint was applied. This could mean that the REM response was either under direct photic or circadian control. Therefore, restraint stress was applied at the onset of either the rest or activity period in DD. Under both restraint stress times in DD, REM sleep increased only during the active phase, indicating that the REM response was regulated by a circadian process.

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0283.E

Long-term Outcome of Adolescents with Delayed Sleep Phase Disorder

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Introduction: Delayed sleep phase disorder (DSPD), a condition where patients consistently cannot fall asleep or awaken until after the desired time, is most commonly diagnosed in younger patients. This condition has been strongly associated with depression (Regestein, 1995). The long-term outcomes of DSPD are little studied, and degree of psychosocial impairment is unknown (Dagan, 1998). We hypothesized that DSPD subjects would have higher rates of psychosocial problems than normal subjects but a lower rate than psychiatric controls.
Methods: The Mayo Foundation IRB approved this study and all participants consented to participate. The database includes of 118 subjects diagnosed with DSPD between the ages of 9-18 (Kubas, 2002). Duration of follow-up ranged from 2-8 years. The control group consisted of 232 normal controls and 235 with psychiatric disorders matched for age, gender, and date of visit. The mailed survey, developed by the investigators, investigated sleep schedules, treatment, coexisting psychiatric issues, and psychosocial functioning. Non-respondents were contacted by telephone. Two sets of unconditional logistic regression analyses were performed.
Results: Seventy-one DSPD subjects responded (60%). Data were available for 51 normal controls (22%) and 41 psychiatric controls (17%). The median age of onset of DSPD was 13-14 years (28% of the sample). The majority of subjects pursued treatment (66%) with a median duration of treatment of 2-5 months. Only 17% of subjects were treated for one year or longer with 13% still in treatment at follow-up. The most common treatments were phototherapy (51%), melatonin (11%) and chronotherapy (10%). Only 42% of respondents reported that the treatment was of any benefit (mild to very high). A substantial number had been treated for depression (47%). At the time of follow-up, the median initial sleep onset was 30 minutes or less with only 28% taking greater than 60 minutes to fall asleep. Compared to normal controls, DSPD patients have longer sleep onset (odds ratio 2.22), poorer general health (3.70), sadness during winter (5.05), missed days of high school (1.68), social problems (6.00) and were more frequently treated for depression (9.33) (p 0.002 for all). Compared to psychiatric controls, poorer general health (OR 1.90) was the only statistically significant difference (p 0.016).
Conclusions: At follow-up, most respondents described a sleep onset of less than an hour. Few DSPD subjects pursue treatment for longer than one year. Subjects with DSPD seen at a tertiary medical center appear to have depression, poorer general health and more psychosocial problems when compared to normal controls. With the exception of poorer general health, few differences emerge when compared to psychiatric controls. These similarities suggest the importance of pursuing psychotherapy and other psychiatric treatments for these patients.

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0284.E

Absence of Detectable Effect of Modafinil on Daytime Sleep After A Simulated Night Shift in SWSD Patients

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Introduction: Shift Work Sleep Disorder (SWSD) is characterized by excessive sleepiness during waking periods and/or insomnia that are temporally associated with shift work schedules. The combination of circadian misalignment and cumulative sleep loss may lead to dangerous lapses of attention, unintended sleep episodes, and occupational and vehicular accidents among night workers. Previous simulated night work studies demonstrated that modafinil improved objective and subjective measures of wakefulness without affecting daytime sleep. We report the effect of modafinil upon daytime sleep in a large-scale clinical trial of patients with SWSD.
Methods: Patients who met the diagnostic criteria for SWSD were enrolled in this 12-week, multicenter, randomized, double-blind, parallel-group study. Eligible patients must have also worked ³5 night shifts/month, of which ³3 were consecutive; had mean sleep latency £6 minutes on a nighttime Multiple Sleep Latency Test (MSLT); and had £87.5% sleep efficiency on daytime polysomnography (PSG). Sleep pathologies other than SWSD and uncontrolled illnesses were excluded. Patients were randomized to modafinil 200 mg (n=96) or placebo (n=108) given once per day, 30 to 60 minutes prior to each night. Daytime sleep was assessed by PSG conducted (>480 minutes, starting minutes) after the simulated night shift at baseline and Week 12 (final visit).
Results: Daytime PSG data were available for 204 patients (mean age 38 years). Modafinil had no effect relative to placebo on daytime sleep parameters, measured as change from baseline. Mean change in scores (in minutes) for the modafinil group were: time in bed, -3.0; time awake, -11.7; total sleep time, 1.4. Mean change in percentages of time in sleep stages for the modafinil group were: REM 0.5%; stage 1, 1.4%; stage 2, -0.4%; and stages 3 and 4, -1.4%. Additionally, modafinil did not affect sleep consolidation as evidenced by a lack of mean changes from baseline in the number of awakenings and the time awake after sleep onset. For patients receiving placebo, similar change from baseline results were found.
Conclusions: We were unable to detect a significant effect of modafinil administered 30 to 60 minutes prior to the night shift on daytime sleep parameters in patients with excessive sleepiness associated with chronic SWSD.

Research supported by Cephalon, Inc., West Chester, PA

0285.F

Signatures Of Sleep In A Paper Wasp

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Introduction: The study of sleep within invertebrates has received recent attention, most notably within fruit flies (Drosophila melanogaster), honey bees (Apis mellifera), and crayfish (Procambarus clarkii). I assembled a set of behavioral and physiological criteria that have served as "sleep signs" in the literature, and investigated these criteria in social paper wasps (Class Insecta, Order Hymenoptera, Family Vespidae: Polistes flavus).
Methods: Three complete colonies of Polistes flavus were collected from the Sonoran Desert (Pima Co., AZ, USA), and reared under ambient light and temperature conditions. Members of each colony (mean = six wasps) were individually marked, and observed and tested for sleep signs, including exhibiting a specific posture during (1) extended, (2) recurrent, and (3) reversible bouts of relative immobility (twitching of antennae or tarsi discounted), as well as displaying a (4) decreased body temperature relative to the surrounding temperature, along with (5) increased arousal threshold during these periods, and (6) a homeostatic

regulatory mechanism. Videotaping, behavior-recording software, and CO2 metabolic measures (with Allen Gibbs) were implemented to address the first two criteria. Infrared imagery and accompanying software enabled specific behaviors to be correlated with relative body temperatures. Individually housed wasps were perturbed with a sonicator at different times under red light to quantify arousal threshold and reversibility. Sleep deprivation experiments, in which wasps were made to locomote every five minutes for 12 hour periods (day versus night versus control), served as tests for a homeostat.

Results: P. flavus paper wasps spent extended periods (criteria 1, 2) from dusk until several hours after sunrise in a relatively motionless state, with bodies usually contacting the substrate, antennae lowered, and with occasional limb-dangling in the direction of gravity. During these states, wasps typically engaged in discontinuous ventilation, versus active-state rapid cycling ventilation, as measured by CO2 expired. The more time wasps remained immobile, the lower were their metabolic rates (P<.0001, n = 12 wasps). Relative body temperatures were lower (4) when wasps remained immobile than when locomoting or grooming (ca. 2.5 and .9 degrees C differences, respectively). Wasps could be aroused (3, 5) from this state with an increasing vibratory stimulus. When disturbed at five minute intervals during sleep deprivation (6), wasps more quickly returned to an immobile state as the night progressed (P=.01, n = four wasps, one colony), although the night's disturbance did not appear to create a greater propensity (n = three colonies) to become quiescent the following day relative to controls and daytime perturbation treatments.

Conclusions: P. flavus, by the criteria outlined above, appear to engage in sleep. Additional work to fortify this assertion should include increasing sensitivity of the homeostat measure, testing for habituation during sleep deprivation, and reversing sleep schedules. Paper wasps can have small populations and reside on open, easily manipulated and observed nests, making them candidates for future study within certain social contexts of sleep.

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0286.F

Ontogenesis Of Rest Behavior In Killer Whales

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Introduction: At birth, sleep (particularly REM) and immobility are elevated relative to adult levels in all terrestrial mammals that have been studied. The aim of the present study was to document the developmental changes of rest behavior in newborn Cetaceans and their mothers after parturition.

Methods: We video recorded and visually monitored the behavior of two killer whale (Orcinus orca) calves (male and female) and their mothers at Sea World in San Diego since their birth (6 days and 3 hours in calf 1 and 2, respectively) until 12 and 5 months old (calf 1 and 2). The behavior of mother-calf pairs was documented at 1-2 week (months 1-3) and 3 month (months 3-12) intervals. The duration of each observation was 2-3 days (first two weeks for both calves), and later – two consecutive nights.

Results: Killer whale females abruptly ceased their typical rest behavior (hanging motionless at the surface or in depth and lying on the bottom of the pools) after parturition to continuously tend to their calves during the 3-week postpartum period. The calves were also continuously active after birth. Slow circular swimming was the only behavior that might represent sleep in the calves and their mothers during this period (<18% of 24-h in both the mother and calf of pair 1 when the calf was 1 week old). Both mothers resumed resting at the surface starting when the calves were about 3 weeks old, although the two calves remained active 24/h/day, swimming near their mothers. Both calves began to perform short episodes of rest at the surface after they reached 1 month of age. During the second month, the calves progressively increased the duration of rest at the surface (14-33% and 2%-8% of the nighttime in calves 1 and 2, respectively) but were never completely immobile as their mothers. The total amount of this behavior in calves was significantly smaller than in their mothers (45-54% and 5-19% in mothers 1 and 2, respectively). In both calves we documented single (<29 per night) and occasionally serial (<10 per night) myoclonic jerks when they rested at the surface. We saw only a few single jerks in the mothers and calves during the 3 week post partum period.

Conclusions: 1) Unlike all terrestrial mammals, newborn killer whales are highly active after birth. At no point do killer whale calves show rest behavior exceeding that shown by adult killer whales. 2) Killer whale females show an abolition of typical rest behavior for the first 3 weeks postpartum. 3) There is no behavioral evidence for REM sleep during the 3 week postpartum period in either mother or calf. The developmental profile of rest in killer whale calves and the postpartum rest behavior of their mothers differs dramatically from that of all previously studied terrestrial mammals.

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0287.F

Characterization of Rest Behavior in the Nematode Caenorhabditis elegans

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Introduction: A fundamental understanding of sleep requires a detailed anatomic characterization of the underlying neuronal circuits, as well as a genetic analysis of the molecular processes. Research during the past three years has validated the use of *Drosophila melanogaster* to study the molecular genetic mechanisms of sleep, though understanding the neuronal circuitry of sleep in *Drosophila* is still at a primitive stage. With respect to understanding neuronal circuits, the nematode *Caenorhabditis elegans* offers the advantage of a relatively small nervous system of 302 neurons and of a complete description of all neuronal connectivities. Further, the roles of individual neurons can be tested by killing them with a laser microbeam. Two recent reports have shown that *C. elegans* has circadian rhythms, but a sleep-like state has not been described. As a first step toward identifying a sleep-like state, we tested the hypothesis that *C. elegans* has a distinct resting behavioral state and that the likelihood that this state will occur varies across the 24-hour cycle.

Methods: First larval stage worms were kept on an agar surface in the absence of food and exposed to temperature cycles, 12 hours at 18 deg alternating with 12 hours at 23 deg. Temperature cycling, rather than light cycling, was used because *C. elegans* does not have photoreceptors; it has a robust behavioral response to temperature but not to light; and it does not have gene products that are obvious orthologues to photoreceptor proteins in other systems. The population of worms was videotaped continuously by a camera mounted on a microscope. After acquiring the video, behavior was analyzed at 12x the acquisition speed to ease detection of worm movements. Every 20 minutes, two minutes of video were analyzed. During those two minutes, worms that did not move were considered resting whereas those that moved were considered active. The fraction of resting worms was then plotted as a function of time.

Results: We found that first larval stage worms can be maintained on an agar surface in the absence of food with little attrition for over a week. Active worm behavior was variable and consisted of forward sinusoidal

movements, brief backing movements, and small foraging movements of the head. There was a distinct rest state. Most resting worms assumed a coiled and compact body posture. The probability of rest behavior was maximal during the cool half of the day, and the probability of active behavior was maximal two hours following the temperature shift up.
Conclusions: We provide the first description of a rest state in the genetically tractable animal model *C. elegans*. We show that this state is influenced by temperature and we hypothesize that it is controlled by a circadian clock.

0288.F

Migratory Sleeplessness In The White-crowned Sparrow (Zonotrichia leucophrys gambelii)

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Introduction: During the spring and fall, migratory songbirds such as the white-crowned sparrow (WCS) fly thousands of kilometers to reach their breeding and wintering grounds, respectively. Despite sleeping at night during the non-migratory seasons, songbirds fly at night during migration and remain active throughout much of the day. Whether such birds sleep in flight, engage in brief bouts of intense daytime sleep or curtail sleeping altogether during migration is unknown. We herein present preliminary behavioral observations of the WCS that indicate a capacity to reduce time spent sleeping during migration.
Methods: Adult migratory WCS (N=30) were captured in the spring on their breeding grounds in Alaska and transported to UW. Sleep-wakefulness behavior was recorded via continuous infra-red activity monitoring and digital video recording. Awake birds kept their eyes open, held their heads erect and away from their body and engaged in active behaviors. Drowsy birds blinked their eyes frequently, held their heads close to their body, facing forward and displayed frequent small head movements. Asleep birds closed their eyes and held their heads still, either facing forward or laying over a wing.
Results: In synchrony with the timing of their normal fall migration in the wild, all of the birds showed a shift in activity in August from being primarily active in the day to being active throughout much of the day and night. Nocturnal behavior included hopping back and forth in the cage and flapping their wings while holding onto a perch, as if attempting to initiate flight. During such migratory restlessness (or zugunruhe), the birds kept both eyes open and appeared alert. The extent of nocturnal activity varied among birds and across phases of the migration. In extreme cases, unequivocal sleep was suspended altogether (24 hr behavioral state scoring: sleep=0.00 %; drowsiness=29.29 %; wakefulness=70.71 % during migration vs. sleep=25.32 %; drowsiness=21.35 %; wakefulness=53.32 % during the non-migratory season).
Conclusions: Our behavioral observations of the WCS suggest that migratory songbirds have the capacity to curtail sleep during migration. Despite the reduction in sleep, drowsiness encompassed a large proportion of the migratory birds' time. Why the birds engaged in drowsiness rather than unequivocal sleep is unclear, but may reflect the overall activated state of sparrows during the migratory season. Electrophysiological studies during the upcoming spring migration will quantify the changes in wakefulness, slow-wave sleep and REM sleep occurring across the migratory and non-migratory seasons. This natural model of sustained sleeplessness provides an opportunity to examine the relationship between sleep and memory consolidation without the potential confounding effects of stress associated with experimental sleep deprivation paradigms. Migratory sleeplessness may also provide insight into psychiatric disorders such as bipolar disorder, where bouts of sleeplessness are diagnostic of mania. Finally, understanding the mechanisms that mediate sleeplessness in songbirds may provide clues to the function of sleep.

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0289.F

Octodon Lunatus: A Nocturnal Octodontid Of Northern Chile

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Introduction: The genus Octodon (RODENTIA: HYSTRICOGNATHI) comprises three species distributed circa 1000 kilometers in the north-south axis of center Chile. Field reports described O. degus, a semi-fossorial inhabitant of xeric areas of center Chile, as diurnal specie. In controlled condition displays a crepuscular profile, with diverse chronotypes. Kas and Edgar reported that wheel-running produces a rapid diurnal-nocturnal inversion in phase preference in the diurnal chronotype of O. degus. We have demonstrated that under controlled condition, wheel running does not change phase preference in the nocturnal O. bridgesi, the inhabitant of center-south Chilean temperate forest. Here, we describe the effect of wheel-running exposure on rest-activity rhythm in O. lunatus, semi-fossorial specie that inhabits coastal humid spots of the Atacama desert (northern Chile).
Methods: Male adult O. lunatus and O. degus were captured in the field and installed in cages contained in individual isolation chambers under a 12:12 Light-Dark schedule (300 Lux) and at 23ºC, with food and water ad libitum. A running-wheel was inside the cage, that could be locked or unlocked (NO WHEEL and WHEEL condition respectively). An acquisition system recorded with a 15-second resolution the activity detected by a movement transducer. After a period of adaptation, O. lunatus were subjected to four conditions (A) entrained to a 12:12 LD schedule with running-wheel locked (LD-NO WHEEL condition); (B) entrained with unlocked running-wheel (LD-WHEEL condition); (C) free-running (constant darkness, DD) with running-wheel locked (DD-NO WHEEL condition), and (D) free-running with unlocked running-wheel (DD-WHEEL condition). O degus were exposed to entrained conditions only (A and B). Angular statistics (cosinor rhythmometry) were applied for hourly incidence of 15-second bins with the highest 20% activity events. Acrophases (mean angles) are expressed in hours respect to lights-on (zeitgeber-time, ZT).
Results: O. degus show the typical crepuscular pattern. Diurnal-nocturnal inversion was evident after exposure to wheel running in diurnal chronotype. No crepuscular pattern was evident for activity rhythm of O. lunatus and achrophases were centered around ZT=18 (objective night) under both LD-NO WHEEL and LD-WHEEL conditions. A period shorter than 24 hours was observed during three weeks of free running under DD-WHEEL condition. Under DD-NO-WHEEL, the period found was shorter than under DD-WHEEL condition. Achrophases of activity remain centered in subjective nights under both DD-WHEEL and DD-NO-WHEEL condition.
Conclusions: O. lunatus is nocturnal and exposed to wheel-running does not change phase preference of activity under neither LD nor DD condition. O. bridgesi and O. lunatus live under different ecological pressures and share nocturnal activity preference. O. degus crepuscular-diurnal preference could be a recent evolutionary acquisition.

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0290.F

Electrophysiological Signs Of Sleep In Crayfish

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Introduction: Behavioral studies have suggested the possibility that invertebrates possess a resting state similar to that of sleep in mammals. Recent results showing that Drosophila has genetic variations similar to those of mammals during sleep (Shaw et al. 2000. Science 287: 1834; Hendricks et al. 2000. Neuron 25: 129; Greenspan et al. 2001 TINS 24: 142) have strenghthened that possibility. However, no electro-physiological signs of sleep in invertebrates have been obtained. For this purpose we developed a preparation of crayfish chronically implanted with extracellular electrodes on the brain and recorded the multiunitary activity from the brain of an animal behaving normally in an aquarium with other crayfish.
Methods: 3-5 free crayfish (Procambarus clarkii) were kept in an aquarium with well aereated water under light:dark cycles of 12:12 hrs. Behavior was studied videotaping the animals during periods of 24 hours and analyzing the records off-line at slow motion. To record the brain electrical activity some animals were implanted with stainless-steel tubes containing 2 teflon-isolated silver electrodes of 25 um diameter. Mechanical threshold was measured attaching a DC brushless-motor ('pancake') to the dorsal cephalothorax and activating it with pulses of variable duration and intensity. Mild cognition was tested stimulating with a paradigm of trains of light flashes and measuring the Omitted Stimulus Potentials (OSP, Ramón et al. 2001. J.Exp.Biol. 204:4291).
Results: Crayfish locomotor activity occurs day or night, but mainly during transitions light-dark and dark-light. The brain electrical activity of an active animal is comprised of numerous spikes isolated and in bursts on an almost flat baseline. Power spectrum graphs show power up to at least 2 kHz, without a dominant frequency. In these animals threshold to mechanical stimulation is low and they show OSPs.Interspersed within bouts of activity, during both day or night crayfish push themselves on a side position against the water surface. At these times animals are motionless, mechanical threshold is about ten times higher than at rest, light stimulation does not result in OSPs, and the brain electrical activity becomes dominated by slow waves with a main frequency around 10 Hz.
Conclusions: At variable lengths of time during day or night crayfish pass through a sleep state similar to the phases 3 & 4 of the N-REM state of mammals, but with an on-going, prominent 10 Hz oscillation.

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0291.F

Sleep in the Cuttlefish Sepia Officinalis

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Introduction: Our laboratory has demonstrated that the cuttlefish Sepia Pharaonis exhibits features of behavioral sleep including a rapidly reversible species specific resting posture; a circadian pattern of consolidated rest periods; an elevated arousal threshold during rest, and homeostatic regulation. In addition, there appeared to be two distinct types of sleep: a quiescent state with stable skin and color pattern (QS) and a state characterized by stereotypic chromatophore activity (CAS) with minor tentacle movements. It was hypothesized that this latter state may be analogous to mammalian REM sleep. This study was an attempt to further characterize this state.
Methods: Ten juvenile sepia pharaonis were habituated in individual aquariums with a bright light-dim light cycle for a minimum of five days. Baseline data was recorded for three days, followed by two days of sleep deprivation, and an additional three days of recovery sleep. Simultaneous video recording for determination of sleep state, and measurement of eye movements and respirations were performed. In addition, in one animal, EEG telemetry was performed utilizing a DSI F-50 telemetry system with bipolar recording from the optic lobe referenced to a subcutaneous electrode.
Results: Cuttlefish averaged 611.3 minutes/day of total sleep during baseline, with 4.12% being CAS; 47.1 minutes/day during deprivation with no CAS present; and 937.8 minutes of total sleep during the first recovery day, with 9.1 % being CAS. Cuttlefish averaged 887.1 minutes of total sleep on the second recovery night with 5.6% being CAS; and 647.6 minutes of total sleep on the third recovery night with 3.96% being CAS. During QS, discrete eye movements were rare, occurring on average only 0.06/minute. During CAS, discrete eye movements were more common, averaging 2.3/minute. Complex color changes surrounding the eyes made it difficult to evaluate eye movements during CAS, with 8.7 such equivocal eye movements/minute. EEG monitoring revealed stable waking patterns consisting of theta, alpha, and beta activity of approximately equal prominence and amplitude. Lower amplitude gamma frequency activity was also present, along with frequent, relatively high amplitude spikes. With the onset of QS, there was an abrupt decrease in amplitude of all frequencies, with the occurrence of intermittent delta frequency activity. No CAS was obtained during the acute preparation.
Conclusions: This study provides further evidence that CAS is a distinct sleep stage in the cuttlefish sepia pharaonis and that it has some similarities to mammalian REM sleep. Both QS and CAS are under homeostatic control, with a more prominent rebound in CAS than QS during the first recovery day. Like mammalian REM sleep, eye movements occur during CAS. Although CAS was not obtained during the acute EEG telemetry recording, this data demonstrates the feasibility of such recording. Chronic implantation and long-term recording is currently being performed.

0292.G

Obstructive Sleep Apnea (OSA) in Pediatric Psychiatic Clinic Patients With Daytime Sleepiness: Incidence and Correlation With Attention Deficit / Hyperactivity Disorder (Ad/Hd)

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Introduction: HYPOTHESIS (1) Children in the pediatric psychiatry clinic population describing daytime sleepiness on questionnaire are postulated to have a high frequency of OSA. Children selected for this study responded positively to one or more of the following questions utilized to screen for pediatric daytime sleepiness (Chervin et. al. 2001):a)Waking unrefreshed, b) Sleepiness during the day, c)A teacher or responsible adult reporting daytime sleepiness, d)Hard to wake in the morning.HYPOTHESIS (2) Children with daytime sleepiness and AD/HD as diagnosed by a Pediatric Psychiatrist using DSM-IV criteria will be significantly more likely to have OSA compared to the non-AD/HD grouping in the same population.
Methods: Children between the ages of 3 and 16 referred to a Pediatric Psychiatric Clinic for evaluation by a Board Certified Pediatric Psychiatrist. Exclusions: adenotonsillectomy (T&A), cleft palate repair, Trisomy – 21. Individuals were evaluated by a Board Certified Sleep Medicine Physician for a sleep history and physical including an assessment of tonsillar size. All children underwent a full night of diagnostic polysomnography in an AASM accredited sleep center.
Results: 1)For this population of sleepy psychiatric clinic patients (N=74), average respiratory disturbance index (RDI) is 5.5 (Range 0-28). The number of these patients with RDI>5.0 is 29/74 (39.2%). The

number of children with an RDI>4.0 is 39/74 (52.7%).2)The sleepy child with AD/HD symptoms (Mean RDI = 7.1) is 2.6 times more likely to have OSA (RDI > 4) than the sleepy child without AD/HD symptoms (Mean RDI = 4.5)(Sig. p<0.05). Mean RDI for children with AD/HD is significantly higher (p<0.05) than mean RDI for children without AD/HD.3)The sleepy child with tonsillar hypertrophy on physical exam is 5.6 times more likely to have OSA (RDI > 4) than the sleepy child without tonsillar hypertrophy (Sig. p<0.001).
Conclusions: This population of sleepy patients being evaluated in a pediatric psychiatric clinic, has a high frequency of OSA (39-53% based on cutoff RDI). Both AD/HD and tonsillar hypertrophy are significant risk factors for OSA in this population.

Research supported by Lexicor

0293.G

A Determination of the Clinically Significant Pediatric Respiratory Disturbance Index (RDI) in a Sleepy Pediatric Psychiatry Clinic Population (N=74)

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Introduction: This study includes children between the ages of 3 and 16 referred to a Pediatric Psychiatric Clinic for evaluation by a Board Certified Pediatric Psychiatrist.The children and parents completed a seventeen-item pediatric sleep questionnaire based on questions validated by Chervin (2001) to correlate with pediatric obstructive sleep apnea (OSA). Children included in this study responded positively to one or more of the following questions used to screen for daytime sleepiness: a) Waking unrefreshed b) Sleepiness during the day, c) A responsible adult reporting daytime sleepiness,d)Hard to wake in the morning. These children were evaluated with a sleep history and physical including an assessment of tonsillar size. Exclusions: previous tonsillectomy and adenoidectomy (T&A), cleft palate repair, Trisomy – 21.
Methods: All children underwent a full night of diagnostic polysomnography in an AASM accredited sleep center. RDI in these children included apneas >10 s in duration, and hypopneas >10 s in duration, with 2-4 % SaO2 desat. and at least a 30% decrease in respiratory effort. The children included in this study were evaluated by a Pediatric Psychiatrist, a Sleep Medicine Physician, and an Otolaryngologist who made in consultation with parents and child the decision for treatment of OSA. For those patients who chose treatment, 96% received (T&A).
Results: (1)In the histogram representation of RDI values for this pediatric clinical population the average RDI is 5.5 (Range 0-28), there are two discrete peaks. a)The first peak lies between RDI = 1.5 to 2.0. The second peak lies between RDI=4.4 to 5.3 b)The classically utilized cutoff RDI = 5.0 bisects the middle of the second peak. c)The minimum point between the two peaks lies in the range (RDI 3.7 - 4.1). In order to represent the natural dispersion of RDI values, a cutoff was tested at the RDI of 4.0.(2)An RDI of 4.0 separates the population into two discrete groups with significant differences in clinical symptoms which correlate with pediatric OSA. The more classically utilized RDI of 5.0 has fewer significant results. a) The significant differences using an RDI of 4.0 include differences in: tonsillar hypertrophy (p<0.001),low O2 saturation (p<0.05), and arousal index (p<0.1), as well as, AD/HD (p<0.05). Significant differences in questionnaire responses are found for reported daytime sleepiness (p<0.001), question: snores always (p<0.05), and question: stops breathing (p<0.1). b)Using an RDI of 5.0, the apparent differences between groups occur at a lower level of significance and are limited to tonsillar hypertrophy (p<0.1), low O2 saturation (p<0.05), arousal index (p<0.05) and the question: daytime sleepiness (p<0.1). (3)The clinical decision for treatment by T&A was better characterized by an RDI of 4.0 than by an RDI of 5.0. a) No child with an RDI<4.0 underwent T&A; 92% of children with RDI>4.0 had surgery. b) 18% of children with an RDI<5.0, and 77% with an RDI>5.0 were treated with T&A.
Conclusions: For this pediatric clinical population an RDI of 4.0 separates the population into two discrete groups based on RDI peaks, clinical symptoms, and decision for treatment better than the classically utilized RDI of 5.0

Research supported by Lexicor Health Systems

0294.G

The Yield of Esophageal pH Monitoring During Polysomnography in Infants with Sleep Disordered Breathing

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Introduction: Polysomnography (PSG) is commonly used in the evaluation of sleep disordered breathing (SDB) during infancy. At this age group, the causes for SDB differ from those in older children in whom obstructive sleep apnea syndrome (OSAS) due to adenotonsillar hypertrophy is the leading cause. Gastroesophageal reflux (GER) can provoke respiratory events in infants. These events may occur solely during sleep as SDB, and thus present as the only clinical manifestation of GER in these infants. The most common symptoms include OSAS, cessation of breathing (central apneas), desaturations, bradycardia, cyanotic episodes and apparent life threatening events (ALTE). The diagnosis of GER related SDB requires simultaneous recording of PSG variables and esophageal pH. The analysis of such recordings allows to formulate specific treatment towards the underlying mechanism. The purpose of this study was to evaluate the yield of esophageal pH monitoring during PSG in infants with unexplained SDB.
Methods: Forty-one infants with unexplained SDB underwent complete nocturnal PSG with simultaneous esophageal pH monitoring of the distal esophagus using an esophageal pH probe. Correct probe positioning was confirmed by chest radiography in each case. Abnormal pH study was defined as pH values under 4 persisting for more than 4% of the total pH monitoring time and was used to diagnose GER. The relations of respiratory events (apneas, desaturations etc.) to both the presence or absence of GER and to synchronous episodes of reflux were analyzed from the simultaneous polysomnographic and pH tracings.
Results: Patients age ranged from 1 week to 1 year (mean= 15.2 ± 13 weeks). The causes for referring the infants to PSG combined with pH monitoring were: cyanotic episodes (22%), apneas (20%), choking episodes related to feedings (15%) followed by ALTE, home apnea monitor alarms, nocturnal tachypnea/dyspnea and nocturnal cough. No gender differences were found. 20% of the infants were born prematurly. PSG was abnormal in 8/41 (20%). 50% of them (4/8 infants) had also GER. Overall, abnormal pH studies compatible with GER were observed in 12/41 (29%). In 4/12 (33%) PSG showed related respiratory events. Nevertheless additional 5/12 infants (42%) with GER whose PSG was normal had apneas and/or desaturation episods as the presenting symptom.
Conclusions: Infants with unexplained respiratory events (apneas, cyanotic events, choking episodes) may benefit from PSG with simultaneous esophageal pH monitoring. In infants with apneas and desaturation events confirmed by PSG, the yield of adding esophageal pH monitoring is relatively high and may help in understanding the mechanism behind the events and thus focus treatment. GER may also be found in infants with cyanotic episodes in whom apneas and desaturations are not detected during PSG. The addition of pH monitoring to PSG should be considered in infants presenting with unexplained sleep disordered breathing.

0295.G

Patients With Attention Deficit Hyperactivity Disorder Have Normal Sleep On Polysomnography

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Introduction: There is continuing speculation about the relationship between attention deficit-hyperactivity disorder (ADHD) and obstructive sleep apnea syndrome (OSAS) or periodic limb movement disorder (PLMD). This is a report on a completed polysomnographic study on 30 children with ADHD.
Methods: Six to 15 years old patients were enrolled. They met DSM-IV criteria for ADHD (inattentive, hyperactive, or combined). They had scores on the ADHD rating scale (ADHD-RS, consisting of 9 inattention items rated from 0-3 for a possible total score of 27, and 9 hyperactivity items similarly rated) at least 1.0 SD above age and gender norms. They had a Clinical Global Impression (CGI) score of at least 4 (moderately ill). They met the same criteria at a subsequent visit 10-24 days later. They had normal lab results and ECG, and had no clinical evidence of primary sleep disorders including OSAS (evidenced by snoring accompanied by excessive daytime sleepiness or observed apneic episodes), bipolar disorder, major depression, hypertension, or drug or alcohol abuse. One patient was excluded because of snoring with daytime sleepiness. A subset of patients (30 out of 64) volunteered for two nights of polysomnography (PSG) as part of the latter visit. The first night recording included EEG, EOG, submental EMG, ECG, nasal pressure, piezo abdominal belt, oximetry, and leg movements. The second night recording included EEG, EOG, submental EMG and ECG.
Results: The 30 patients (mean age 10.4, SD 2.0, range 6.4-14.6, 24 boys, 6 girls) had severe ADHD. On the ADHD-RS, patients had mean inattention score of 22.4 (SD 4.0, range 11-27) and mean hyperactivity score of 17.3 (SD 7.2, range 0-27). Mean Respiratory Disturbance Index was 1.7/h sleep (range 0-4.9). Mean Periodic Limb Movement (with arousal) index was 0.7/h sleep (range 0-5.0). The only significant correlations between ADHD ratings and polysomnographic variables on night one were for inattention score with sleep efficiency ($r=0.37$, $p=0.04$) and with PLM index ($r=-0.46$, $p=0.01$); and for CGI with sleep efficiency ($r=0.36$, $p=0.05$) and with PLM index ($r=-0.51$, $p=0.04$). On night 2, inattention score was correlated with sleep efficiency ($r=0.61$, $p<0.001$) and wake after sleep onset (WASO) ($r=-0.62$, $p<0.001$); as was CGI with sleep efficiency ($r=0.45$, $p=0.01$) and with WASO ($r=-0.51$, $p<0.01$).
Conclusions: ADHD is likely a multi-etiological syndrome. However, there was no evidence of OSAS or PLMD being one of the significant etiologies in this sample of patients. Clinical screening for snoring accompanied by EDS or observed apneic episodes successfully eliminated any patients who might have had OSAS. Patients did not have to be excluded simply for snoring. The inattention score and CGI were positively correlated with sleep efficiency and negatively with PLM index and with WASO, and were not correlated with Time in Bed, or with percentage of delta or REM sleep. This suggests that more inattentive patients do not sleep worse or have more PLMs, and their better sleep efficiency is not merely related to insufficient sleep.

0296.G

Peak End-tidal Carbon Dioxide (ETPCOs2s) in the Diagnosis of Pediatric Obstructive Sleep Apnea (OSA)

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Introduction: Several publications have suggested 1) that the polysomnographic features of pediatric OSA differ from those of adult OSA and 2) that using adult criteria to interpret pediatric sleep studies would miss cases of significant sleep-disordered breathing. The American Thoracic Society's published standards for performing and interpreting cardiopulmonary sleep studies in children recommend measurement of COs2s retention. However, these standards are largely based on a single study that investigated asymptomatic children and adolescents. Few studies have reported on the usefulness of ETPCOs2s measurements in clinical populations. The aim of the present study was to determine the usefulness of measuring peak ETPCOs2s in children suspected of having OSA.
Methods: We reviewed the polysomnogaphic data of all children, ages 1 through 11, who had full-night diagnostic polysomnograms at our sleep lab between 9/99 and 9/02 for the clinical suspicion of OSA. Data from patients with sickle cell disease, neuromuscular disease, or chronic pulmonary disease (other than asthma) was excluded. Also excluded was data from sleep studies in which reliable ETPCOs2s values were not obtained. Peak ETPCOs2s had been measured using a Capnocheck Plus ETPCOs2s monitor (BCI International, Waukesha, Wisconsin). For children who had more than one polysomnogram performed at our center, only data from the earliest polysomnogram meeting criteria was included in the study.
Results: Data from 78 children was included in the analysis. The mean of the peak ETPCOs2s values was 48.9 (SD=5.1, range=32-59). The mean AHI was 5.4 (SD=11.2, range=0-85.1). Peak ETPCOs2s correlated weakly with the apnea-hypopnea index (AHI) ($r=.15$), both in children with ($n=18$, $r=.40$) and without ($n=59$, $r=.13$) a prior adenotonsillectomy (data from one child with an isolated adenoidectomy was not included in sub-group analysis). Thirteen (17%) children had elevated peak ETPCOs2s values (greater than 53 mm Hg). Nine of the 21 children (43%) with an elevated AHI had an elevated peak ETPCOs2s. Ten of the thirteen children (77%) with an elevated peak ETPCOs2s had an AHI^{3}5 or an obstructive apnea index^{3}1, and thus met criteria for pediatric OSA even without ETPCOs2s data.
Conclusions: Although most cases of pediatric OSA could be identified based on AHI alone, peak ETPCO2s2s was useful in identifying additional cases. A weak correlation between AHI and peak ETPCOs2s was present. Studies examining the usefulness of other ETPCOs2s parameters are needed, as are studies comparing the usefulness of nasal pressure transducers versus ETPCOs2s monitors (which can not ordinarily be used simultaneously) in the diagnosis of pediatric OSA. In conclusion, clinicians should consider that peak ETPCOs2s may not be abnormal in all cases of pediatric OSA. Nevertheless, an elevated peak ETCOs2s may identify a small but significant number of children who do not meet OSA criteria on the basis of AHI alone.

0297.G

Cosleeping And Sleep Problems Among Swiss Children In The First 10 Years Of Life: Prevalence, Correlations And Secular Trends

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Introduction: Children sleeping in the same bed (bedsharing) or in the same room (roomsharing) with parents has been referred to in the literature as cosleeping. Cosleeping is generally described as decreasing with age, although large cultural differences exist. Associations between cosleeping and sleep problems have been reported, but whether sleep problems are antecedent to cosleeping rather than the opposite is still unclear. The Zurich Longitudinal Studies between 1974 and 2001 provided a unique opportunity to study cosleeping practices and sleep problems among Swiss families.
Methods: A total of 472 children (141 preterm, 331 full-term, 224 girls, 248 boys) were followed using structured sleep-related interviews at 1, 3, 6, 9, 12, 18, and 24 months after birth, and then at annual intervals until 10 years of age. Parents were queried about bedsharing, roomsharing, night wakings, bedtime resistance and sleep onset difficulties during the 3 months preceding the consultation. Descriptive statistical methods

were used to describe developmental trends across age.
Results: No differences were found between children born preterm or full-term, or between boys and girls. While in the first year of life relatively few children slept with their parents (< 10%), bedsharing increased with age and reached a maximum between 3 and 5 years (37.0% at 4y). Roomsharing with the parents decreased across age (from 20.3% at 1m to 3.9% at 1y), whereas roomsharing with siblings increased to a maximum at 5 years (42.2 %). In the first months of life, a remarkable decrease of nocturnal wakings (from 81.8% at 1m to 33.5% at 3m) was seen. After 3 months wakings increased again to a maximum at 3 to 4 years, when over half of all children woke up at least occasionally during the night (20.0% every night at 3y). Less than 10% of all children demonstrated regular bedtime resistance. Bedsharing was significantly correlated with nocturnal wakings at all ages except for age 3 months (r = 0.28 to 0.59), but less consistently with bedtime resistance or sleep onset difficulties. No consistent cohort trends were found except for bedtime resistance, which decreased significantly between 1974 and 2001.
Conclusions: Swiss children frequently wake up during the night and share the bed with their parents. Bedsharing may be more a reaction to nocturnal wakings than a lifestyle habit of Swiss families. The strong temporal correlation between bedsharing and nocturnal wakings indicates that a considerable number of children may need parental proximity during the night. The secular trends of bedtime resistance may indicate that child rearing practice have become more child-oriented over the last decades.

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0298.G

Disturbing Trends in the Sleep of "Normal" Children and Adolescents

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Introduction: The current state of the art of normative data for sleep structure in children is based on a few classic laboratory studies conducted many years ago with healthy children. These studies had very few subjects, but there have been many other studies where at least a few "normal control" children received comprehensive sleep evaluations. Pooling the polysomnogram (PSG) results from multiple studies using healthy subjects creates a much larger sample and affords the opportunity to assess changes in various sleep parameters over time. The aim of this study was to assess changes in sleep architecture in normal children and adolescents over time.
Methods: A search of the sleep literature was conducted to find all studies in the past 30 years in which healthy children and/or adolescents received complete PSG assessments. Studies were retained if they carefully screened subjects for factors that might influence sleep such as sleep-disordered breathing, depression, obesity, medication use, illness, and poor sleep prior to arriving in the sleep laboratory. A further requirement was that numbers of subjects, means, and standard deviations were reported for each sleep parameter. Thirty-five studies from 1974-2001, with a total of 670 subjects met all of these requirements. Subjects aged 4-12 who did not exceed stage 2 on Tanner's scale of pubertal development were considered children and those aged 13-19 who were at least in Tanner stage 3 were considered adolescents.
Results: Means and standard deviations were computed for the following sleep parameters: sleep efficiency, percentage of time spent in stages 1, 2, slow-wave, and REM sleep, REM latency, and number of REM periods. Separate computations were done for studies published prior to 1990 and those from 1990 to 2001. 1990 was chosen as a dividing year in order to retain a substantial number of subjects in earlier vs. later studies. Significant shifts from pre 1990 to post 1990 were as follows: For children: Sleep efficiency dropped from 94.96% to 91.17% (T=5.73 p<.001).Slow wave sleep increased from 23.76% to 26.28% (T=3.21 p<.001).REM sleep decreased from 23.3% to 20.16% (T=5.16 p<.001).Number of REM periods decreased from 5.0 to 4.0 (T=2.95 p<.002).For adolescents: Stage 1 sleep increased from 5.63% to 6.72% (T=2.00 p<.025).Stage 2 sleep increased from 48.74% to 52.95% (T=4.23 p<.001).Slow wave sleep decreased from 22.21% to 18.72% (T=3.34 p<.001).REM sleep decreased from 22.01% to 18.92% (T=4.9 p<.001).REM latency dropped from 116.3 minutes to 100.5 minutes (T=3.68 p<.001).These differences cannot be attributed to increased age of subjects in the post-1990 groups, as the post-1990 subjects were actually slightly younger.
Conclusions: Analyses of sleep studies of children and adolescents suggest that the sleep of normal healthy children is acquiring some attributes of adolescent sleep and that the sleep of normal adolescents is deteriorating. While the absolute size of these effects is relatively small, the consistent pattern is disturbing.

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0299.G

Maternal Feelings And Infants' Nightwaking

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Introduction: From a maturational perspective, by the end of the first year, sleep-wake states are well regulated. Nevertheless, many infants continue to wake-up during the night. While sleep disorders in early years may be a marker of disturbed mother-child relationships (Benoit et al. 1992), from a developmental perspective, settling difficulties and nightwaking around 1 year of age are normative. As the child becomes more aware of separation from caregivers (Bowlby, 1969), and is better able to control the environment (Piaget, 1952), prolonged nighttime interactions are expected. For the parents, nighttime separation from the infant, is often a source of concern, hence, attending to the child's signals and taking an active part in sleep regulation may be perceived as sensitive parenting. The goal of this study was to focus on mothers' feelings towards the infant, and examine the hypothesis that in a non-referred sample, mothers who enjoy interacting with their child will be more involved with the infant during the night.
Methods: 68 Israeli mothers, of 9- to 15-month-old healthy infants, participated in the study. Mothers completed the Infant Sleep Questionnaire (ISQ-Morrell, 1999). Based on Richman's (1981) criteria, the severity of the infant's nightwaking was scored (1 to 4). Mothers' feelings towards the infant were assessed with a modified version of "parent-to-infant attachment instrument" (Condon & Corkindale, 1998): the Maternal Feelings Questionnaire (MFQ), included 16 items (e.g., " when I am with the baby I usually try to shorten the time I spend with him/her"), scored 1 to 4, high score indicates positive feelings. Test re-test reliability has been established (.87). A factor analysis on the MFQ produced two scales "maternal hostility" (alpha .67) and "pleasure in interaction" (alpha .72).
Results: The ISQ indicated that 43% of the infants had a sleep problem. Higher levels of "pleasure in interaction" were associated with more sleep difficulties r=.28 (p<.05). In a regression analysis it was indicated that "pleasure" predicted 8% of the sleep problem variance. When dividing the mothers into two groups, based on median split of "pleasure", more awakenings were reported by mothers who scored high in "pleasure" (t=2.03, p<.05). Mothers who occasionally co-slept (35%) reported more positive feelings toward their infant compared to mothers who refrained from taking the infant into the parents' bed (t=3.00, p<01).
Conclusions: Around one year of age, sleep difficulties, in non-referred infants, are common. Nightwaking, and subsequent co-sleeping, were associated with mothers' pleasure in caring for, and interacting with, the

infant. This finding is in line with Scher (2001) who found that positive mother-child interaction during play was associated with more night-waking. The association between positive mother-child relationships and more sleep difficulties may be explained in terms of a bi-directional developmental model of sleep regulation (Anders et al., 2000). How maternal feelings and sleep characteristics correlate across time needs to be examined longitudinally. Given the present methodology, disentangling the contribution of constitutional child factors and contextual-parenting variables awaits future studies.

0300.G

Periodic Limb Movements in Sleep(PLMS) and Restless Leg Syndrome(RLS) in Children with "Growing Pains"

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Introduction: The purpose of the study is to determine if children with "growing pains" have RLS and PLMS. The next goal is to determine if "growing pains" respond to dopaminergic drugs. There have been no studies done to evaluate the prevalence of PLMS in children with "growing pains". Many children with RLS have been misdiagnosed as "growing pains". The prevalence of PLMS in children with RLS is not known. RLS and PLMS occur more commonly in children with ADHD.
Methods: Children between the ages of 5-18 complaining of "growing pains" were entered in the study. Initial growing pain questionnaires were filled out by a parent and child. They had 2 nights of standard polysomnogram(PSG) except 2 of these children had only one night of PSG. PSG parameters of the 2 nights were averaged. The children were interviewed by a Neurologist and Sleep specialist regarding the symptoms of RLS. They had clinical evaluation done by our Pediatric Neurologist for ADHD prior to referral for the "growing pains" study. Children with significant "growing pains" who were found to have RLS were started on Carbidopa/Levodopa (Sinemet) 25/100 at night. They were given an RLS rating scale to assess the severity of RLS, pre-treatment and post-treatment. The RLS rating scale assessed the severity of RLS in a scale of 0 to 40.
Results: A total of 10 children with "growing pains" were evaluated. Nine of these 10 children met criteria for RLS. One of these 9 had pain in the arms predominantly in addition to the legs. The average PLMS of the 9 children with RLS was 4.9 per hour. The range was 0.3 to 27. Only 3 of these 9 children had PLMS index more than 5 per hour of sleep. The Apnea index average of these 9 children with RLS was 0.61 with a range of 0 to 2.65. Two children had apnea index more than 1. Four of these 9 children with RLS were started on L-Dopa treatment. Two of these children had an average pre-treatment RLS rating scale of 30.5 that went down to 11 in two months follow-up. The other 2 children on treatment need follow-up evaluation in 2 months. Preliminary results of the RLS rating scale after treatment showed significant improvement in the complaint of growing pains and RLS symptoms. Four children of 10 with "growing pains" have ADHD. RLS was misdiagnosed as "growing pains" in 9 of 10 children.
Conclusions: A PLMS index of more than 5 per hour seems to occur less frequently in children with RLS compared to adults, but further investigation is warranted. This study further confirms that RLS can be misdiagnosed as "growing pains". As with other previous studies, there seems to be a high correlation between ADHD and RLS/PLMS. As in other previous limited studies, childhood RLS seems to respond well to L-Dopa therapy.

0301.G

Hyperactivity Symptoms Are Related To Poor Sleep In Children With ADHD

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Introduction: ADHD is the most commonly diagnosed behavioral disorder of childhood. Subjective and objective reports have shown that children with ADHD have extensive sleep disturbances and age-inappropriate increases in daytime and nighttime activity levels. This study therefore, examined whether there is a relationship between objectively recorded sleep and severity of ADHD hyperactivity symptoms.
Methods: Six Caucasian boys (mean age 8.5 yrs, SD 1.9, range 6-11 yrs) diagnosed with ADHD-Hyperactive/Impulsive Type or Combined Type (according to DSM-IV criteria) participated. Each child wore a Mini-Motionlogger Actigraph (Ambulatory Monitoring, Inc., Ardsley, NY) for 96 consecutive hours (2 weekend days and 2 weekdays) and filled out a daily sleep log (with parental assistance). Parents and teachers also filled out comprehensive questionnaires on each child's academic, emotional, medical, and behavioral history, including DuPaul ADHD ratings for Home/School, which provide ADHD symptomatology and symptom severity.
Results: On weeknights, the mean total sleep time (TST) was 9.7 hours, (SD=0.6), wake after sleep onset (WASO) was 1.6 hours, (SD=0.8), and number awakenings were 23.0, (SD=5.4). On weekend nights mean TST was 9.2, (SD=0.7), WASO was 1.3 hours, (SD=0.7), and number awakenings was 25.8, (SD=9.9). One-sample t-tests showed that there were no differences in WASO and number of awakenings between weekend and week nights, however, there was a trend for increased sleep duration on weekend nights when compared to week nights ($t5=-2.2$, $p<.083$). Spearman correlations were computed between objective sleep variables and the DuPaul ADHD Home scales (severity of hyperactivity symptoms; range of scores=0-27). Higher ADHD hyperactivity scores (mean=19.5, SD=3.5, range=14.0-23.0) were associated with more WASO (rho=.84; p=.038) and number awakenings (rho=.97; p=.001) on weekend nights but not on weeknights. No relationships were found between TST and hyperactivity scores. Due to the small sample size (n=6) at this phase of the study, more through analyses will be reported in future.
Conclusions: These data suggest a possible relationship between daytime hyperactivity levels in children with ADHD, number of nighttime awakenings, and time spent awake during the night. Children with ADHD are known to have extensive increases in arousal levels and daytime activity patterns, which may be extending into their nighttime period and thus affecting their nighttime sleep. We are continuing to collect data to further examine these possible relationships.

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0302.G

Does Slow Release Melatonin (SR) Prevent Recurrent Night Wakenings in Children with Neurodisability?

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Introduction: Sleep deprivation has a devastating effect on the individual child and family, affecting the health of parents, siblings and the overall functioning of the family unit. An evaluation of fast release melatonin in our unit suggested it had little impact on recurrent night wakening. Our hypothesis was that slow release melatonin (Melatonin 6 hour Timed Release) is superior to fast release melatonin in maintaining sleep in children with neurological disability.
Methods: Data was collected prospectively from children attending a nurse led sleep clinic for children with neurological disability. Families

received behavioural management and sleep hygiene advice. Parents completed one hour block sleep diaries for fouteen days prior to open label melatonin SR prescription (3mg or 6mg), and for twenty eight days on treatment. If relevant, parents were asked to keep seizure diaries. We were unable to source a suitable placebo preparation.
Results: 15 prescriptions were issued from 2001-2002. 2 diaries were not returned, 1 uninterpretable,1 prescription was not adhered to, 11 could be studied. The group comprised 5 males, 6 females age range 2.5 to 14y. All had learning disability and 8 had epilepsy. There was no reported increase in seizures while taking melatonin.Wilcoxon Signed Rank Test suggested the number of night awakenings was significantly lower (p=0.015, 95% confidence intervals 3-15). The number of hours slept increased significantly (p=0.014, 95% confidence interval 0.32-2.67).
Conclusions: Melatonin SR appears to be associated with a significant reduction in night wakening and an improvement in sleep duration. The numbers are small and confidence limits wide. We are continuing to collect data prospectively. There was no change in seizure frequency in those with epilepsy.

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0303.G

Impact of a Nurse Led Sleep Clinic on the Use and Evaluation of Melatonin FR (Fast Release) for Sleep Problems in Children with Neurodisability

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Introduction: Initiating and maintaining sleep are common problems for children with neurological disorders. Though there is little evidence to support its use, melatonin is widely used for this indication. We evaluated the use of melatonin, before and after the institution of a dedicated sleep clinic.
Methods: Since 1995 melatonin prescription has been evaluated by an initial double blind placebo/melatonin crossover trial. Parents complete 1hr block sleep diaries 10 days prior to treatment, 10 days on capsule A, 4 days washout and 10 days on capsule B. Decision to continue melatonin prescription is made by visual assessment of the diary once the code is broken. Before 2001, neurologists prescribed melatonin. From 2001 melatonin prescriptions were prescibed by the neurologist but issued through a nurse led sleep clinic, data was collected prospectively and the families received behavioural management and sleep hygiene advice. Diaries were reviewed with respect to number of hours slept, recurrent night wakening and patient details.
Results: From 1995-2001 pharmacy issued 33 trial prescriptions. 18 diaries were untraceable, 3 unidentifiable, 5 uninterpretable, and 7 auditable. 2001-2002, of 9 diaries issued, 2 were uninterpretable. The 1995-2001 group comprised 5 males, 2 females (age 18m-11y). The clinic group (2001-2002) comprised 2 males, 5 females (age 4-13y).Wilcoxon signed rank test in the pre clinic group showed no evidence that number of hours slept with or without melatonin were different (p=0.205). In the clinic group the difference in the number of hours slept prior to taking Melatonin and after is statistically significant (p=0.036). There was no significant difference in time taken to fall into continuous sleep in either group.
Conclusions: We have demonstrated an association between use of fast release melatonin with number of hours slept only when it was prescribed in the setting of a dedicated sleep clinic. Families attending the clinic received structured behavioural management advice. The clinic allowed improvements in ongoing follow up, record keeping and family support. The patient numbers are small and we are continuing the prospective evaluation.

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0304.G

Snoring Is In The Ear Of The Beholder

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Introduction: Sleep-disordered breathing (SDB) in pediatric populations has recently emerged as a significant health problem. Snoring is the major symptom for SDB in children. Thus, screening of all children for presence of snoring has been recommended by the American Academy of Pediatrics. However, the validity of parental report for snoring has rarely been examined. We sought to compare the sensitivity of parental report of snoring with presence of objectively recorded snoring during overnight polysomnography (PSG) in a large sample of pre-school and first-grade students.
Methods: A previously validated questionnaire was distributed to the parents of all students attending public pre-school and first grade classes; target questions included "How often does your child snore?" and response options included "Never" (never in the past 6 months), "Rarely" (once a week), "Occasionally" (2 times a week), "Frequently" (3-4 times a week), or "Almost Always" (more than 4 times a week). At-risk for SDB and control subjects were invited to participate in standard overnight PSG as part of two ongoing studies. Parental report of snoring was compared to presence or absence of snoring during PSG; sensitivity and specificity of the instrument was measured in the two age groups by defining risk for SDB to include 1) report of snoring that occurred "occasionally", "frequently", and "almost always" (OFA), or 2) "frequently" and "almost always" (FA).
Results: 123 pre-schoolers and 269 first-graders had both parental report and overnight PSG. The likelihood ratios for pre-school and first-grade samples in each reporting frequency were: 0.29 and 0.22 for Never; 0.00 and 0.44 for Rarely; 0.81 and 0.52 for Occasionally; 0.81 and 1.75 for Frequently; and 2.73 and 3.47 for Almost Always. Sensitivity and specificity for pre-schoolers were 0.92 and 0.21 for OFA, and 0.62 and 0.57 for FA. For first graders sensitivity and specificity were 0.85 and 0.50 for OFA, and 0.73 and 0.74 for FA.
Conclusions: Parental report of snoring is sensitive for identifying children who indeed snore. As expected, agreement between parental report and objectively recorded snoring was highest at the highest frequency of snoring. Inclusion of "occasional" snoring in the criteria for overnight PSG will increase the sensitivity of the instrument but decrease the specificity, with reciprocal effects when occasional snorers are excluded. Thus, operational decisions on PSG indication by parental report may need to include occasional snoring to insure proper detection and diagnosis of SDB in early childhood.

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0305.G

Prevalence Of Risk For Sleep-Disordered Breathing (SDB) Among Infants And Toddlers

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Introduction: The prevalence of SDB in school-age children is estimated at 2-3%. However, reliable data on the incidence of SDB during infancy are not currently available. Accordingly, the goal of this study was to survey a broad, cross-sectional sample of the general community to determine the prevalence of infants and toddlers who may be at-risk

for SDB.
Methods: Parents attending local pediatric offices for well-baby check-ups with children ages 0-2 years answered an abbreviated modification of a previously validated questionnaire. In addition to demographics and general medical history, sleeping location (in the parent bed or room, or in the child's own room), and snoring frequency and loudness were assessed. At-risk for SDB included infants whose parent reported snoring to occur "Frequently" or "Almost Always", provided snoring was "Loud", "Very Loud", or "Extremely Loud".
Results: 767 respondents were evenly distributed over ten check-up time-points from birth-2 years. The percent of patients reported to be at-risk for SDB was 0% at 1 month and younger, 5% at two months, 1% at four and six months, 3% at nine and twelve months, 7% at fifteen months, 4% at eighteen months, and 5% at twenty-four months. There was a significant increase in the number of toddlers (>12 months) reported to be at-risk for SDB, compared to infants (£ 12 months) (2 = 4.1, p<.05). Overall, 2% of infants and 6% of toddlers were found to be at high risk for SDB. Sleeping location was associated with a difference in reporting frequency among parents of infants, but not toddlers: At-risk for SDB among infants sleeping in the parent bed or room was 3.6% compared to 1.3% for infants sleeping in their own room (p=.052). 54% of infants at-risk for SDB and 30% of those not at-risk had at least one parent who smoked, while smoking rates were similar in toddlers (33% and 32% respectively). 92% of infants at-risk for SDB and 64% of those not at-risk had at least one parent who snored, while among toddlers, rates were 75% and 66% respectively.
Conclusions: The prevalence of infants and toddlers reported to be at-risk for SDB suggests that an increased rate of SDB exists among toddlers compared to infants, and may reflect the growth of upper airway lymphatic tissue. Among infants, proximity of the parent during the night affects report of snoring prevalence. Furthermore, infants, but not toddlers, are at higher risk for SDB, if at least one parent smokes. Similarly, higher risk for SDB occurs in both infants and toddlers when a family history of snoring is present. Thus, screening for the potential presence of SDB in infants and toddlers will require incorporation of multifactorial elements in the parental questionnaire.

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0306.G

Quality of Life and Depressive Symptoms Among Children with Suspected Sleep-Disordered Breathing

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Introduction: Sleep-disordered breathing (SDB) has been associated with depression in adults and with impaired quality of life in children. However, it remains unclear whether SDB impacts children's mood, and what role obesity may play.
Methods: Twenty-seven children with suspected SDB (15 males), ages 8-12, have been thus far recruited. Children were asked to complete the Children's Depression Inventory (CDI) and the Child Report version of the Pediatric Quality of Life Inventory (PedsQL). Parents were asked to complete the Parent Report version of the PedsQL. Twelve children were classified as overweight, with a body mass index (BMI) above the 95th percentile for age and gender, and the remainder were classified as normal weight.
Results: Mean age was 10.5 ± 1.4 years, with similar age in the overweight and normal weight groups. No ethnic differences were observed between the two groups, with 74% of the total sample Caucasian, 22% African American, and 4% biracial. Mean BMI for the overweight group was 31.7 ± 7.8, and 17.7 ± 2.3 in the normal weight group ($p < .0001$). While no differences were observed between the two groups on child-reported measures of quality of life, parent reports revealed significantly poorer PedsQL scores in the overweight group, including total quality of life, physical health, and social functioning ($t = 2.38$, $p = .025$; $t = 3.18$, $p = .004$; $t = 2.37$, $p = .026$, respectively). Mean total PedsQL scores for the combined sample was 61.9 ± 18.0 by parent report and 66.14 ± 15.9 by child report. Mean CDI T-score was 51.5 ± 8.4, and 30% had T-scores above 55. Mean Anhedonia T-score was 55.9 ± 9.5, with 44% of the sample having T-scores above 55.
Conclusions: Children with suspected SDB, regardless of weight status, report substantially poorer quality of life than even chronically ill children previously studied with the PedsQL. Additionally, regardless of weight status, children with suspected SDB are at high risk for overall depression and anhedonia, possibly related to the fatigue associated with poor sleep quality. Furthermore, parent-reported quality of life in children who are overweight appears significantly impaired in comparison with children of normal weight. Thus, depressive manifestations and decreased quality of life are highly prevalent in children suspected for SDB, particularly when obesity is present.

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0307.G

Parental Stress and Sleep Structure in Children

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Introduction: Parental stress and anxiety may impact on their children's emotional functioning. However, the role of parental stress on children's sleep architecture has not been specifically examined.
Methods: A clinical sample of 60 children referred to a pediatric sleep medicine center (clinic group; mean age = 7.1 ± 2.6; 60% male) and a community sample of 65 children recruited through the public school system (research group; mean age = 5.7 ± 1.3; 52% male) were assessed with overnight polysomnography (PSG). The children's parents completed the State Trait Anxiety Inventory and the Parenting Stress Index (PSI). Children whose parents responded defensively to the PSI were not included in the analyses. The clinic group included 28% with psychiatric disorders. Suspected sleep-disordered breathing was the chief complaint for 73%, and 38% had been referred with initial complaints of behaviorally-related sleep problems.
Results: The clinic group was significantly older than the research group ($t = 3.75$, $p < .001$) and was significantly more likely to have problems that contributed to parental stress levels ($t = 2.33$, $p = .02$). Furthermore, parents of children in the clinic group were significantly more likely to report problems on the PSI related to their children's adaptability, demandingness, mood, and acceptability ($t = 2.89$, $p = .005$; $t = 2.5$, $p = .01$; $t = 2.15$, $p = .03$; $t = 2.27$, $p = .025$, respectively) than parents in the research group. When controlling for recruitment status, problems related to child adaptability to changes were positively correlated with slow-wave sleep (SWS; $r = .24$, $p = .006$). SWS was also positively correlated with increased parental isolation, role restriction, overall parent-reported stress, and total stress ($r = .22$, $p = .01$; $r = .20$, $p = .01$; $r = .18$, $p = .047$; $r = .20$, $p = .03$, respectively). Parentally-reported marital problems were negatively correlated with proportion of non-REM sleep and REM latency and positively correlated with proportion of REM sleep ($r = -.22$, $p = .02$; $r = -.25$, $p = .006$; $r = .22$, $p = .02$, respectively).
Conclusions: Children who are referred to a pediatric sleep medicine center are more likely to present problems related to parental stress levels than control children. Regardless of referral status, parental stress is associated with SWS increases in their children, while reports of marital problems are associated with REM sleep disturbances. These alterations in sleep architecture may reflect sleep loss and indicate stress and

depression in children. Thus, children's sleep appears to be vulnerable to parental stress.

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0308.G

Modafinil In The Treatment Of Excessive Daytime Sleepiness In Children

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Introduction: Modafinil is an alerting agent approved for the treatment of narcolepsy in adults. There are no studies examining the long-term effects and safety profile of modafinil in children with excessive daytime somnolence (EDS).
Methods: To determine the effects of modafinil on clinical manifestations of narcolepsy and idiopathic hypersomnia a systematic chart review was conducted on 13 children (mean age 11±5.3years, six males, 10 with narcolepsy and 3 with idiopathic hypersomnia) receiving modafinil.
Results: The mean modafinil dose was 346±119 mg/day, with a mean treatment duration of 15.6±7.8 months. In approximately 90% of children, a favorable response was reported by the parents with a reduction in sudden sleep attacks being documented by sleep-wake diaries. One child failed to improve on 400 mg/day modafininl and was switched to methylphenidate, and two other children showed only partial improvement and required additional stimulant medication to control EDS symptoms. Seven children underwent nocturnal polysomnography and multiple sleep latency test (MSLT) while on modafinil. Compared to baseline MSLT measures (mean sleep latency: 6.6 ±3.7 min) modafinil prolonged mean sleep latency (10.2±4.8 min, p=0.02) without significant alteration in nocturnal polysomnographic measures. However, a trend towards REM sleep reduction was noted with modafinil (16.8±5.1%TST vs. 11.8±6.2%TST). No adverse reactions were reported with modafinil therapy, and hematological and hepatic functions assessed every 3 months remained unaltered.
Conclusions: Modafinil has a modest, yet significant effect on EDS in children and appears to be safe and well-tolerated for long-term use.

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0309.G

Vascular Dysfunction In Children With Sleep-Disordered Breathing

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Introduction: Autonomic nervous system (ANS) dysfunction is highly prevalent among adult patients with sleep disordered breathing (SDB). However, the effect of SDB on ANS in childhood has not been systematically investigated. Pulse Arterial Tonometry (PAT) is a noninvasive beat-to-beat technique (finger-mounted probe) that is exquisitely sensitive to changes in sympathetic autonomic nervous system tone.
Methods: Cold hand pressor tests were performed in 4 healthy control children and 4 children with SDB as diagnosed from an overnight polysomnography. The left hand was immersed in ice cold water for 30 seconds while right hand PAT signal and cutaneous blood flow (CBF; laser Doppler flowmetry) were continuously monitored during immersion and recovery periods. Changes in signal amplitudes were calculated by averaging the mean amplitude over a 10-sec period before the pressor test (baseline), during the test (challenge), and immediately following removal of the hand from the water (post challenge), and then at one minute intervals during the 20 minute recovery phase. Amplitudes were expressed as % change from corresponding baseline.
Results: The magnitude of sympathetic discharge-induced attenuation of PAT signal and of CBF were similar during the cold hand pressor test. Furthermore, no differences occurred between children with SDB (signal attenuation of 87.8%) compared to controls (signal attenuation of 70.8%, p=ns). However, the recovery dynamics of control children were faster than those of children with SDB, with the control children demonstrating a return to baseline in 5 minutes post challenge, compared with a recovery time of 13 minutes for the SDB children ($p<0.01$). None of the SDB children and all of the control children displayed the typical CBF overshoot that develops during recovery.
Conclusions: Children with SDB have altered ANS regulation as evidenced by alteration in vascular reactivity. The reversibility of these findings with treatment remains to be determined.

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0310.G

Potential Usefulness Of Non-Invasive Autonomic Monitoring In Recognition Of Arousals In Children

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Introduction: Overnight polysomnographic studies are considered the gold standard for the diagnosis of sleep disordered breathing in children. Current methods employed for the scoring of arousals in children rely on adult-defined criteria, and may not be sensitive in children. In addition, previous work suggests that arousals may manifest as movement in children. In general, arousals from sleep are associated with increases in sympathetic tone and therefore, measurement of sympathetic activity using non-invasive approaches, e.g., Pulse Transit Time (PTT) and Peripheral Arterial Tonometry (PAT), have become useful surrogate markers for arousals in adults.
Methods: To validate the use of PTT and PAT measures in the identification of arousals in children, 5 healthy children underwent overnight polysomnographic assessment with PTT and PAT being measured simultaneously. Arousals (EEG and/or movement) were identified. A moving average (4 sec) of PTT signal was constructed to remove respiratory variation and declines in PTT of at least 10 msec for a minimum duration of 3 seconds were classified as PTT arousal events. PAT signal attenuations of at least 20% from the preceding baseline were counted as PAT arousal events. Analysis of arousals, PTT events, and PAT events were performed independently with scorers blinded to the other signals. PAT and PTT movement-related artifacts were also recorded. The sensitivity and specificity of PTT and PAT for recognizing arousals were assessed.
Results: A total of 822 events were identified in the 5 records. Of these, 277 were arousals, and 223 (80.5%) were identified by either PTT and/or PAT. The sensitivity and specificity of PTT for recognizing arousals was 0.66 and 0.34, respectively, while the sensitivity and specificity of PAT for recognizing arousals was 0.56 and 0.13, respectively (PAT vs. PTT, p=NS). Since movement arousals result in brief periods of artifact on the PTT and PAT signals, we re-analyzed the PTT and PAT events to include artifact events. Re-analysis increased the sensitivity of PTT for recognizing arousals to 0.99 and that of the PAT to 0.97, without affecting their specificity.
Conclusions: Both PTT and PAT events are extremely sensitive in recognizing arousals in children, particularly when brief signal artifacts characteristically associated with movement arousals are included. However, a substantial proportion of autonomic events occur in children without accompanying visually-recognizable EEG changes, thereby reducing the specificity of PAT and PTT methods. Thus, PAT and PTT

may provide useful alternatives for arousal recognition during ambulatory sleep monitoring in children.

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0311.G

Sleepwalking, Sleep-Disordered Breathing, and Restless Leg

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Introduction: The pathophysiology of sleep terrors and sleepwalking is poorly understood.
Methods: Patients with sleep terrors with or without sleepwalking were studied and compared to controls. Each subject had: 1) Pediatric Sleep Questionnaire; 2) Interview regarding medical, social and family history of medical and sleep disorders, orthodontic history, schooling, psychological difficulties, and medications; 3) General pediatric physical, neurological, otolaryngological, and craniofacial examination; 4) Polysomnography including EEG, chin and leg EMG, EOG, ECG, nasal cannula/pressure transducer system, mouth thermistor, chest and abdominal bands, pulse oximeter, neck microphone and calibrated esophageal manometry. 5)Available family members with sleep terrors and sleepwalking received similar clinical evaluations, and ambulatory monitoring with Edentrace. Data AnalysisAll recordings were re-scored by two of four blinded specialists.Mann-Whitney U test was used for group comparison. Non-parametric chi-square test was used to compare percentages of symptoms in symptomatic versus control children.
Results: Eighty-four children (5 with sleep terrors and 79 with sleep terrors and sleepwalking) and 36 controls were studied. All subjects were Tanner stage I. No controls had parasomnias. Fifty-one of the 84 children (61%) were diagnosed with an additional sleep disorder: 49 with sleep disordered breathing (SDB) and 2 with restless leg syndrome (RLS). Twenty-nine of the children with both parasomnia and SDB had a family history of parasomnias, and 24 of the 29 also had a family history of SDB. 45 of 51 children with associated sleep disorders were treated. Forty-three children with SDB were treated with tonsillectomy, adenoidectomy and/or turbinate revision, and the 2 RLS children were treated with Pramipexole. Treatment of the precipitating sleep disorder eliminated parasomnias in all 45 children. EEG arousals > 3 seconds/hour during total sleep time decreased from a mean of 9 + 2.6 to 3 + 1.5 (p=0.0001), and during the first sleep cycle of Slow Wave Sleep, from 4 + 1.4 to 1+ 0.2 (p=0.01). Parasomnias resolved in all the surgical cases. In RLS children, the PLMS arousal index decreased from 11 and 16 to 0 and 0.2, respectively, with treatment. Parasomnia persisted in the 6 untreated SDB children.
Conclusions: Children with chronic parasomnias may often present with SDB or RLS. The resolution of the parasomnias after treatment of the SDB or RLS/PLMS suggests that the latter may trigger the former. Children with parasomnias are not systematically monitored during sleep, even though past studies have suggested patients with sleep terrors or sleepwalking have more EEG arousals. When children receive polysomnographies, evidence of SDB should be sought. Children's respiration during sleep should be monitored with nasal cannula/pressure transducer system and/or esophageal manometry, which are more sensitive than the thermistors or thermocouples currently used in many laboratories. Also noteworthy is the report of familial presence of parasomnia. It remains to be determined whether a genetic factor directly influences sleep terror and sleepwalking, or instead influences other disorders that fragment sleep and lead to confusional arousals.

0312.G

Breathing Patterns in Prepubertal Children with Sleep Disordered Breathing

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Introduction: Clinical practice suggests that breathing patterns other than those described in the literature are indicative of abnormal breathing during sleep. Consequently, snoring children with clinical symptoms but with "negative polysomnograms" have undergone tonsillectomy and adenoidectomy. We studied breathing patterns during sleep using more accurate recording devices, and we examined the validity of attributing pathological significance to specific breathing patterns by evaluating the presence/absence of clinical complaints, the results of polysomnography, and the effect of tonsillectomy and adenoidectomy on the selected breathing patterns.
Methods: 400 children referred for suspicion of sleep disordered breathing and 60 control children were studied. Analysis of clinical signs and symptoms was performed at entry and three months post-otolarygological treatment. Determination of the frequency of pre-defined breathing patterns during sleep through blind analysis of polysomnograms was obtained once in control subjects and twice in referred children (pre- and post-adenotonsillectomy), utilizing EEG, EOG, chin and leg EMG, ECG, nasal cannula/pressure transducer system, mouth thermistor, esophageal manometry (Pes), microphone, pulse oximetry and transcutaneous CO2 electrode. The relationship between breathing patterns during sleep pre- and post-surgery, and residual post-surgery symptoms was determined.
Results: 99 SDB and 6 control children presented with a non-apneic, non-hypopneic respiratory pattern. These patterns were tachypnea, persistently elevated breathing effort, and progressively increased breath effort with discrete flattening of nasal airflow. They were monitored with nasal cannula/ pressure transducer system and were unaccompanied by oxygen saturation drops. These abnormal breathing patterns were significantly more frequently seen as residual breathing disturbances when either tonsillectomy or adenoidectomy was performed compared to adenotonsillectomy, and they were associated with residual clinical complaints.
Conclusions: Currently published polysomnographic scoring recommendations overlook common breathing abnormalities during sleep that are associated with clinical complaints, and may persist with partial surgery on the upper airway.

0313.G

Actigraphically-Estimated Sleep Patterns of Middle School Students

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Introduction: Sleep patterns of US adolescents across the high-school years include progressively later bedtime, earlier rising time for school days, and less sleep. This trend may begin as early as middle school according to several small studies that relied on self-report. The present study assessed actigraphically-estimated sleep patterns of younger adolescents.
Methods: Students from grades 6, 7, and 8 (46 girls, 42 boys, ages 11.0 - 14.8 yr (M=12.7)) recruited from an urban, public middle school, wore an actigraph (AMI) for 8 days while keeping a sleep diary. Actigraph data were analyzed using Action-W2 software (AMI) and a validated algorithm to estimate the following variables for school nights and weekend nights: sleep period (SP = sleep onset - sleep offset), sleep onset (time of first consolidated sleep after bedtime), and sleep offset (time of last consolidated sleep before rise time). Effects of grade level and sex were assessed for each variable.

Results: Significant (F's ≥ 3.63, p's £ .03) effects of grade level were found for all school night variables: SP: M(6) = 500, M(7) = 498, M(8) = 473; Onset: M(6) = 22:08, M(7) = 22:13, M(8) = 22:44; Offset: M(6) = 6:26, M(7) = 6:29, M(8) = 6:35. Post hoc analyses demonstrated that school night differences were attributable to the 8th grade group. Sex differences on school nights included only a significant (p = .007) delay of sleep offset by about 50 minutes from grades 6 to 7 for boys. Weekend sleep patterns were not significantly affected by grade level (overall means: SP = 528; Onset = 23:33; Offset = 8:17). The only significant (p = .03) sex difference for weekend sleep patterns was a delay of offset by 43 minutes from grades 6 to 7 in boys.
Conclusions: These data confirm with objective measures that the trend for delays and reductions of school-night sleep begin in early adolescence. In comparison with laboratory based findings regarding adolescent sleep need, these young adolescents are not obtaining adequate sleep. In summary, according to actigraphy, 40% of the middle school students fell asleep after 10:30 P.M. on school nights; 25% fell asleep after midnight on weekends. Furthermore, 20% slept 7.5 hours or less and only 10% obtained 9 hours or more on school nights. Future analyses need to assess daytime sleep and examine factors that may contribute to young adolescents' sleep patterns.

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0314.G

Daytime Sleepiness And Sleeping Habits Of High School Students

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Introduction: Poor sleep hygiene and sleep deprivation in adolescents have been linked to unintentional injuries, low grades and poor school performance, negative moods and increased likelihood of stimulant use. To date there is limited research information on the effects of sleep disturbance on adolescents. There is also lack of awareness of the problem of sleep deprivation in adolescent students and daytime sleepiness or decreased alertness are still not recognized as significant obstacles to the education. However the combination of late night social schedule, part-time jobs, sport or other activities of high school students are significantly compressing the hours available for sleep, causing daytime sleepiness and lack of attention in the classroom. The purpose of this study was to investigate sleeping habits in a group of randomly selected grade 11-12 students.
Methods: Fifty high school students (25 females and 25 males, 16-17 years old) participated in the study. Consent forms were obtained from the students and their parents/guardians. 17- item Sleep/Wake Assessment Questionnaires (SWAQ) containing questions regarding diurnal and nocturnal routines and habits were distributed to the students. Students also kept sleep diaries for 7 consecutive days.
Results: SWAQs showed that total sleep time on weekdays and weekends was 6.6h±1.2 and 8.0h±2.3 respectively. However sleep diaries revealed less comforting results: 5.6h±2.3 on weekdays and 6.9h±2.1 on weekends. More than the third of the students reported difficulty falling asleep. High percentage of respondents reported daytime sleepiness (82%) and concentration difficulties (73%). 82% of the students were carrying part-time jobs.
Conclusions: This study showed evidence of significant sleep deprivation and daytime sleepiness in high school students. Surprisingly the high proportion of students who reported difficulty initiating sleep despite chronic sleep deprivation implies disturbed circadian mechanisms regulating sleep/wake cycle in this population.

0315.G

Daytime Sleepiness In Children With Attention Deficit Hyperactive Disorder

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Introduction: Children with attention deficit hyperactive disorder (ADHD), although hyperactive, benefit from stimulant treatment. We hypothesized that children with ADHD are in fact sleepy during the day, and sought to test it objectively.
Methods: Thirty four children with a previous diagnosis of ADHD (age 12.4±4.6 (mean ± STD)) and 32 matched controls (age 12.0 ± 3.6y) were studied. All underwent a full night polysomnographic study followed by a multiple sleep latency test (MSLT).
Results: During the night study, sleep latency, total sleep time and sleep efficiency were comparable between the groups. Yet, ADHD children were significantly sleepier than controls during the day (mean MSLT score of 21.9±5.5min vs. 27.9±2.0min, $p<0.005$). Eighteen of the ADHD children have been found to suffer from obstructive sleep apnea syndrome (50%) vs. 7 of the control group (22%, $p<0.05$). Five of the ADHD group had periodic limb movement of sleep (PLM, 15%) vs. none in the control group. However, surprisingly, within the ADHD group, children with OSA were not sleepier than children without OSA. Children without a notable primary sleep disorder had the lowest nocturnal sleep efficiency and total sleep time.
Conclusions: Children with ADHD demonstrate objective daytime somnolence, which can explain the beneficial effects of stimulant medications. Sleep disorders should be looked for in children with ADHD, as many of them (over 50% in this study) may suffer from a primary sleep disorder. ADHD children without a primary sleep disorder may have low sleep efficiencies and short total sleep time.

0316.G

Forced Long Daytime Nap Delays Bedtime In Nursery School Children And Their Delayed Nighttime Sleep Pattern Persists During Early Elementary School Period

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Introduction: Fukuda & Sakashita (2002) investigated sleep pattern of kindergartners and nursery school children in Japan. In Japanese nursery schools the children have to take an afternoon nap for about 1.5 hr. They found the long afternoon nap delayed the children's bedtime and significantly affect the daytime functioning adversely. The present study investigated their sleep pattern after entering elementary school where a daytime nap is no more obligatory and aimed at finding whether their delayed sleep pattern persists during elementary school period.
Methods: A questionnaire asking their sleep pattern was mailed to elementary school children. Their parents were asked to fill out the questionnaire. The survey was conducted annually from 1999 to 2001. The cummulative number of children who participated in the survey was 1,518. Several parameters concerning sleep pattern were compared between the elementary school children who formerly attended kindergarten (ex-kindergartners) and nursery school (ex-nursery school children).
Results: Bedtime was significantly delayed in ex-nursery school children compared with ex-kindergartners until grade 4 (grade 1 & 2: $p<.001$, grade 3 & 4: $p<.001$). Subjective insufficiency of sleep length was greater in ex-nursery school children in the grade 1 & 2 ($p<.05$). Several parasomnias (e.g., night terror and sleep walking, $p<.05$, both) were more frequent in ex-nursery school children during grade 1 & 2.
Conclusions: In ex-nursery school children, their delayed sleep pattern, which was caused by the institutional daytime nap in their nursery

school days, persists during early elementary school period after the custom of taking the long afternoon nap ceased. Several parasomnias were also significantly more prevalent in ex-nursery school children.

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0317.G

REM Sleep Architecture in Depressed Children and Adolescents

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Introduction: While subjective sleep complaints are common in children and adolescents with major depressive disorder (MDD), polysomnographic findings have been more equivocal. Some studies have reported shorter REM latency and prolonged sleep onset in childhood depression, whereas others have failed to distinguish patients from healthy controls. Methodological issues such as the potential influence of gender or incomplete age-matching between patients and controls may contribute to the discrepant findings among studies. The present study evaluated potential gender differences between depressed outpatients, 8-17 years of age, compared to age-matched healthy normal controls. A secondary aim of the study was to examine the characteristics of individual REM periods, in addition to all-night summaries.
Methods: 100 children and adolescents spent two consecutive nights in the laboratory after a 5-day regularized home sleep schedule, confirmed by actigraphy and diary. All subjects were run on the weekend. The 59 patients (28 females, 31 males) met DSM-IV criteria for MDD and were symptomatic and unmedicated at the time of study. 41 (20 females, 21 males) normal controls (NC) with no personal or family history of psychopathy also participated. Each night of sleep was scored visually according to strict Rechtschaffen and Kales criteria. The latencies, durations, densities and minutes of REM in each REM period were calculated along with standard sleep measures. Data were coded for group (MDD vs NC), gender and age, using a cutpoint of 12 years. A 3-way factorial ANOVA evaluated between-group differences. Multiple comparisons contrasted differences between individual groups.
Results: With the exception of REM sleep measures, none of the standard sleep measures differed between patients and controls. REM latency, % REM, and the durations of the individual REM periods all showed significant group by gender by age interactions. Adolescent males with MDD showed significantly shorter REM latency and higher % REM than all other groups ($p<.05$). Moreover, MDD males showed a very large age-related change in REM latency, contrasting 8-12 yr olds to 13-17 yr olds ($p<.001$), in sharp contrast to all other groups. Males with MDD also showed a longer first REM period in both children and adolescents. Interestingly, females in both MDD and NC groups showed a progressive increase in the duration of the individual REM periods, regardless of age, whereas males showed an increase in duration from the first to second REM period with no subsequent increase. In addition, all groups of 8-12 year olds showed a high correlation between the 1st REM period duration and the minutes of slow-wave sleep (SWS) in the 1st NREM period (>.80, $p<.010$) that was lower in those 13-17, except MDD males. The MDD males actually showed only a moderate correlation between REM latency and minutes of SWS in the 1st NREM period that was significantly higher in the 13-17 yr olds.
Conclusions: REM sleep architecture in MDD is strongly influenced by age and gender. REM sleep abnormalities are more prominent in MDD male adolescents. Further, the relationship between REM characteristics and slow-wave sleep also appears to be disease-, gender- and age-dependent.

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0318.G

Glucose Homeostasis And Serum Lipids Among Snoring Children

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Introduction: In adults, sleep-disordered breathing (SDB) is associated with insulin resistance and dyslipidemia, independently of obesity. Similarly, SDB severity correlates with insulin resistance among obese children. Furthermore, hypertriglyceridemia and decreased HDL levels coincide with insulin resistance among obese children. However, the prevalence of insulin resistance and dyslipidemia among snoring children is unknown.
Methods: In consecutive children, fasting serum lipids, glucose, and insulin were obtained the morning after undergoing polysomnographic evaluation for suspected SDB. Scoring of variables during sleep was performed using standard criteria. Insulin resistance was assessed using the homeostasis model assessment (HOMA) and the insulin/glucose ratio (I/G). Body mass index was calculated as weight/height^2. To linearize BMI data, the relative BMI (RelBMI) was calculated as BMI/BMI at 50th percentile for age and gender x 100. Obesity was defined as relBMI >170%.
Results: 29 children (12 males), ages 5-18 years (mean age: 9.54±2.99) were studied; 10 children (34%) had SDB (Obstructive apnea/hypopnea index (AHI) > 5), and 11 (38%) were obese. In the SDB group 4/10 (40%) were obese (p-NS vs. non-SDB). Mean insulin levels in the obese group were 319.9±166.7 compared to 61.3±15.1 pmol/L in the nonobese children ($p<0.05$). Insulin resistance was present in 8 children, and 7 of these were obese. No significant correlations were found between AHI, lowest SpO2, or arousal index and serum insulin or lipids for either the whole group or the obese children only. However, significant correlations were found between HOMA and relBMI ($r=0.5$ $p=0.006$), relBMI and HDL ($r=-0.59$, $p=0.006$) and relBMI and TG levels ($r=0.47$, $p=0.04$). In addition, age and insulin level were also positively correlated ($r=0.50$, $p=0.007$)
Conclusions: Among children with suspected SDB, insulin resistance and dyslipidemia appear to be primarily determined by their ponderosity, rather than by the severity of SDB.

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0319.G

Sleep Characteristics In Children With ADHD And Other Psychiatric Disorders Referred To A Pediatric Sleep Medicine Center

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Introduction: The primary goal of the present study was to compare parental reports of sleep problems and polysomnographic findings of pre-pubertal children formally diagnosed with ADHD to sleep characteristics of children with other psychiatric disorders (anxiety and mood disorders) referred to a pediatric sleep medicine center.
Methods: A retrospective, consecutive case-series examination of patients seen in the sleep medicine clinic was conducted. Parents of 120 pre-adolescent children with a DSM-IV diagnosis of ADHD (mean age: 7.8±2.2 years) provided information regarding their children's sleep patterns using a problem-based survey instrument. Sixty-five had a professional diagnosis of ADHD alone (ADHD group), 23 had ADHD with other psychiatric co-morbidities (ADHD/Psych group), and 32 were diagnosed with either anxiety or mood disorder (Psych group). Of the 120 children, 85 (ADHD-48; ADHD/Psych-18; Psych-19) underwent overnight polysomnography (PSG). Sleep data from 41 children with snoring, but no DSM-IV diagnosis, were used as a control group.

Results: Parents of children with ADHD reported more nocturnal awakenings ($p< 0.05$), daytime somnolence ($p<0.001$), and were more likely to view their children as having a sleep disturbance of moderate severity ($p< 0.01$) than the other two clinical groups. Parents of ADHD/Psych reported longer sleep latencies ($p< 0.05$) and more frequent leg jerks ($p< 0.05$) than the other two groups. However, no differences were identified between the groups on any of the PSG measures. When PSG measures among the three groups were compared to children evaluated for sleep-disordered breathing, PLMI was higher ($p< 0.01$) in all 3 groups.
Conclusions: Parental complaints of children with mood or anxiety psychiatric conditions evaluated at the sleep medicine center are similar to those of children with ADHD. The presence of psychiatric co-morbidities is not a contributing factor to the frequency of subjective sleep complaints among parents of children with ADHD referred to a sleep medicine center. However, PLMD is a frequent condition in this group of children.

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0320.G

Association Between Human Leukocyte Antigen (HLA) And Development Of Obstructive Sleep Apnea Syndrome (OSAS) In Infants

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Introduction: Adult studies have emphasized the role of HLA in OSAS (Internal Medicine 1993;32:94-97)however no data are available in childhood (Chest 1995;107:1545-51). In order to investigate the possible role of HLA in the development of OSAS in childhood, we assessed the HLA on a group of children with OSAS, and compared with the HLA frequencies in the population of our geographic area.
Methods: Between 1999 and 2001, we performed HLA analysis on 39 consecutive children[28 M (72%); median age of 3,7 (range 4 month to 10,6)] diagnosed as having OSAS; in all the diagnosis was based on nocturnal polygraphic monitoring (NPM) study. All presented excessive snoring, apnoeic episodes during sleep, oral breathing, daily sleepiness. The frequencies of HLA alleles in children with OSAS were then compared with the HLA frequencies in the Apulian population as assessed by the Apulian HLA Distribution Study (VII Meeting AIBT).
Results: We found that the frequency of HLA-DRB1*03, DQB1*02 and HLA-A33 antigens was markedly increased in the patient with OSAS compared with Apulian population (25.64% vs 12.8% , p=0.03; 46.15% vs. 29.08%, p=0.03 and 12.82% vs. 4.2%, p 0.02 respectively). We found no difference in the frequencies of HLA-B and –C among the two groups. When we divided children with OSAS in HLA-A33, -DRB1*03, -DQB1*02 positive and negative groups, we found no difference in terms of age, Body Mass Index (BMI), Apnoea Index (AI), Oxigen Desaturatin Index (ODI), atopy and smoking habits in the family.
Conclusions: Our study suggests that having an HLA-A33, HLA-DRB1*03 or HLA-DQB1*02 may increase the likelihood of having OSAS however further studies on larger series are needed to confirm this observation. The identification of sensible genetic markers for OSAS may be of great help in selecting children at risk for this condition to whom address an effective environmental and pharmacological prophylaxis.

0321.G

Home Literacy Environment, TV Viewing, And Sleep Hygiene In Children

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Introduction: Parental activities in the home are of great importance to early literacy development in children. In addition, restricted sleep and increased TV viewing could affect child development. The present study was undertaken to evaluate sleep habits and literacy environment of community children and to determine their relationship to each other.
Methods: Parents of children, ages 3- to- 8 years, enrolled in the Jefferson County Public School system completed a home literacy questionnaire (modified from the STIM Q Inventory), which included information on the sleep habits of the child. The literacy instrument contained information on four broad subscales: namely, environment (description of resources in home-e.g. books, crayons, scissors), language (resources stressing language skills), reading (resources stressing reading skills), and parental involvement (activities of literacy shared with parent and child). Higher scores indicate a more positive literacy environment.
Results: 374 questionnaires were available for analysis; mean age was 6.3±1.2 years; 212 were male (56.2%); and ethnic distribution was: C, 298 [79%]; AA, 57 [5.1%]; other 11 [2.9%]; unknown, 11 [2.9%]. Mean sleep duration was 9.2±1.4 hr per night, and TV viewing was 1.9 ±0.8 hr per day. Literacy subscales were as follows – environment: 11.9±2.6 (max. 15); language: 7.2±2.0 (max. 10); reading: 9.7±2.6 (max. 13); parental involvement: 16.5± 3.4 (max. 19). Positive correlations emerged between sleep time and all literacy subscales ($p<0.01$), while inverse correlations were found between TV viewing and environmental subscale ($p = 0.02$) and TV viewing and sleep time ($p = 0.02$). In AA, sleep time was shorter (8.5±1.8 vs. 9.4±1.3 hrs in C; p =0 .0001), and TV viewing was longer (2.3±0.9 vs. 1.8±0.7 hrs in C; p =0 .002). AA and C had similar literacy subscales except for environment (C = 12.4±2.2 vs. AA = 9.5±3.3, $p < 0.0001$), and the latter accounted for most of the disparities in total sleeping time, and to a lesser extent in the duration of TV viewing.
Conclusions: Home literacy in general, and more particularly environmental literacy resources (books, crayons, puzzles, etc.) are a major determinant of sleep hygiene and TV viewing in children, the latter imposing a major detrimental effect on sleep duration. Ethnic-related disparities in sleep duration were primarily ascribable to the environmental subscale of home literacy. We postulate that improved parental education on home environment activities may not only ameliorate sleep hygiene, but may ultimately lead to improved literacy skills in their children.

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0322.G

The Significance of CSF Hypocretin-1 (Orexin-A) Measurement in Pediatric and Adolescent Neurologic Disorders

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Introduction: Narcolepsy and other sleep problems are under-recognized in children and the final diagnosis and initiation of treatment is often delayed. This is partially due to the fact that the expression of the sleep-related symptoms in children is often different from those in adults. Hypersomnia is often expressed as a behavioral hyperactivity and/or deficient attention in children. Furthermore, polysomnographical

examinations are generally difficult to perform in children, and the interpretation of the results is often difficult (especially for diagnostic purposes). An establishment of a specific diagnostic tool for sleep disorders in children would thus be an urgent issue. Recent CSF hypocretin-1 measurements and postmortem studies in narcolepsy suggest that hypocretin deficiency is the major pathophysiology of the disease. CSF hypocretin-1 in various neurologic and sleep disorders in adults further demonstrated that low CSF hypocretin-1 levels are highly specific to narcolepsy, and the CSF hypocretin measures are now being established as a new diagnostic tool. In this study, we studied CSF hypocretin-1 levels in 105 children with narcolepsy and various neurologic disorders, in order to determine the diagnostic values of low CSF hypocretin levels of narcolepsy in children.

Methods: CSF samples were collected from patients under 19 years of age with 1) neurologic diseases common to all generations: narcolepsy (n=6), other sleep disorders (n=5), CNS infection (n=10), post-infectious encephalo/radiculo pathy (n=17) such as Guillain Barre syndrome (GBS) and acute disseminated encephalomyelitis (ADEM), head trauma (n=3), brain tumor (n=3), malignancy without CNS invasion (n=13), and psychological problems (n=3). 2) neurologic diseases mainly observed in children: CNS malformation (n=4), systemic disorder (n=4), epilepsy or mental retardation (n=13), perinatal trauma or asphyxia (n=6), metabolic disease (n=5), subacute sclerosing panencephalitis (SSPE) (n=2), epileptic encephalopathy (n=3), motor unit disease (n=4), cerebral hypertension (n=2), and transient conditions (n=2). CSF hypocretin-1 was measured in the crude CSF without extraction using commercially available radioimmunoassay (RIA) kits (Phoenix Pharmaceuticals). Intra-assay variability of the RIA was 4.3% and detection limit was 40pg/ml. We used the cut-off of 110pg/ml as abnormally low, and values above 200pg/ml were considered normal as described by Mignot et al (2002).

Results: In 80 subjects out of 105, hypocretin-1 was in the normal range (>200pg/ml). All subjects with narcolepsy-cataplexy showed low hypocretin-1 levels (<110pg/ml). Besides narcolepsy, we found 7 subjects who belong to 4 neurologic categories that had low hypocretin-1 levels. The results that low hypocretin levels in the GBS, headtrauma and brain tumor were consistent with the finding previously reported in the adults. Two low cases with SSPE were under intrathecal interferon-alpha therapy (Ogawa 2003) and the influence of the treatment on CSF hypocretin levels should be further examined. An ADEM case with hypersomnia (Kubota 2002), 1 out of 7 cases had low level. Intermediate hypocretin-1 levels (between 110-200 pg/ml) were found cases with Niemann-Pick type C (1 out of 2), Prader-Willi syndrome (1 out of 1) and birth trauma (2 out of 3).

Conclusions: Abnormally low hypocretin-1 levels are specific for narcolepsy-cataplexy. Although some neurologic disorders showed low hypocretin-1 levels (as seen in GBS, ADEM, SSPE, head trauma and brain tumor), clinical symptoms of these disease are different from narcolepsy, and the findings do not confound the diagnostic value of CSF hypocretin measures for narcolepsy. A measurement of hypocretin-1 level is useful diagnostic tool in pediatric narcolepsy especially when other diagnostic information is not sufficient. The role of low hypocretin levels in neurologic conditions such as ADEM, Niemann-Pick type C and Prader-Willi syndrome C in relationship to the occurrence of EDS and cataplexy should further be studied.

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0323.G

Sleep-Related Childhood Crying in Japan

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Introduction: In Japan, sleep-related childhood crying (SRCC) has been very often observed and parents become exhausted because of insufficient sleep. Difficulty produced by full awakening and of prompt return to sleep after awakening at night can cause sleep-related problems in infancy and early childhood. The background mechanisms of this kind of sleep disorder and appropriate and effective suggestions for the parents remain unsolved. Therefore, the present study aimed to examine the factors involved in SRCC.

Methods: Subjects were parents of 170 infants (3-6 months of age: group A), 174 toddlers (1 year 6-9months of age: group B) and 137 children (3 years 0-5 months of age: group C). We made a survey on SRCC using our questionnaire which parents filled out at well baby clinic held at public health centers. Our questionnaire includes childcare methods, sleep-wake cycle and sleep environment. We defined SRCC as unexplained crying during night on a daily basis. Colic was also defined as unexplained crying in the evening or crying for estimated more than 3 hours in a daytime. We asked them to fill in the answer sheets.

Results: The frequency of SRCC was the same in boys and girls. The incidence of SRCC till the age of group A, B and C was 18.8, 64.9, 59.9%, respectively. In group A, colic was seen in 4.1% of infants and only 2 infants had both colic and SRCC. Eighty-four% of SRCC disappeared in group C. In group B, bedtime irregularity seemed to be associated with more SRCC compared with that of regularity. In group C, children who sleep stable hours of 9.5-10.5 had less SRCC than those of longer or shorter sleepers. Late bedtime hours and the way of taking nap were not related with SRCC. Infants who bedshare or co-sleep with parents had more SRCC than infants who sleep alone in group A. In group B, Children who are taken care of at daycare had more SRCC than non-users of daycare. Moreover, children whose parents considered as crybabies had more SRCC than non-crybabies in group B. In group B and C, children with bruxism show more SRCC than those without it. The other factors such as usage of sleep aids and nursing arrangements were not statistically significant of incidence of SRCC.

Conclusions: Colic has no relation with SRCC and the occurrence was low in Japan as compared with Western countries. Sleeping through the night in the Western countries could be similar to sleep without SRCC in Japan. We speculate SRCC is caused by immature or inappropriate sleep-wake rhythm based on the present study. Daytime stress may be another candidate of SRCC because of the presence of frequent bruxism in daycare users. We also suggest that Japanese custom of infant fs co-sleeping with their parents increase the incidence of SRCC.

0324.G

Levels of Hypocretin-1 (Orexin A) in the Cerebrospinal Fluid of Two Young Hypersomniacs Suspected of Being Narcoleptic

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Introduction: It has been reported that the level of cerebrospinal fluid (CSF) hypocretin-1 or orexin A is low in subjects with narcolepsy. It is important to clarify the relationship between the CSF level of hypocretin-1 and a variant of hypersomnia. A recently reported case of childhood-onset narcolepsy manifested a low level of CSF hypocretin-1 when cataplexy appeared. In this study, we measured the level of CSF hypocretin-1 in two young hypersomniacs suspected of being narcoleptic: one subject was a childhood-onset hypersomniac, while the other was an adolescence-onset hypersomniac.CASE 1: 9-year-old male (138 cm; 33 kg; HLA-DR2 positive).The subjectÕs excessive daytime sleepiness (EDS) was noticed at home and at school ca. 6 months prior to con-

sultation at our outpatient clinic. The patient often fell due to muscle atonia. A pediatrician was consulted, but identified no decrement of muscle strength. At the same time that the patient began to suffer from EDS, his family members noticed an increased appetite and a weight gain of 5 kg. A polysomnogram (PSG) was attempted, although recording could not be continued longer than 4 hours due to the subjectÕs restlessness. Although the PSG did not demonstrate sleep-onset REM period (SOREMP), a multiple sleep latency test (MSLT) demonstrated 5 SOREMPs occurring over the 5 MSLT sessions. CASE 2: 16-year-old male (161 cm; 51 kg; HLA-DR2 negative).When this patient entered high school student, he began to experience EDS. He often fell asleep while traveling by train to school. During PSG, no SOREMP was observed, although SOREMPs were identified in 4 of the 5 MSLT sessions. Neither increased appetite nor weight gain were noted.

Methods: After receiving informed consent from the patients and their parents, we obtained CSF samples from each patient. The samples were stored at -80°C until use. The concentration of hypocretin-1 in the CSF samples was measured by use of a radioimmunoassay kit (Phoenix Pharmaceuticals).

Results: In the sample from CASE 1, the concentration of hypocretin-1 was under the detection limit (40 pg/ml). In the sample from CASE 2, the concentration of hypocretin-1 was 288 pg/ml, which was within normal limits.

Conclusions: In each of these two cases, EDS occurred in the form of sleep attack. In accordance with the guidelines established by the Diagnostic Classification Steering Committee, 1990, these cases could be diagnosed as narcolepsy. However, Case 2 was demonstrated to be HLA-DR2 negative, and experienced no episodes of cataplexy. Furthermore, neither increased appetite nor weight gain were observed. Lastly, there was no decrement in the CSF level of hypocretin-1. Based on these features, which were different from those of Case 1, we infer that Case 2 represents a form of hypersomnia totally different from that of Case 1. We suggest that a decreased hypocretin-1 CSF level is a critical marker for the diagnosis and treatment of narcolepsy. In addition, we suggest that increased appetite and weight gain are also reliable indices for the diagnosis of narcolepsy.

0325.G

Rapid Eye Movements Density Within Active Sleep In Former Iron Deficient Anemic Children Is Most Affected At The End Of The Night

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Introduction: Iron deficiency anemia (IDA) in infancy alters the organization of several sleep-wake patterns. It is also associated with long-lasting behavioral, neurofunctional and cognitive effects, despite the correction of hematological variables after treatment (Algarín C et al: Long-lasting effects of iron deficiency anemia in infancy on auditory and visual system functioning. Pediatr Res, 2003, in press). Therefore, it is conceivable that long-term disruption of sleep patterns in former IDA children may be apparent as well. In fact, we previously reported that the density of REMs within AS is reduced in former IDA (FIDA) children. In this study we evaluated whether this AS characteristic in former IDA children prevails in a specific portion of the night.

Methods: In a prospective long-term follow-up of a randomized controlled trial of IDA prevention in infancy, we performed all-night polysomnographic recordings at the age of 4.5 years in a group of FIDA children (n=24) 3 years after the correction of all hematologic variables, and in a group of nonanemic matched controls (n=24). Sleep-wake states were determined by combining usual EEG, EOG and EMG criteria. The EOG signal of all AS episodes was processed off-line using an automated system that detects the beginning and end of each REM, and REMs were separated in isolated and non-isolated (at least 2 separated by no more than 0.5 sec). For each individual child the corresponding sleep episode was divided in thirds, and the following REMs parameters within AS were determined for the 1st, 2nd and 3rd thirds: (a) index (number/min) of isolated and (b) non-isolated REMs; (c) mean duration of isolated and (d) non-isolated REMs; (e) mean duration of intervals between isolated and (f) non-isolated REMs.

Results: In FIDA children the index of isolated REMs was lower in the 1st and 3rd thirds ($p < .04$ and $< .0007$, respectively); the same was also true for the index of non-isolated REMs in the 3rd third ($p < .007$). Duration of both isolated and non-isolated REMs was similar in both groups. In the last third the intervals between isolated REMs were significantly shorter in FIDA children ($p < .01$), whereas the intervals between non-isolated REMs tended to be longer in controls ($p < .08$).

Conclusions: Our results show that the reduction in the density of REMs within AS in FIDA children is more evident in the last third of the night. They also emphasize that IDA in infancy is associated with long-lasting effects on sleep organization, and support the role of iron in the temporal patterning of AS phasic events. Finally, the prevalence of between-group differences in the last portion of the night, might indicate that early IDA affects the developmental consolidation of AS .

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0326.G

Cyclic Alternating Pattern In Obstructive Sleep Apnea Children

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Introduction: Sleep maintains an oscillating pattern reflecting different levels of arousal during NREM, coded as cyclic alternating pattern (CAP) by Terzano. Several studies analyzed its role in different pathologies such as sleep apnea, insomnia, epilepsy, etc., mainly in adults. Because only few studies are available on CAP in normal and pathologic children, we analyzed CAP in children with obstructive sleep apnea (OSA).

Methods: Nine children (5 M, 4 F, mean age 7.1 yrs) with OSA evaluated by polysomnography were included and compared to 10 healthy age-matched subjects (6 M, 4 F, mean age 8.3 yrs; t= 1.39; NS). All subjects underwent polysomnography recordings for two consecutive nights in a standard laboratory setting using a digital system. Sleep macrostructure was visually scored according to the R&K criteria and CAP was visually scored following the criteria by Terzano et al.

Results: In normal children, CAP rate showed a progressive increase with deepness of sleep. A1 CAP subtypes were the most numerous (84.45%) followed by A3 (9.14%) and by A2 (6.44%). The OSA children showed a mean apnea-hypopnea index (AHI) of 20.36 (range 7.4-50.7) and their mean SaO2 was 96.48 (range 93.1-98.6); mean duration of apneas was 14.7 s (range 7.7-19.8). No differences in macrostructural parameters and in CAP rate were found between OSA and normal children. The percentage of A1 was significantly reduced and A2% and A3% increased; arousal index was augmented (table 1). A1 index (number of A1 per hour of NREM) in Stage2 was reduced (23.67 vs. 40.07; $p < 0.0005$) while A2 index in Stage2 was increased (16.26 vs. 3.74; $p < 0.0005$). CAP duration showed a positive relationship with number of apneas (r=0.71), AHI (r=0.78) and mean duration of apneas (r=0.86). Also, the duration of B phases correlated with AHI (r=0.80), and mean duration of apneas (r=0.91). A1 index in NREM negatively correlated with AHI in NREM (r=*f*{0.72) and with the mean duration of apneas (r=*f*{0.87). Table 1.

	Control		OSA	
	Mean	SD	Mean	SD
p <CAP rate	33.43	5.27	29.99	7.212
NSA1%	84.45	3.39	56.42	

12.89	0.001	A2%	6.44	1.83	27.38	13.46
0.001	A3%	9.14	3.93	16.20	13.62	N S C A P
rate A1	39.54	6.39	28.79	13.95	0.05	CAP rate A2
2.66	0.96	11.31	7.02	0.001	CAP rate A3	3.30
1.90	5.73	4.40	NS	Arousal index NREM		8.69
2.03	24.15	8.33	0.001	Arousal index REM		4.18
2.57	15.14	11.92	0.01	Phase A mean duration		6.28
0.64	6.81	1.10	NS	Phase B mean duration		24.68
1.10	21.14	2.24	0.001			

Conclusions: Our study shows that, although no significant differences between control and OSA children in macrostructural parameters were found, CAP analysis was able to reveal important differences in microstructural sleep parameters.

0327.G

Prevalence, Evolution And Associations Between Various Parasomnias In Early Childhood

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Introduction: To our knowledge, no epidemiological research has studied simultaneously various parasomnias in early childhood in a prospective and longitudinal way. Our aims were to show the prevalence of various parasomnias at around 1½, 2½ and 3½ years of age, to describe their evolution and to measure the associations between various parasomnias at 3½ years of age.
Methods: Longitudinal data on 1839 children were collected by questionnaires and interviews. Parasomnias were classified into "presence" (sometimes, often or always) or "absence" (never) according to the mother's opinion. Night terrors, body rocking and teeth grinding were studied at around 1½, 2½ and 3½ years of age whereas sleepwalking, sleeptalking and nightmares were evaluated at 2½ and 3½ years of age. McNemar tests were performed to determine the evolution of parasomnias from 1½ and 2½ years of age (first transition) and from 2½ to 3½ years of age (second transition). Contingency coefficients were used to represent the strength of the associations between parasomnias. The associations were considered significant at $p<0.002$ (Bonferroni correction).
Results: At 2½ and 3½ years of age, some parasomnias had a high prevalence (at least occasionally) such as sleeptalking (46.4%; 53.0%) and nightmares (64.6%; 67.2%) whereas others parasomnias had a low prevalence, i.e. sleepwalking (3.8%; 2.6%) and body rocking (3.2%) at 3½ years of age. However, the prevalences at 2½ and 3½ years of age of frequent (often and always) sleeptalking were 2.9% and 3.7% and frequent nightmares were 2.4% and 3.2%. Teeth grinding and sleeptalking increased significantly for both transitions ($p<0.0001$) whereas body rocking decreased significantly for both transitions ($p<0.0001$). The percentage of children having night terrors decreased significantly ($p<0.0001$) during the first transition and remained stable between 2½ and 3½ years of age. Significant (albeit weak) associations were found for sleeptalking and nightmares (0.26), night terrors (0.16), teeth grinding (.10) and sleepwalking (.08). Night terrors were also significantly associated with nightmares (.28), teeth grinding (0.09) and sleepwalking (0.08).
Conclusions: Our results show that occasional sleeptalking and nightmares are highly prevalent in early childhood. The parasomnias studied did not have the same evolution through time. In addition, parasomnias seem to manifest themselves in clusters, except for body rocking which did not show an association with any other parasomnia.

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0328.G

Sleep EEG Topography In Human Infants

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Introduction: The analysis of regional characteristics in EEG power spectra of baseline sleep in adults demonstrated that antero-posterior gradients are not homogenous, but exhibit site-specific and state-related changes in different frequency bands. In the first nonREM sleep episode, power in the 2-Hz band was highest in the anterior derivation; over the subsequent episodes, the anterior predominance of power declined and eventually vanished. In infants, however, topographical aspects of the EEG during sleep have not been studied in detail.
Methods: Investigations of longitudinal all-night home sleep recordings in 5 healthy full-term infants at 2 weeks, and then at 2, 4, 6, and 9 months after birth were performed. Sleep stages (quiet sleep, QS; active sleep, AS) were scored for 20s epochs (derivation C3A2) according to standard criteria for infant sleep. EEG power spectra of anterior (F4C4) and posterior (P4O2) derivations were computed.
Results: The typical declining trend of EEG power with increasing frequency as well as frequency-specific, state-dependent modulations of power in the course of the sleep episode were common features in both the anterior and the posterior derivation. In addition, topographic differences were observed in a broad frequency range. Between 4 and 9 months of age low delta activity in QS (EEG power < 2 Hz) showed high levels only in every second QS episode and predominated over posterior regions. In contrast, power in the theta band (6.5 - 9 Hz) showed a monotonic decline in the course of the night from 2 months onwards. Theta activity was higher in anterior derivations at the ages 2 weeks and 2 and 9 months. Sleep spindles emerged before the age of 2 months and their quantitative EEG measure, sigma activity (12 - 15 Hz), exhibited a marked anterior predominance at all ages form 2 months onwards. Antero-posterior gradients in the low delta, theta and sigma band did not change in the course of the sleep episode. Before the age of 4 months, an anterior predominance of power over broad frequency ranges was observed in both AS and QS.
Conclusions: Regional differences in the sleep EEG of human infants indicate that sleep during ontogeny is not only a global process, but in addition exhibits local phenomena involving different areas of the developing brain. In contrast to adults, the low delta band showed a posterior predominance between 4 and 9 months, whereas theta activity was highest in anterior regions at the age of 9 months. These frequency-specific topographic features may reflect their different functional significance in the sleep process.

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0329.G

Late In and Out of Bed in Teenagers: Delayed Sleep Phase Syndrome, Sleep Hygiene or Other Sleep Disorders?

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Introduction: Surveys of large teenage populations have revealed that sleep disorders often occur in this age category. In particular complaints about late sleeponset and too short duration of sleep are frequently

heard. The disorder sometimes has disastrous influence on social life. Lifestyle (sleephygiene) is mentioned as its main cause, but delayed sleep phase syndrome (DSPS) is another possibility. Details on sleep and behaviour in such teenagers are not well known and were the objective of this decriptive study

Methods: Thirty-one patients with major implications of persistent late sleeponset and tiredness in the morning, consecutively seen in our center over a period of 2.5 years, were systematically asked about sleep and behaviour and underwent polysomnography (PSG). The disorder had to have started before the age of 15. At the moment of study 9 patients were 10-13 yrs old (group 1), 10 14-16 yrs (group 2) and 12 17-21 yrs old (group 3).

Results: The mean duration of the disorder in the 3 age categories was respectively 7.5, 7.1 and 11.5 yrs. In 16 patients the first symptoms occurred before the age of 5. Compared to normal children in the Netherlands, the median bedtimes were late: 10 p.m. for group 1, 11 p.m. for group 2 and 1.15 a.m. for group 3. Patients in both younger categories came out of bed early as dictated by their school regime. The eldest category had a median out of bed time of 11 a.m. Seventeen children indicated their sleep quality as satisfactory or better. Children in group 1 had a long sleep onset latency(SOLAT: median 74 min; range up to 269 min) in contrast to the patients in groups 2 and 3 with median SOLATs of 25 and 16 min. Obviously, patients in the latter two categories have learnt that early bedtimes are contraproductive and have long SOLAT as a consequence. The other parameters of sleep as measured from the PSG (sleep efficiency, REM and NREM parameters, WASO, awakenings and number of sleep cycli) were within normal values. Temperature curves were available for 23 patients. In 8 of these patients a late nadir suggested a DSPS. The final diagnoses were insomnia due to aberrant sleep hygiene in 7, DSPS or free running rhythm in 17, psychophysiological insomnia in 3 and misperception in 4 patients. Treatment was tailored to the diagnosis and needs of the patient and was succesful in about half of the cases.

Conclusions: Teenagers are prone to sleep/wake rhythms that are socially unacceptable. The disorder often starts before the age of 5. As there are various diagnoses behind the aberrant behaviour, careful work-up and treatment tailored to the diagnosis is important

0330.G

Periodic Limb Movement Disorder in Children and Adolescents: Accuracy of Clinical History

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Introduction: This study is a preliminary examination of whether symptoms reported in a questionnaire or clinical history are related to periodic limb movement disorder (PLMD) as diagnosed by nocturnal polysomnography (PSG). The accuracy of the clinical diagnosis of PLMD in children and adolescents has not been previously examined, but if determined to be related, may reduce the need for PSG.

Methods: 16 subjects (12 boys and 4 girls), ages 7-18 years (mean age = 11.6, standard deviation = 4.3), were seen in a pediatric sleep disorders specialty clinic. Eight subjects were diagnosed with PLMD based on PSG findings. The remaining eight subjects, matched for age and sex, were used as controls. Data were collected from existing records and included (1) an intake questionnaire completed by parents; (2) the clinical history as reported by the primary clinician; and (3) patient's PSG findings that document the presence/absence of PLMD. Six parental reported symptoms of PLMD were examined (restless sleep, kicks legs during sleep, wakes up at night, trouble waking in the morning, daytime sleepiness, and ADHD).

Results: Correlation analyses were conducted to examine the relationship between both questionnaire (Q) and clinical history (CH) reported symptoms and the periodic limb movement index score from the PSG. No significant relationships were found (*restless sleep* rsQs = .13, rsCHs = .45; *kicks legs* rsQs = .14, \underrsCHs = -.33; wakes at night \underrsQs = -.05, rsCHs = -.39; *trouble waking in AM* rsQs = .12, rsCHs = .26; *daytime sleepiness* rsQs = -.13, rsCHs = -.23; *ADHD* rsQs = .31, \underrsCHs = .33). Chi-square analyses also demonstrated no significant differences in reported symptoms between subjects who were and were not diagnosed with PLMD (*restless sleep*: PLMD 86%, No PLMD 57%; *kicks legs*: PLMD 83%, No PLMD 40%; *wakes at night*: PLMD 100%, No PLMD 83%; *trouble waking in AM*: PLMD 88%, No PLMD 63%; *daytime sleepiness*: PLMD 71%, No PLMD 88%; *ADHD*: PLMD 38%, No PLMD 25%).

Conclusions: This pilot study provides little evidence of a relationship between parental reported symptoms of PLMD and objective findings based on PSG. This suggests the importance of utilizing PSG findings for the diagnosis of PLMD. Unlike symptoms of obstructive sleep apnea that are easily observed (e.g., snoring, pauses in breathing), parents may not be aware of the symptoms of PLMD (e.g., leg kicking, restless sleep). In addition, due to the age of our sample (mean 11.6), parents are likely less involved with their child's sleep than parents of younger children. Finally, this study was significantly limited by a small sample size. Future studies should continue to examine the relationship between symptoms reported by questionnaire, in a clinical interview, and through PSG, using larger samples, helping to determine the need of using PSG as a diagnostic tool for this disorder.

0331.G

Sleep Of Children With Frequent Nightmares : A Preliminary Study

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Introduction: Although they frequently complain of sleep problems, very few polysomnographic studies of nightmare sufferers have been published. Hartmann (1984) reported no sleep abnormalities, whereas Newell, et al. (1992) reported reductions in total sleep time and slow wave sleep and more night awakenings. Recently, Germain and Nielsen (2001) observed no difference between sleep variables of adult idiopathic nightmares sufferers compared to control participants. We report here on a first study of prepubertal children with frequent nightmares.

Methods: Twelve children aged between 9 to 11 spent a single night in the laboratory with polysomnographic and infrared camera. Six children had moderate to severe nightmares without PTSD and six children were free of nightmares. Four of the six nightmare sufferers were in the first few weeks of an 8 weeks imagery rehearsal treatment. A basic montage of nine electrodes was applied (EMG, EOG, EEG). Sleep was scored following Rechschaffen and Kales (1968) criterias. The following sleep variables were examined : TST, WBS, SOL, WASO, sleep efficiency, REM latency, REM density, REM efficacy, absolute and relative time in the stages. The number of sleep positions, postural immobility period and the trunk position were scored from the video recordings. No children reported experiencing a nightmare in the laboratory.

Results: T-tests revealed no significant difference between the groups for TST, WBS, SOL, WASO, and sleep efficiency. Also, their was no significant difference between groups for REM latency, REM density, absolute and relative time in REM. Separate ANOVAs for the absolute time in each sleep stages across thirds of the night revealed no significant differences between groups, except for the stage 4 ($F(1,10)=5.57$, $p<0.04$). Children with nightmares spent less minutes in total in stage 4 than children without nightmares. Moreover, no significant difference was observed between the groups for the number of position adopted, although children with nightmares had fewer trunk position changes than the control group ($t(10)=2.80$, $p<0.02$). No trunk position was preferred by neither one of the groups. Although statistical comparisons could not be made between the nightmare sufferers who had begun treatment and those who had not, no trends could be detected suggesting that the treatment has not affected their sleep patterns.

Conclusions: These results are consistent with previous findings with

adults (Germain & Nielsen, 2001; Hartmann, 1984). Sleep electrophysiology and sleep positions of children with frequent nightmares do not seem to present any abnormality on nights without nightmares when compared with control children. The lower level of stage 4 is consistent with the findings of Newell et al. (1992), but it was the only difference observed and would not seem to be related to nightmares since they typically occurs in late REM periods. It is still possible that the beginning of treatment in four of our six nightmare sufferers could have resolve any prior sleep problems. Finally, the laboratory situation might have affected positively their sleep. A larger sample with more nights of recording would be required to test these interpretations.

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0332.G

Sleep, Vagal Regulation, and Risk Outcomes for Children Exposed to Marital Conflict

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Introduction: While marital conflict, and disrupted parenting have been identified as risk factors for negative outcomes in children, the processes responsible for these outcomes are less well understood. Although emotion regulation has been identified as one process that moderates these outcomes (El-Sheikh, 2001), sleep has not been studied in this context. As a beginning to test an integrated conceptual model we have developed incorporating emotion regulation (Cummings & Davies, 1996; Porges, 1998), and the relation of sleep regulation to arousal, emotion regulation, and development (Carskadon & Acebo, 2002; Dahl, 1996), children's sleep, emotional reactivity, and vagal regulation, were measured along with family risk variables and child outcomes.
Methods: Sleep was actigraphically monitored for 44 children (M 9yrs.), and parents and/or children completed: Sleep Habits Survey; Sleep/Wake Diary; Marital Conflict Tactics Scale; Personality Inventory for Children; Cornell Medical Index, RAND; Childhood Behavior Questionnaire; Children's Perceptions of Interparental Conflict Scale; Parent-Child Conflict Tactics Scale; Woodcock-Johnson Tests of Cognitive Ability; 2 computer-administered reaction time tasks. Children also had vagal tone and skin conductance (SCL) assessed while performing a cognitive task and listening to an argument between two adults in a well–established laboratory paradigm (El-Sheikh, 2001).
Results: 1. Marital and parent-child conflict were related to children's adjustment and health problems, and to cognitive functioning. 2. Reported sleep problems were associated with many family conflict and child variables, e.g. children's depression (.50) and anxiety (.38), social (.37) and cognitive (.32) problems, anger (.43), emotion regulation (-.33), health problems (.37), and reaction time (.43). 3. Numerous actigraphic variables were related to many risk variables e.g., marital and parent-child conflict, and children's anger, externalizing and internalizing problems, and cognitive performance (.32-.49). Sleep efficiency was associated with parent-child conflict (-.34), health (.40), variability (-.37) and speed (-.51) on reaction time tasks. 4. Sleep variables were also associated with children's emotionality and regulation (anger, vagal suppression, SCL). Sleep efficiency was associated with lower SCL reactivity to the cognitive task (-.35), while sleep latency was related to lower vagal suppression both to the cognitive task (-.34), and the argument (.50), and higher SCL reactivity to the cognitive task (.45). Sleep movement and fragmentation was associated with lower vagal suppression during the cognitive task (-.37) and the argument (boys,-.63); and higher levels of resting SCL (.37), and SCL reactivity (.34) to the cognitive task.
Conclusions: While these results are preliminary, and full tests of mediation or moderation roles for sleep in the well-established link between marital conflict and negative child outcomes must be done with larger samples, the results suggest that understanding how sleep relates to emotion regulation may help elucidate processes involved in risks posed to children by marital conflict.

0333.G

Mouth Breather Children Presents a Similar Cephalometric Pattern Observed in OSAS Adults Patients

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Introduction: Mouth breathing during childhood is responsible for a sequence of events that commonly result in alterations of maxilo-mandibular growth and development, contributing to the appearance of sleep disordered breathing during childhood, specially the Obstructive Sleep Apnea Syndrome (OSAS). Many studies have shown a connection between the anatomical constitution of upper airway in mouth breather(MB) patients and alterations of craniofacial morphology. Objective: To analyze cephalometric studies between mouth and nasal breather(NB) children and also compare the craniofacial pattern similarities of MB patients with that of apnea patients .
Methods: It was analyzed the standing lateral skull radiograph of 23 MB children (13 boys) aged 5 to 14 years (mean 8.1 years) to determinate angular and linear craniofacial measures and upper airway dimensions. We compared the cephalometric patterns of our patients with those found in OSAS patients, and to values observed in 10 NB children (5 boys/ mean 10.4 years). We measured the following parameters: A-Nperp, Pog-Nperp, PAS, C3-H, Mandibular Angulation (FH-MP) and Facial Axis Angle(Ba-PTM-Gn). We called apnea cephalometric pattern, if the patients have at least four altered measures characteristic of OSAS. Statistical analysis was based on t-Test or Fisher Exact Test.
Results: : The majority of our MB children presented abnormal cephalometric values ensuing a reduced Upper Pharyngeal Airway Space. The apnea cephalometric pattern was observed in 15 MB patients (65.21%) and in none of the NB patients ($p<0.001$).Mean and standart measurements were as following for MB and NB patients respectively: A-Nperp= -0.5mm $\pm$ 3.1; 2.4mm $\pm$ 3.8; p=0.05, Pog-Nperp= -8.6mm $\pm$ 5.6; -4.8 $\pm$ 4.6; p=0.05, Mand-Plan-Angle = 30º $\pm$ 6.5º; 25.3 $\pm$ 3.6; p=0.01, Facial-axis-angle= -4.2º +-4.7; -0.1 $\pm$ 1.8; p=0.001, Up-Pharyn-Space= 6.2mm $\pm$ 1.6; 10.9mm $\pm$ 3.5; p=0.002, PAS=10mm $\pm$ 3.9 11.4mm $\pm$ 3.0; p=0.28 and C3=32.9mm $\pm$ 3.1; 33.5mm $\pm$ 2.5; p=0.57. There were no difference between MB and NB regarding the distance hyoid bone to C3.
Conclusions: Mouth breather children showed Upper Pharyngeal Airway Space decreased, and more than a half presented the cephalometric pattern of OSAS.

0334.G

Sleep Habits in Brazilian Children 7 to 10 Years Old

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Introduction: Cultural differences influence sleep habits considerably and sleep patterns in the childhood vary with the age, and some normal or abnormal behaviors are age-dependent, associated to some limits imposed by the social activity, especially the school. This study analyzes sleep habits in Brazilian children and focus the influence of school period (morning or afternoon) adopted in Brazil for children`s basic education.
Methods: The sleep pattern of 2,482 children (7 to 10 years old), of 9 public schools from São Paulo city, Brazil, was evaluated. All children received a sleep questionnaire to assess sleep habits and sleep disorders

(SD). The questionnaire was answered by the parents, and children without SD were included according to the criteria of the test (Bruni et al, 1996). We analyzed the prevalence of naps, use of transitional object, rituals before sleep, room sharing, feeding before sleeping and total sleep time (TST) according to sex, age (7, 8, 9 and 10 years) and school period (morning and afternoon).
Results: Fifty two were female and 48% were male. Seventeen per cent presented naps, being more prevalente among children that study in the morning ($p< 0,001$). Sixty one percent presented some rituals before sleeping, 41% drunk milk, 28% needed brightness and 13% used transitional object, 2,3% presented the three rituals. Mean TST was 10 hours and 25min, 91% had TST above 8 hours and 8,4% less than 8 hours. Children studding in the morning presented smaller TST ($p< 0.001$) and more naps than children studding in the afternoon. The rituals to sleep decreased with the age.
Conclusions: Our data showed that some sleep habits like feeding at bedtime, a lit bedroom, and transitional object decrease with the age as expected and also showed that school period (morning and afternoon) has a definite influence on TST and napping of 1st grade students in Brazil.

0335.G

Parental Sleep Complaints Among Children With Psychiatric Disorders

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Introduction: Sleep problems are highly prevalent across the lifespan and there is substantial evidence indicating a relationship between sleep problems and psychiatric illness in adults. However, little is known about the prevalence of sleep problems in children with emotional and behavioral disturbances, and more specifically whether any particular psychiatric disorder carries a high sleep morbidity.
Methods: To examine these issues, parents of 174 children (mean age = 10.5±3.6 years) attending a child psychiatric outpatient clinic completed a 47-item Childhood Sleep Questionnaire for assessment of sleep-related behaviors and perceived sleep problems. Frequency of occurrence for any item was coded on a likert scale from 1 to 4, with 1 = never present and 4 = always present. A retrospective review of psychiatric records was conducted to obtain the psychiatric diagnoses for the children whose parents participated in the study. Respondents were divided into 4 diagnostic categories: ADHD alone (n=29), ADHD with other psychiatric comorbidities, such as mood and anxiety disorders (ADHD+; n=50), mood and anxiety disorders alone (MAnx; n=67), and other psychiatric disorders, e.g., adjustment disorder, autism (OT; n= 28). Chi Square analysis and one-way ANOVA were used to compare parental responses between the groups with a statistical significance set at $p< 0.05$.
Results: For the whole cohort, a high frequency of sleep problems (sometimes, often or always) was noted for: delayed sleep onset (25.3%), nocturnal awakenings (85.6%), bedwetting (27%), restless sleep (67.8%), leg jerks (57.5%), daytime sleepiness (66.7%), fears of dark (49.4%), bedtime refusal (62.6%), struggles at bedtime (64.4%), and snoring (55.7%). The ADHD+ group had more frequent nocturnal awakenings than the ADHD group ($p< 0.04$) and than OT ($p<0.001$), more bad dreams ($p<0.04$) than OT, and more frequent bed refusals ($p<0.003$) than the MAnx group. Leg jerks were more likely to occur in children in the ADHD and ADHD+ groups compared to children in the Manx group ($p<0.03$) and the OT group ($p<0.04$). Nighttime awakenings were similar in the ADHD+ and MAnx groups. However, more frequent nighttime awakenings were present in the MAnx group than in OT children ($p < 0.0001$). No differences were detected between the groups for any other sleep variable.
Conclusions: Sleep problems, as reported by parents, are highly prevalent among children with psychiatric disorders evaluated at an outpatient child psychiatric clinic. Of all children however, those with ADHD+ are more likely to report sleep disturbances. Objective assessments of sleep architecture are needed in these patient populations.

0336.G

Cognitive Dysfunction in Sleep Breathing Disorders Children

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Introduction: Because in Brazil we have less classroom than we need to teach our children, we have the morning (starting at 7:00AM) and afternoon (starting at 1:00PM) periods to accomplish 1st grade education. The relation between sleep disorders and learning problems has been observed in children that have bad quality of sleep, irregular hours to go to the bed and fatigue during the classes. Among the sleep disorders (SD), sleep breathing disorder (SBD) presents association with the cognitive performance, memory, attention, and visoconstructive ability. Objective: To evaluate the association between SBD and cognitive dysfunction (CD) in 7 to 10 years old children of public schools in São Paulo, Brazil.
Methods: We studied 1,180 children, 7 to 10 years old, from public Schools of Sao Paulo city, Brazil. Parents answered a sleep questionnaire adapted of Bruni et al (1996). We had three groups: SBD (79 children), nonrespiratory sleep disorders – NR (468 children), where we took out the SBD group, and a control group (CG) without SD (633 children). NR group included children with disorders of initiation and maintenance of sleep, sleep wake transition disorders, disorders of arousal and disorders of excessive somnolence. The diagnosis of CD was done throughout Bender Gestaltic Visomotor Test (BG). The data were analyzed throughout Logistic Regression for SBD in relation to the CG, taking in account periods (morning/afternoon) and grades (1st , 2nd , 3rd and 4th).
Results: The interaction between SBD and period (p=0,09), SBD and grades (p=0,08) showed more odds for CD. First grade children with SBD that study in the afternoon showed a odds for CD of 1.18 compared to those studding in the morning. For the other grades the odds for CD is greater for children studing in the morning: 3.69; 4.07; 3.41 for 2nd, 3rd, and 4th grades, respectively. The odds for CD for children with SBD studing in the morning is greater than the children without SD for 1st grades (8.04) and 3rd grades (1.39). Only the 1st grade children with SBD that study in the afternoon, present greater odds for CD in relation to the children without SD (2.92).
Conclusions: CD is associated to SBD and the time of the day and the grade play a role in that finding. The SBD analyzed with periods and grades, presents greater odds for CD. The odds for CD increase with the age when children are compared among the grades. When compared between the periods (morning and afternoon) the young children with SBD that study in the afternoon, presented more odds for CD than those studding in the morning, and the opposite was observed for the oldest children. When compared with the children that do not have SD, the 1st grade children with SBD that study in the morning or in the afternoon presented more odds for CD.

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0337.G

The Association Between the Conduction Time of the Brainstem Auditory Evoked Response (BAER) and Apnea Index in Preterm Infants

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Introduction: Previous study has shown the brainstem conduction time is longer in preterm infants who have apnea of prematurity. However, this study assessed only the prolonged apneas from apnea monitors without multi-channel polysomnographic evaluation. The association between short apnea and brainstem conduction time is currently unknown.
Methods: A retrospective review of overnight polysomonographic studies and BAER studies was performed in preterm infants. These tests were performed routinely in preterm infants at our nursery before discharge. The standard infant montage was performed with simultaneous monitoring of the following parameters; body position, left and right EOG, 3 channel EEG, chin EMG, thoracic and abdominal inductance plethysmography, nasal thermister, pulse oximetry and pulse wave form, end-tidal pCO2, transcutaneous pO2 and pCO2. Infants with neuromuscular, cardiac, lung or metabolic diseases were excluded from the study.
Results: Twenty seven preterm infants met the criteria for entry into the analysis. There was a significant difference between infants with apnea <15/hr (A) and infants with apnea >15/hr (B) in the interpeak latency of brainstem conduction time of BAER in the wave III and I interval (III-I) (T=2.07$\pm$0.42 [A] vs T= 2.56$\pm$0.36 [B], p=0.01) and wave V and I interval (V-I) (T=4.65$\pm$0.51 [A] vs T=5.21$\pm$0.55 [B], p=0.03). In addition, there was a significant correlation between III-I interpeak latency and apnea index (r=0.42, p=0.04) but no significant correlation between V-I interpeak latency and apnea index (r=0.31, p=NS)
Conclusions: It is concluded that the conduction time of BAER correlated with the number of apnea in preterm infants. It is further speculated that the immaturity of the brainstem center as indicated by brainstem conduction time may underlie an important pathophysiologic mechanism in the apnea of prematurity.

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0338.G

Activity And Sleep In Children With ADHD

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Introduction: Sleep deprivation, causing daytime malfunctioning, could lead to attention deficit hyperactivity disorder (ADHD)-like symptoms in normal children. Although sleep problems are often reported by parents to children with ADHD (CADHD), sleep studies of CADHD are scarce and show inconsistent results. We aimed to assess sleep patterns and daytime activity in CADHD investigated at home, and to study a probable causal relationship between sleep dysfunction and behavior.
Methods: CADHD (combined subtype - inattention and hyperactivity/impulsivity), with reported difficulties in falling asleep, were investigated and compared to healthy children. Studies were made at home. Children and parents gave their consent. The protocol was submitted to the ethical committee.Questionnaires about children's sleep habits/quality/daytime sleepiness were answered by children and parents. Sleep diaries were filled in during a two-week period. Motor activity (actigraphy) was continuously monitored during the same period. Sleep was studied two consecutive nights using sensor pad and pulse oxymeter. The signal was filtered to detect heart, respiratory and body movements, allowing activity-based sleep monitoring. Body movements were grouped according to duration. Polysomnography (16 channels plus sensor pad and oxymeter) was done another night, with questionnaires answered before and after each recording (daytime activity, sleep quality…). Axillary and peripheral (finger nail and plantar foot) temperatures were continuously measured.
Results: CADHD did not sleep enough according to the questionnaire answered by parents. Time in bed was 10-11 hours.Actigraphy: CADHD had increased daytime activity, with short periods of rest. Averaging activity of the two-week periods showed differences (P<0.009) between the two groups for the ratio day/night activity, reflecting the increased motor activity of CADHD during the day. Peak of activity seemed to occur earlier during the day in CADHD. No significant differences in night activity.Sensor pad: During sleep CADHD had more movements of long duration (P< 0.03), more turns per hour (P<0.04), and the first turn occurred much earlier than in controls (P<0.003).Polysomnography: CADHD had decreased total sleep time (P<0.01). There were small differences in sleep structure between the controls and the patients. CADHD had normal sleep efficiency, slightly more stage I sleep, less REM and turned more often in bed. Their sleep was more fractionated, shifting more often between sleep stages (P<0.03), indicating a more restless sleep. Deep and REM sleep were more discontinuous, spread along the night. EEG was normal. No breathing disorders nor periodic limb movements were observed.Temperature profile during the night was similar in the two groups. Heat loss increased at sleep onset faster in the finger than in the foot.
Conclusions: A novelty is that children were investigated at home. Sleep of CADHD was more fractionated, seemed to be more restless than controls and probably non-restorative. This may produce a chronic sleep deprivation. It is tempting to suggest that CADHD use part of their hyperactivity to remain awake.

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0339.G

Restless Legs Syndrome and Serum Ferritin Levels in ADHD Children

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Introduction: Sleep disorders, including sleep disruption through restless leg syndrome (RLS) are often reported in Attention Deficit/Hyperactivity Disorder (ADHD) children. RLS and Periodic limb movement disorder (PLMD) are associated with low serum ferritin levels in adults. Iron deficiency (ID) in childhood (10-15 microgr/L) could affect the developing central nervous system. ID is also known to affect the modulation of motor activity in sleeping infants. Our hypothesis is that iron status measured with serum ferritin level may have an important role in the dopaminergic regulation and could explain an overlap with RLS, PLMD and ADHD in children.
Methods: Forty-three ADHD children (DSM IV), 36 boys and 7 girls, mean age 9.2 $\pm$ 2.2 years, were included in the study. Children were assessed for RLS according to International Restless Legs Syndrome Study Group criteria and for hyperactivity/impulsivity and inattention severity with the Conners Parent Rating Scales (CPRS). Children were investigated for serum iron level and ferritin level (EIA, Abbott). Children were medication free for at least 2 months and none of them had previously been supplemented with iron.
Results: Serum ferritin levels were abnormally low (mean: 13 $\pm$ 2

microgr/L) in 11 (25%) ADHD children and subnormal (mean: 23 ± 5 microgr/L) in 22 (51%). Serum ferritin levels were not correlated with age or gender. Serum iron levels, hemoglobin and hematocrit levels were within normal ranges in all children. ADHD index was significantly correlated with ferritin level (R = - 0,407 ; p<0.001). Nineteen (44%) ADHD children met positive criteria for RLS.
Conclusions: This is the first study reporting low serum ferritin levels in ADHD children. Serum ferritin levels correlated with ADHD index and RLS severity in ADHD children. These findings strongly suggest that iron supplementation could enhance the effects of dopaminergic agents in RLS/ADHD children.

0340.G

Phasic and Tonic Chin Muscle Activity in Child Patients With Sleep Disordered Breathing

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Introduction: Children with sleep disordered breathing (SDB) show neurocognitive deficits, such as poor learning, behavioral problems and attention deficit hyperactivity disorder. Though the cause of these disturbances could be attributed to the impairment of the cortical structures, more than half of apneas in child SDB patients were not associated with EEG arousal (McNamara et al., 1996). Subcortical activation might be involved in the disturbance of the higher brain functions in SDB patients. However, few sleep studies have succeeded in assessing subcortical function in child SDB patients. We have proposed that phasic and tonic inhibition indices (PII and TII) are useful to assess atonia during REM sleep (Kohyama, 1996; Kohyama et al., 1997). Since atonia during REM sleep is maintained by the activity of the brainstem cholinoceptive and/or cholinergic systems, PII and TII might reflect the function of these neuronal systems. Muscle activity during non-REM sleep is maintained through the brainstem serotonergic and noradrenergic systems, and atonia during non-REM sleep might reflect the disturbance of these systems. In the current study, we assess PII, TII and atonia during non-REM sleep in child patients with SDB before and after adenotonsillectomy.
Methods: Five children with complaints of SDB aged 3 to 5 years were diagnosed as having obstructive sleep apnea by means of one all night polysomnography, and underwent adenotonsillectomy. They had the second polysomnographical assessment within six months after the adenotonsillectomy. One all night poysomnography was also performed for four control subjects aged 3 to 4 years. PII is a geometric mean of the following 2 values; 1) the percentage of phasic chin muscle activity (PCMAs) that occur with rapid eye movements f burst (RB), in relation to the total number of PCMAs, and 2) the percentage of RB, that appear with PCMAs, in relation to the total number of bursts. TII quantified the shortness of PCMA. TII is the number of short PCMAs during REM sleep divided by the sum of short and long PCMAs during REM sleep. An elevation of PII and a decrease of TII indicate the disturbance of atonia during REM sleep. Atonia during non-REM sleep was expressed as the percentage of chin muscle atonia during non-REM sleep (atonic non-REM, ANR).
Results: All PII values in patients did not exceed the average value (4.50) in the controls. Except for one value (0.68 in the pretreatment records of 3-year-old boy), all the other TII values in patients exceeded the average value (0.72) in the controls. ANR values decreased in four out of five SDB patients after the adenotonsillectomy. The average ANR value in the pretreatment records was 19.8%, whereas that in the posttreatment ones was 8.9%. The average ANR value in the controls was 13.0%, which showed no statistical significance with the average values in both pre- and posttreatment records.
Conclusions: In child SDB patients, brainstem cholinoceptive and/or cholinergic systems might not be disturbed, while brainstem serotonergic and noradrenergic systems might be impaired before the treatment.

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0341.G

Nasal Continuous Positive Airway Pressure Use and Compliance Among Pediatric Patients with Obstructive Sleep Apnea Syndrome

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Introduction: Obstructive sleep apnea (OSA) affects 1-2% of the general pediatric population. While the majority of children have complete resolution of OSA after adenotonsillectomy, a small percentage of patients continue to have persistent OSA requiring nasal continuous positive airway pressure (CPAP) using single or bi-level airway pressure. Compliance, especially among adolescents, remains a major deterrent to its therapeutic success. Studies in adults suggest that high compliance rates to CPAP can be achieved in an environment that fosters patient education, comprehensive follow-up and integrated care. This study aims to determine nasal CPAP compliance in our pediatric patient population over the last 34 months, through a comprehensive program dedicated for CPAP education and follow-up.
Methods: Patient records from January 2000-October 2002 were retrospectively reviewed. Children aged 9 years and older with OSA in spite of indicated adenotonsillectomy were included. Patients on nasal CPAP for reasons other than OSA were excluded. All patients had baseline polysomnogram prior to and after initiation of nasal CPAP. Hours and frequency of nasal CPAP use were determined using parental feedback on clinic follow-up, further verified by an equipment hour meter. Consequent success and compliance with nasal CPAP use, problems encountered and factors that may help improve compliance were identified.
Results: Thirty-eight (38) patients were included. Age ranged between 8-19 years with 22 (58%) males and 16 (42%) females. Length of nasal CPAP use varied from 6 to 30 months. 28 patients (74%) required CPAP with mean pressure of 9cmH2O; 10 patients (28%) required Bi-level positive airway pressure (BiPAP) (range of 12-20 / 6-12 cm H2O). Indications for nasal CPAP included OSA associated with obesity (32/38 ; 84%), chiari malformation (5%), myelomeningocoele (5%), otopalatodigital-syndrome and muscular dystrophy (2.5%). Average Apnea Index was 7.1/hr and 1.0/hr before and after nasal CPAP use. Average Respiratory Disturbance Index was 18.6/hr before and 4.4/hr after nasal CPAP. All patients had nocturnal symptoms which resolved after therapy. 28/38 (74%) had daytime symptoms – all resolved with therapy. Average frequency of use was 5/7 nights (71%) with 6 hours of average use. 87% of patients used nasal CPAP > 5 hours - 39% (15/38) with documented > 8 hours of use. One (3%) patient refused to use nasal CPAP. Six patients (17%) had improved compliance with additional education. 4/38 (10.5%) had initial problems with mask-fit and 3/38 (8%) complained of nasal dryness - all resolved with mask refitting and added humidifier. There was no difference in compliance between CPAP and BiPAP users.
Conclusions: Nasal CPAP is an effective and safe therapeutic modality for pediatric patients with OSA. Tolerance to nasal CPAP may be enhanced by improving patient comfort with mask-fit and added humidity. Enhanced nasal CPAP use and compliance can be achieved, even among adolescent patients with OSA, through patient and family education and a comprehensive follow-up plan.

0342.G

DSM-IV Disruptive Behavior Disorders in Children Before And After Adenotonsillectomy

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Introduction: Sleep-disordered breathing (SDB) has been linked to inattention, hyperactivity, and aggression. Although SDB is present in many children who undergo adenotonsillectomy (AT), little is known about behavioral problems they may have. We previously reported disruptive behavior disorders (DBDs) in 20 of 45 children evaluated before scheduled AT. We now expand these findings to include 77 subjects and 23 controls, and for the first time report diagnostic outcomes in 56 children rigorously assessed just before and one year after adenotonsillectomy.
Methods: AT subjects were 5.3 to 12.5 years-old, and averaged 8.5 ± 1.9 years; 39 (51%) were boys. The one-year follow-up group of 56 children had a mean baseline age of 8.3 ± 1.9 years, and included 30 (54%) boys. Twenty-three controls, recruited at other surgical clinics and often scheduled for hernia repair, received baseline assessments at a mean age of 9.3 ± 1.9; 17 (74%) were boys. Diagnoses were made by board-certified child psychiatrists who interviewed subjects' parent(s) with the Diagnostic Interview Schedule for Children, Present-State version (DISC), a valid and reliable diagnostic instrument widely employed in child psychiatric research. Final psychiatric diagnoses were made in strict conformity with DSM-IV criteria based upon all available information including the DISC interview, interviews of the children, and additional questioning of the parent(s). The same procedure was repeated one year later.Statistical analysis employed Fischer's exact test to compare diagnostic frequencies in AT subjects and controls at baseline, and McNemar's change test to compare diagnostic frequencies before and after AT.
Results: Baseline Diagnoses: 22/77 (29%) of AT subjects met DSM-IV criteria for attention-deficit/hyperactivity disorder (ADHD). Nine AT subjects had inattentive, 2 hyperactive, and 11 the combined subtypes of ADHD, whereas only 1 (4%) of control subjects had ADHD (inattentive subtype, p = .021). Oppositional-defiant disorder (ODD) was diagnosed in 14 AT subjects (18%) and in 1 (4%) of the controls, p =0.180. One AT subject had conduct disorder. Overall, disruptive behavior disorders were found in 29 AT subjects (38%) and in 2 controls (9%), p =.009.Diagnoses One Year After AT: Among 56 AT subjects who completed follow-up interviews, 17 (30%) had ADHD at baseline, whereas only 10 (18%) had ADHD one year later (p=.092). Nine (16%) had ODD at baseline compared with 3 (5%) at follow-up, p=.070. Overall, 22 (39%) of these subjects had at least one DBD prior to AT, but only 11, including 9 with persistent DBDs and 2 newly diagnosed cases, had DBDs at follow-up (p=.007).
Conclusions: DSM-IV disruptive behavior disorders were diagnosed in 38% of the children scheduled for adenotonsillectomy, significantly more than the 9% rate for control children. The frequency of these disorders dropped by 50% one year after surgery. These findings suggest that sleep-disordered breathing may play an important role in the etiology and treatment of disruptive behavior disorders in some children.

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0343.G

Polysomnographic Analysis of Sleep Disrupted Autism Patients

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Introduction: The parents of children with autism frequently complain of sleep disturbance in the children. Previous studies have suggested an increased prevalence of Periodic Limb Movements in Sleep (PLMS) or REM Sleep Behavior Disorder (RBD) in children with autism.
Methods: Eight children with autism referred for sleep disturbance (6 M, 2 F, average age 7.4 years, range 4-16 years) underwent 2 nights of polysomnographic (PSG) study. Patients were evaluated and diagnosed as autism based on DSM-IV and autism diagnostic interview-R (ADI-R) for autism spectrum disorder. Detailed sleep history regarding the child's sleep was provided by the parents through a standard sleep questionnaire. Sleep architecture, respiration, PLMS and parasomnia activity were evaluated by standard methodology. Quantitative values for both nights of the PSG were averaged.
Results: By history, the 8 autism children have difficulty initializing and maintaining sleep and all 8 children have a history of snoring. By history, sleep enuresis is present in 5 of the 8 children. Four of the 8 children have been previously diagnosed with Attention-Deficit-Hyperactivity Disorder (ADHD). One patient has a history compatible with Restless Legs Syndrome (RLS). The neurological and general physical examination was grossly normal in all patients. PSG study showed that three of the 8 children had an apnea index >1.0 (2, 2, 10.5). Five out of 8 patient had sudden awakenings of 10 seconds to a few minutes directly from slow wave sleep (stage III and IV). These events were associated with an increase in cardiac and respiratory rate on PSG and arm and leg movements as documented by video. In no case did any child leave the bed to walk during these episodes. A diagnosis of Confusional Arousals/Sleep Terrors could not definitely be made due to problems of determining the level of awareness in an autistic child. Only one patient had a significant PLMS index > 5.0 (7.3) and that child also had ADHD. No child had evidence of RBD on either night of the polysomnographic study. An arousal index > 10/hour occurred in 2 of the 8 patients (20 and 23.8). Sleep efficiencies were on average above 90%, but sleep times were sometimes shortened and bed times were later than at home due to laboratory schedule demands. The overall sleep architecture for the children as a whole was close to normal except that % REM was lower (average 13.7% TST), perhaps due to the foreshortened sleep times.
Conclusions: A variety of sleep disturbances occur in children with autism and insomnia. The most frequent of these are sleep disordered breathing, enuresis, and polysomnographic findings compatible with confusional arousal/sleep terrors. All together, all 8 of the children with autism had historical evidence of sleep disordered breathing and all 8 had either historical or polysomnographic evidence suggestive of at least one parasomnia.

0344.G

The Relationship between Sleep Hygiene and Sleep Quality in Italian and American Adolescents

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Introduction: Previous research has shown that sleep difficulties are common during adolescence. Furthermore, poor or inadequate sleep is associated with negative outcomes, including daytime sleepiness, emotional dysfunction, and behavioral problems. Sleep hygiene may be importantly related to adolescent sleep quality; however, this relationship has not been well explored. The purpose of this study was to (a) compare the sleep hygiene practices and sleep quality of adolescents from two industrialized societies, Italy and the United States; and (b) investigate the relationship between sleep hygiene and sleep quality in both samples.
Methods: Participants were 1348 adolescents (669 males; 710 females)

aged 12-17 years (*M*=14.6; *SD*=1.6). Data were collected from public school systems in Rome, Italy (*n*=776; response rate=83.3%) and Southern Mississippi, USA (*n*=562; response rate=57.4%). Samples did not differ in mean age but did differ in gender, race, and SES. Participants were administered a pencil-and-paper questionnaire that included: the Self-Rating Scale of Pubertal Development, the Sleepiness and Morningness/Eveningness Scales (School Sleep Habits Survey), the Adolescent Sleep-Wake Scale (ASWS), and the Adolescent Sleep Hygiene Scale (ASHS). The ASWS measures sleep quality along five behavioral dimensions (Going to Bed, Falling Asleep, Maintaining Sleep, Reinitiating Sleep, Returning to Wakefulness). The ASHS assesses several sleep hygiene domains (Substances, Physiological, Cognitive, Emotional, Environmental, Bed Sharing, Sleep Stability).

Results: Italian adolescents reported much better sleep hygiene (ASHS Total Scale effect size = .66 *SD*) and substantially better sleep quality than American adolescents (ASWS Total Scale effect size = .63 *SD*). A strong linear relationship was found between sleep hygiene and sleep quality in both samples (Italians: r=.45, p<.001; Americans: r=.50, p<.001). Separate hierarchical multiple regression analyses were performed on the Italian and American samples. The variables entered in step 1 included demographic characteristics [age, sex, race (Americans only)], SES, medication/illness status, pubertal status, and circadian preference. For both samples, variables in step 1 explained a significant proportion (p<.001) of the variance in sleep quality [Italians: $R2$=.19, F(7, 543)=19.12; Americans: $R2$=.26, F(8, 418)=19.88], with circadian preference accounting for the highest percentage of variance in both samples (15% for Italians; 24% for Americans). ASHS scores were added in step 2. The total variance explained was significantly increased [Italians: $R2$=.38, F(7, 536)=22.93; Americans: $R2$=.44, F(7, 411)=17.68]. Sleep Hygiene was responsible for significant variance above that accounted for by variables entered in step 1 (19% for Italians;: 17% for Americans). A final hierarchical multiple regression analysis with all cases (both samples combined) showed that geographic location (Italy versus USA) only explained an additional 1% of the variance in ASWS scores after controlling for sleep hygiene and all other variables.

Conclusions: This study suggests significant cultural differences in sleep quality and sleep hygiene practices during adolescence. The results also indicate that sleep hygiene practices are importantly, and perhaps causally, related to sleep quality. Further research is needed to determine if practicing good sleep hygiene will result in improved sleep quality, reduced daytime sleepiness, and better daytime functioning during adolescence.

0345.G

Sleep Disordered Breathing in Patients with Mucopolysaccharidosis

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Introduction: Airway obstruction, specially during sleep- obstructive sleep apnea (OSA), has been recognized as a major cause of morbidity and mortality in patients with Mucopolysaccharidoses (MPS). Assessments for diagnosis and the severity based upon clinical history and physical evaluation alone are often inadequate.

Methods: From a cohort study of 69 MPS patients, we are evaluating the occurrence of airway obstruction by means of clinical assessment, bronchoscopy, pulmonary function testing and cardiopulmonary sleep study.

Results: Forty- six patients were seen at the Sleep Disorders Clinic, thirty- three (72%) had a clinical history suggestive of airway obstruction. The more common symptoms were snoring (36/46), frequent arousals (26/46), snorting (26/46), profuse sweating during sleep (24/46) and witnessed apnea (23/46). Two patients were on nasal Cpap during sleep and one patient had a tracheostomy. Cardiopulmonary sleep studies performed during non sedated sleep in 39 patients, showed severe OSA in 14/39 patients (12 patients MPS VI, one MPS I and one MPS IV), moderate OSA in 10/39 patients (two patients MPS I, one MPS II and 7 MPS VI), mild OSA in 6/39 (one MPS I and five patients MPS VI). Seven patients had normal sleep studies (two patients MPS I, one MPS IV and four MPS VI) and two patients (MPS I and MPS VI) had a borderline study.

Conclusions: The results of this study have shown that airway obstruction is an important problem in MPS patients and needs to be carefully evaluated with routine cardiopulmonary sleep studies.

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0346.G

Cosleeping and Sleep Problems Among Chinese School-Aged Children

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Introduction: Sleep problems in children have received more and more attention of parents and medical professionals because of their potentially adverse effects on learning, behavior, and physical development. Child sleep practices and sleep behaviors are not only associated with a large number of biological and psychological factors but also cultural, social and family factors. For example, cosleeping of young children with parents is acceptable practices in many Asian countries but cosleeping is less common in Western countries. Almost all previous studies on cosleeping are limited to young children under 4 years of age, sample size is small, and results on the association between cosleeping and child sleep problems have not been consistent . No studies have examined the association between cosleeping and sleep problems with Chinese children. This questionnaire survey was undertaken in Jinan city of Mainland China (1) to estimate the prevalence of cosleeping and parent-reported sleep problems in Chinese school-aged children; (2) to examine the correlates of cosleeping practices; and (3) to examine if copsleeping is associated with increased risk for sleep problems.

Methods: Participants were recruited from three elementary schools in one representative district of Jinan, the capital city of Shandong Province in the eastern part of Mainland China. After getting permission from target schools, we randomly selected one class from each grade for each school and obtained 565 children as potential participants. The sampled children were asked to take their parents a questionnaire with a letter explaining the project and asking the parents to complete the questionnaire if they were agreeable. The parent-self administered questionnaire included the Chinese version of the Children's Sleep Habit Questionnaire (CSHQ) and a number of questions that asked about child's regularly sleeping practices (i.e., share a bed with parent(s), share a room with parent(s) but not share a bed, or sleep alone in own room) and information on family and child characteristics. Of these 565 sampled children, 517 (92%) returned questionnaires (47.4% boys, mean age 10.5 years, rang 7-13).

Results: Overall, average bedtime and wake time in this sample were 21:06 (SD = 0.74h) and 06:24 (SD = 0.33h), respectively. Average sleep duration was 9.13h, significantly declining with age (F = 19.63, p < .001). More than one-fifth of children often had hard time getting out of bed, and 22% seemed very sleep during daytime. Night wakings, restless and moving a lot during sleep, afraid of sleep in the dark or alone also were very common in this sample of children (>10%). However, breathing stop, bedwetting, and awaken screaming or sweating were less common (<1%).The prevalence of regular cosleeping in Chinese school-aged children was as high as 18.2%. The rate of cosleeping decreased

significantly with age, from 55.8% in 7-year-olds to 7.2% in 11-13-year-olds. No significant differences in the rate of cosleeping were observed between boys and girls. Logistic regression analyses showed that poor physical health of children (OR = 2.79), overcrowded housing (<11m2 per person) (OR = 2.53), and poor parental relationships (OR = 6.33) were associated with increased likelihood for child cosleeping with parent(s). Compared with those children sleeping alone during night, children who coslept with parent(s) woke up later in the morning (F = 7.88, p < .01) and were more likely to have reported sleep anxiety (F = 15.05, p < .001) and daytime sleepiness (F = 7.57, p < .01). Cosleeping children did not significantly differ from those sleeping alone in bedtime, total sleep duration and sleep onset delay, parasomnias and sleep disordered breathing problems.

Conclusions: In summary, regular cosleeping in Chinese school-aged children was very common and significantly decreased with age. Family conflicts and crowded housing increased the likelihood for child cosleeping with parent(s). Cosleeping was associated with increased risk for sleep anxiety and daytime sleepiness. These results suggest that cosleeping might affect sleep quality rather than sleep quantity. Longitudinal studies with multiple informants and possibly objective measures need to examine the causal relationship between cosleeping and sleep problems and long-term effects of cosleeping on child development.

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0347.G

Correlates of Sleep Latency on The Multiple Sleep Latency Test in a Population of Morbidly Obese School Children

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Introduction: The multiple sleep latency test (MSLT) is a commonly used objective measure of sleepiness. A short mean sleep latency (msl) has been variously correlated with disorders of hypersomnolence including Narcolepsy, idiopathic hypersomnia, chronic sleep deprivation from obstructive sleep apnea, periodic limb movement disorders as well as with obesity alone. Limited data of MSLT in children is available in current literature.

Methods: One hundred consecutive children recruited for an obesity screening program were evaluated with an attended nocturnal polysomnogram (PSG) for obstructive sleep apnea hypopnea syndrome (OSAHS) as well as a MSLT for hypersomnolence. PSG and MSLT were done and scored according to current guidelines. Demographic data and data from the nocturnal polysomnogram were correlated with msl on MSLT. Statistical analysis was done using statistical software package (SPSS version 9.0).

Results: One hundred children aged 6-18 years were evaluated. Male to female ratio was 5.8 to 4.2. Racial distribution were 46% Chinese, 46% Malay, 6% Chinese, 2% Others. Their percent idea body weight for height (IBW) ranged from 160% to 346% (median = 188%) and Body mass index (BMI) ranged from 26.8 kg/m2 to 64.8 kg/m2. (median = 36.2 kg/m2). 57% of patients were positive for OSAHS while 15% had excessive daytime somnolence (EDS) defined as mean sleep latency of less than 10 minutes. Presence of OSAHS was not significantly associated with the presence of EDS (p>0.05). Spearman's correlations however revealed significant positive correlation of msl with PSG sleep latency (r = 0.32**) REM sleep latency (r = 0.22*), and percentage of stage 3/4 sleep (r = 0.3**). There was also a negative correlation with sleep respiratory disturbance index RDI (r = 0.25*), REM sleep RDI (r = 0.26**) and sleep efficiency (r = 0.27**). Subset analysis of the disease group revealed only a positive correlation of msl with REM sleep RDI (r = 0.29*). Looking at the normal and primary snoring group, msl correlated inversely with sleep efficiency (r = 0.43**) and IBW (r=0.33*). There was a positive correlation in this group with PSG sleep latency (r = 0.34*). MSL was not otherwise significantly correlated with other variables studied i.e. wake after sleep onset time, arousal index, percentage of stage 1 or 2 sleep, REM sleep time, oxygen nadir, amount of sleep time spent with an oxygen saturation less than 95%, peak end tidal carbon dioxide as well as amount of sleep time spent with end tidal CO2 higher than 50 mmHg.Significant correlation at p<0.05*, p<0.01**

Conclusions: Excessive daytime sleepiness as measured by shortened mean sleep latency was not common in obese children with OSAHS and may be present without sleep apnea. Msl in obese children with OSAHS correlated only with REM sleep RDI.

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0348.G

Sleep Complaints in High School Students

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Introduction: Although the prevalence of sleep disorders is well established in the adult population, fewer studies have been conducted with adolescents. Much research has focussed on delayed sleep times and daytime sleepiness. Changes in circadian rhythms, busy schedules, earlier school start times, increased social and school work demands as well as other factors may predispose adolescents to poor sleep habits. In addition, there may be underlying symptoms of sleep disorders that may further contribute to poor sleep and subsequent daytime sleepiness. The present survey study was designed to determine whether otherwise healthy 10th and 11th grade students (14-17 years old) report symptoms of common sleep disorders.

Methods: The study was conducted as part of an Authentic Science Research Program by a senior high school student. Surveys were designed based on the Brown University web-based sleep survey (http://www.sleepforscience.org/contentmgr/showdetails.php?id=93) with additional questions targeting symptoms related to snoring, restless legs syndrome, insomnia, among others. After IRB approval was obtained, surveys were mailed to the parents of students enrolled at a medium-sized suburban high school. Surveys were returned to the student investigator anonymously. Statistical analyses were conducted using SAS (Chi-square tests). Given the sample sizes, the counts in some of the cells were small.

Results: Surveys were sent to 531 students; 82 were returned (15%). Of the 82, 48 were in 10th grade, and 34 were in 11th grade. More girls returned surveys (64.6% vs. 35.4%) than boys. The highest frequency responses for sleep duration questions were as follows: 76.8 reported not getting enough sleep at least once or twice a week; 32% reported that their sleep was never or hardly ever refreshing; and 43% reported having to wake earlier in the morning than they desired nearly every day. 24.4% of the students reported having racing thoughts at night that interfered with sleeping at least 3-4 times per week. There was a significant difference between 10th and 11th graders, with older students reporting more of this symptom (p = 0.014). There was a trend for more girls to report having a problem falling asleep before 3:00 AM (p < 0.078). About 10% of the students reported snoring at least 3-4 times per week, while only 3.6% reported symptoms of restless legs syndrome. 12.2% of the students considered themselves to be restless sleepers at least 3-4 times per week. There were significant correlations between reporting difficulty falling asleep before 3:00 AM and racing thoughts (p < 0.01), snoring (p < 0.01), restless legs (p < 0.01), and restless sleeping (p < 0.01). Restless sleeping correlated with racing thoughts (p < 0.01) and restless legs (p < 0.01).

Conclusions: The results of the study are consistent with the literature on short and unrefreshing sleep endorsed by adolescents. In addition, the

current survey suggests that there may be other factors impacting sleep that may contribute to daytime sleepiness. When students reported difficulty falling asleep before 3:00 AM, they were also more likely to endorse other sleep symptoms. Thus, it may be important for health professionals to probe into other possible sleep complaints when teens present with sleep delays.

0349.G

Sleep Behaviors of Preschool-aged Children Attending Daycare

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Introduction: Although children who attend daycare may be at high risk for compromised sleep due to hectic working family schedules, a description of the sleep behaviors of this population has never been reported. Optimal sleep is important for normal growth and development, emotional health, and immune function and, therefore, an understanding of the effects of daycare on the sleep of these children is essential. Thus, the purpose of this preliminary study was to describe sleep behaviors typical of preschoolers attending daycare.
Methods: A convenience sample of parents of two- to five-year-old children attending a university-based daycare center completed the Children's Sleep Habits Questionnaire (CSHQ), a 33-item tool that assesses age-relevant sleep domains including: 1) Bedtime Resistance, 2) Sleep Onset Delay, 3) Sleep Duration, 4) Sleep Anxiety, 5) Night Wakings, 6) Parasomnias, 7) Sleep-Disordered Breathing, 8) Daytime Sleepiness. The CSHQ also elicits information regarding the child's usual bedtime, wake time, and the total amount of nocturnal and daytime sleep obtained by the child in a 24-hour period.
Results: The sample of children included 8 males and 11 females with a mean age of 38.9 months ($\pm$ 8.4, range 24-50). The average number of hours spent in daycare per week was 40.9 ($\pm$ 4.6) for a mean of 30 months ($\pm$ 9.7). Average bedtimes and wake times were 20:45 (military time, range 20:00 - 22:00) and 06:54 (range 06:00 - 08:00), respectively. Total sleep obtained during a 24-hour period ranged from 9 to 13.5 hours with a mean of 11.5 ($\pm$ 1.3). Over 26% of parents reported sleep latencies greater than 20 minutes 2 to 4 times per week. Twenty-one percent of children needed a parent in the room to fall asleep 2 to 4 times per week with 26.3% requiring a parent 5 to 7 times per week. Bedtime struggles occurred in 21% of the children between 2 to 4 times per week. Loud snoring (5 to 7 times per week) was reported in 10.5% of the children, with 5% having pauses in breathing and snorts/gasps 2 to 4 times per week. Parents reported that waking in a negative mood (42.1%), falling asleep while watching TV (31.6%), having a hard time getting out of bed (26.3%), and seeming tired (21.1%) were common.
Conclusions: These preliminary results suggest that the total amount of sleep obtained by preschoolers attending daycare is comparable to normative data. Clinical symptoms associated with childhood sleep apnea were also similar to prior reports. However, specific sleep behaviors, including bedtime resistance, delayed sleep onset, and daytime sleepiness, may be more common. Because compromised sleep has the potential to adversely affect a variety of health outcomes, further research designed to study the sleep of preschoolers in daycare is warranted.

0350.G

Genioglossal EMG Activity in Children with Sleep Apnea Versus Controls During Wakefulness, Sleep Onset and Stable NREM Sleep

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Introduction: The upper airway size is determined by the balance between static pharyngeal mechanics, neuromuscular activity, and luminal pressure. Children with the obstructive sleep apnea syndrome (OSAS) have narrower and more collapsible airways compared to normal controls. However, even with sedation, there is considerable overlap in the pharyngeal luminal diameter of children with and without OSAS, suggesting a role for neuromuscular compensation. An active airway neuromuscular mechanism is further evidenced by the lack of obstruction during wakefulness, the REM predominance of apnea, and the tendency for sedatives to induce apnea. The neuromuscular control mechanisms active in maintaining airway patency in children are not well understood.
Methods: Children with OSAS (N = 9) and a control group of non-snoring, asymptomatic subjects (N = 6) were studied. All subjects underwent an overnight polysomnogram including continuous measurement of EMGgg using an intra-oral surface electrode. Maximal EMGgg activity was defined using a tongue protrusion maneuver against the alveolar ridge. For each subject, the mean peak phasic EMGgg (% maximum) was determined supine during; 1) 5 minutes of baseline breathing during eyes-closed wakefulness (approximately 100 breaths); 2) Early sleep onset period (5 breaths); 3) late sleep onset period (5 breaths); 4) Stable stage 2 sleep (20 breaths).
Results: We observed that the EMGgg activity in OSAS patients compared to controls was significantly greater during wakefulness (4.2 ± 2.4 versus 1.8 ± 1.1 % max, $p < 0.05$), and had a greater decline in the sleep onset period (39 ± 9 versus 25 ± 8%, $p < 0.05$). During stable NREM sleep, EMGgg remained below the wakeful baseline in all normal controls, but increased above the baseline in half of the OSAS patients. Phasic EMGgg activity was observed in 5 of the 9 OSAS patients but none of the control subjects. There was no difference between the groups in oxygen saturation or end-tidal carbon dioxide levels during the sleep onset period or stage 2 sleep.
Conclusions: During wakefulness, the mean peak phasic EMGgg activity is greater in children with OSAS than control subjects, although there is some overlap between groups. This is consistent with a reflex-driven neuromuscular compensation for an anatomically compromised airway. The reduction in EMGgg activity during the sleep onset period was greater in OSAS patients than control subjects. This further supports the hypothesis that OSAS patients have an increased reliance on compensatory mechanisms to maintain airway patency while awake. During stable NREM sleep, the EMGgg activity remained at low levels in all control subjects, but increased in some OSAS patients to levels above wakefulness. This indicates that neuromuscular compensatory mechanisms remain at least partially intact during NREM sleep, and may be activated in some children with severe OSAS.

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0351.G

Clonidine For Children's Sleep Disturbance: A Survey Of Pediatricians' Practices

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Introduction: Sleep disruption is on the "Top 10" list of child behavior problems for parents. Twenty to thirty percent of children experience sleep disturbance (i.e., sleep onset difficulties, night-time awakenings, parasomnias, early morning awakenings, sleep schedule problems, and obstructive sleep apnea). Recent data indicate that Clonidine is the psychotropic medication with the largest gain in prescription rates. An alpha-2 adernergic agonist, clonidine is classified as an anti-hypertensive with sedation side effects. It is used in the treatment of multiple conditions (e.g., ADHD, Autism, Hypertension, Aggression, and Tic Disorders). Although clonidine is not labeled for the treatment of pediatric sleep disturbance, there is emerging evidence that it is commonly used among pediatricians. The purpose of this study was to investigate the utilization of clonidine in the treatment of pediatric sleep disturbance.

Methods: Surveys were mailed to 600 pediatricians in 3 states (IA, OR, NC). Information was gathered on pediatrician demographics, sleep disturbance treatment practices, use of clonidine in the treatment of sleep disturbance and other conditions. The response rate resulted in a final sample of 133 practicing pediatricians 39.8% from IA, 33.8% from OR, 19.5% from NC. Eighty-three percent identified their primary specialty as general pediatrics, followed by developmental pediatrics (4.5%) and emergency medicine (3%). Fifty-seven percent were female and the mean age was 44.7 yrs (SD = 9.6). Respondents were primarily Caucasian (85%) with 10.5% Asian/Pacific Islander. Of the respondents 41.4% practiced in urban settings, 38.3% in suburban settings, and 19.5% in rural setting. Mean years in medical practice was 14.2 (SD = 9.1).
Results: The survey results revealed 94% of pediatricians reported seeing pediatric patients who report sleep disturbance. Behavioral treatments were used by 92.5% of the sample, medication alone by 45.1%, behavioral treatments and medication combined by 57.1%. Pediatricians reported using a variety of medications in the treatment of sleep disturbance. The most commonly prescribed drug class was antihistamines (61.7%), followed by clonidine (34.6%), melatonin (32.3%), tricyclic anti-depressants (24.1%), and other anti-depressants (21.8%). Of those pediatricians who reported clondine use, the most common sleep disturbances targeted were sleep onset difficulties (87.0%), sleep schedule problems (26.1%), parasomnias (8.7%), night-time awakenings (6.5%), and morning awakenings (4.3%). Compared to non-prescribers, clonidine prescribers were more likely to practice in Oregon, reported more "comfort" in treating pediatric sleep disturbance, and were more likely to use clonidine to treat non sleep-related problems. No significant differences in age, years in practice, or other demographic variables were identified for clonidine prescribers versus non-prescribers.
Conclusions: Given increasing prescription rates of clonidine, and its reported use with pediatric sleep disturbance, further research investigating clonidine's safety, efficacy, and appropriate dosing for treatment of pediatric sleep disturbance is sorely needed. Reserach investigating pediatrician training in and treatment of sleep disturbance is also needed to examine the effect of training on the choice of treatment modality.

0352.G

Normal Polysomnographic Values of Obstructive Hypopneas for Children and Adolescents

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Introduction: Polysomnography is an established gold standard for diagnosing obstructive sleep apnea in both children and adults. Marcus et al (1992) reported normal polysomnographic criteria for apneas in healthy children, however obstructive hypopneas were not evaluated. Although obstructive hypopnea indices are often measured in sleep laboratories, normative data in children are lacking.
Methods: We analyzed 41 overnight polysomnograms of healthy children, initially perfomed in 1990-1991, for the presence of obstructive hypopneas. OH was defined as a 50% or greater decrease in airflow amplitude by nasal thermistor or end-tidal carbon dioxide waveform (PsETscos2s), accompanied by paradoxical breathing, lasting at least two respiratory cycles. Although hypoxemia and arousals were scored, if present, they were not considered essential for defining OH.
Results: 13/41 (32%) were females. The mean age was 10.1 $\pm$ 4.3 SD years (range 1.1 – 17.5 yrs). The duration of total sleep time was 6.1 $\pm$ 1.7 hrs. Only 6/41 (15%) had any OH. The OH index was 0.3 $\pm$ 0.2 events/hour (range of 0.17 - 0.67 events/hour). The mean duration of OH was 12.8 sec (range 3.5 – 40 sec), the Sspsos2s nadir post OH was 95-99%. None of the OH was associated with desaturation greater than 2%. The peak PsETscos2s post OH was 40 mmHg. Only one child had arousals with OH. 2/6 children with OH also had obstructive apneas (OA), however 6 children with OA did not have any OH. There was no relationship between children who had OA versus OH (p=0.58 *NS*).
Conclusions: We conclude that in normal children, OH is rare and OH index is < 1 event per hour. Furthermore, OH, if present, is not accompanied by hypoxemia or hypercarbia.

0353.G

Temperament And Sleep-Waking Behavior In The Neonate and Toddler

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Introduction: The progression toward sleep consolidation and circadian control of sleep and waking during infancy is known to be influenced by maturation, temperament and psychosocial milieu. Temperament, defined as biological predispositions in reactivity, responsiveness and arousal, has been associated with sleep disturbance in infants and children. This longitudinal study examines temperament in the context of developing sleep-wake behavior including the incidence of nightwaking.
Methods: Infants (N=170) were evaluated at 6 weeks and 16months of age. At 6 weeks, sleep and waking across 24 hours was examined using a sleep diary for 3 days in the home. Sleep, waking, crying and fussiness are recorded at 5-min intervals across 24 hours. This method produces a record of the distribution and proportion of different behavioral states. At 16 months, parents completed the Sleep Habits Inventory (SHI) which measures sleep hygiene, onset, continuity, nightwaking, parent-seeking, bedsharing and use of sleep aids. Sleeping arrangements, naps, bed and wake-up times were also measured. Six week assessments of developmental level and temperament was done in the laboratory in a videotaped session of the motor scale of the Bayley Scales of Infant Development II (BSID). Temperament was assessed during the test by tabulation of fussing and crying episodes; and ratings of infant consolability and activity level. Parents separately completed the Infant Characteristics Questionnaire (ICQ) which yields subscores of difficult-fussy, unadaptable, dullness and unpredictability. At 16 months, the Physical Activity Scale and Infant/Toddler Symptom Checklist (SC) and subscores were used to assess temperament.
Results: Time 1: 6-weeks Maternal and paternal ICQ scores strongly concurred for composite scores (r=.79, p<.0001) and the difficult-fussy factor (r=.52; p<.0001). ICQ fussiness scores reliably predicted several Sleep Diary fussiness measures (r range=. 34 to.53; p<. 0001) and videotaped observations of crying and activity level. Lab crying and fussing epochs also predicted Sleep Diary nightwaking, 24 h crying and were negatively associated with awake-content Sleep Diary measures. Time 2: 16-months. ICQ measures at 6 weeks predicted 16-month Symptom Checklist (SC) composite score and self regulation, touch and attachment subscores. Lab fuss/cry at 6 weeks was associated with Physical Activity Scale scores and the movement subscale of the SC. Six-week Sleep Diary nightwaking and several fuss measures were negatively associated with developmental level as measured by motor milestones, but Sleep Diary fussing levels predicted SC self regulation and attention symptoms. ICQ scores at 6 weeks predicted 16-month sleep habits (SHI) items related to sleep onset ease, use of sleep aids and bedtime routine. Sleeping arrangements were associated with SHI measures and SC sleep symptoms.
Conclusions: In this study, infant measures of temperament using parental report and laboratory measures were related to sleep-wake behaviors at both 6 weeks and 16 months. Measures of fussiness and crying in infancy were convergent arguing for the validity of these behaviors as a trait markers. At 16 months, fuss measures were associated with toddler temperament and particularly sleep onset skills. Sleeping arrangements were related to SHI measures and temperament.

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0354.G

Automated Arousal Detection in Neonates

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Introduction: Arousal events punctuate the sleep cycle across the human lifespan, and are important physiologic phenomena influencing sleep continuity and maintenance. Insufficient or excessive arousals reflect transient or profound sleep disruptions which may be surrogate markers for brain disorders and/or systemic disease states. Arousals are prominent behaviors during neonatal sleep. However, no uniform definition of arousal yet exists. Clinical applications of arousal analysis include neonatal populations who express alterations in arousal number and duration which reflect prenatal or postnatal brain disorders.
Methods: Our research consortium is developing a computerized arousal detector for neonates as part of a comprehensive program for automated neonatal state detection. A statistical model, hidden Markov modeling (HMM), is being used to categorize the statistical properties of arousal signals. The development of the HMM-based arousal detector begins by creating a training set of physiologic behaviors defined as arousal events that were identified by an experienced neonatal polysomnographer. In the recognition phase of this detector the trained HMM is used to evaluate given signal inputs against a set of codes, trained in the supervised learning phase for arousal recognition. The training set utilizes features obtained from the short-time Fourier transforms of EEG and respiratory signals. These features were used to analyze changes in EEG frequencies across the four EEG-sleep state segments in the testing set, (i.e. mixed frequency active sleep, high voltage slow quiet sleep, tracé alternant quiet sleep, and low voltage irregular active sleep). The respiratory frequencies were assessed only during the tracé alternant quiet sleep. Eight neonates were used for the training phase and 10 neonates were used for the testing phase of this study.
Results: We identified by visual analysis 28,401 seconds of neonatal arousal epochs with a correct detection rate of 83.7% by our automated technique.
Conclusions: Arousals constitute a prominent physiologic phenomena during neonatal sleep and can be readily identified by an automated technique. This arousal detector may also assist in medical management of the high risk neonate. Future studies will refine this arousal detector by identifying arousal subtypes which can then be applied to our training sets to improve the accuracy for feature extraction.

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0355.G

Sleep Spindles During Rem Sleep – a Family Study

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Introduction: Analysis of phasic events during sleep has been suggested as being useful to differentiate between normal and abnormal sleep, even though sleep architecture has shown to be adequate. Observation of atypical phasic events during REM sleep has been discribed in patients with some psychiatric disorders, i.e. depression. We described sleep spindles during REM sleep in a child with difficulties initiating and maintaining sleep and her mother.
Methods: We performed 3 polysomnographic (PSG) studies over a two-year period with recordings at intervals of 6 and 12 months in a girl (aged 9 at initial point of study). Data were compared with age and gender matched control subject. We also performed a single PSG recording in all members of the family (parents and younger female sibling). Psychological evaluation consisted of a psycho-diagnosis using Rorschach tests along with psycho-dynamic sessions.
Results: The 3 PSG studies of the subject presented with sleep spindles intrusion during REM sleep. An identical pattern could be observed in the mother's recording. Quantification of sleep spindles during stage 2 of NREM sleep was similar to the observed in healthy children. The father and younger sister revealed normal sleep patterns. The Rorschach test highlighted an immature response to environment stimuli in the subject. Psychodynamic sessions outlined similarities in personality traits between the subject and her mother.
Conclusions: As part of the neurophysiological development, indeterminate sleep stage is defined as a indefinate sleep stage because there is a mixture of wave frequencies and amplitudes along with phasic elements. Indeterminate sleep is frequently used as a marker of neurophysiologic maturation – the smaller the concepcional age the greater the percentage of this stage over the total sleep time. The observation of phasic elements typical of NREM sleep during REM sleep gave us in some way the impression of undefined sleep insted of REM sleep, during PSG recording analysis. In this case, the observation of similar sleep patterns in the child and her mother and the association of immature traits observed during psychological diagnosis led us to hypothesize a possible link between "immature" sleep patterns and the psychological "immature" traits observed.

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0356.G

Sleep Disturbances Following Pediatric Traumatic Brain Injury

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Introduction: Adult traumatic brain injury (TBI) has been linked to post-injury sleep complaints and sleep disturbances. The only published study on sleep after pediatric TBI indicates that, in a sample of adolescents recruited because of sleep complaints three years after a mild TBI, objective sleep disturbances are prevalent. Despite clinical experience that such disturbances are present more broadly, no published studies have examined sleep problems in grade school children with TBI. This study examines the presence, nature, and persistence of parent-reported sleep disturbances in children with moderate to severe TBI.
Methods: As part of a larger longitudinal study of neuropsychological and family system outcome after pediatric TBI, 109 children with moderate to severe traumatic brain injuries (TBI) were compared to 80 children who sustained orthopedic injuries (OI) without brain involvement. Data were collected at baseline (parent report of pre-injury functioning) and at 6-month, 1 year, and 4 month follow-ups. Mean age of injury was 9.7 years for the TBI group and 9.3 for the OI controls (range: 6-12). The dependent measures were seven sleep-related items from the Achenbach Child Behavior Checklist (CBCL), a broad-spectrum parent behavior rating form. These seven items (each rated never, sometimes, or often) were: nightmares, overtired, sleep less than most kids, sleeps more than most kids, talks or walks in sleep (parasomnias), trouble sleeping, and wets the bed (enuresis).
Results: Group differences on the sleep items were assessed at each time point using MANOVA, with univariate ANOVA follow-up tests. MANOVA indicated no significant differences between the groups at baseline ($p>.6$), but a significant difference at 1 year ($p=.01$) and trends towards significance at 6 months and 4 years ($p<.10$). Univariate follow-up analyses indicated that the groups did not differ at any time point in parasomnias, sleeping less than most children, or enuresis ($p>.05$). However, compared to the OI group, the TBI group was reported to be overtired and to have trouble sleeping at all post-injury time points ($p<.05$). In addition, the TBI group was reported to have nightmares at the 1- and

4-year post-injury assessments (p£.01) and more sleep than normal at the 1-year follow up (p<.01). Compared to CBCL norms, the TBI group tended to have greater reported sleep problems across time points, whereas the OI controls were generally similar to the normative sample.
Conclusions: Results from this study indicate that children with TBI have greater reported sleep problems than children with orthopedic injuries, including daytime sleepiness, nightmares, excessive sleeping, and difficulty sleeping. Sleep problems in the TBI group were evident by 6 months following injury and peaked at one year post injury, but were still evident four years post injury. These findings argue for routine sleep screening following pediatric TBI, as well as more detailed research into the nature and etiology of sleep abnormalities after pediatric brain injury.

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0357.G

Sleep Disordered Breathing (SDB) in 971 Consecutive Children Aged 3 to 6: Association with Risk Factors

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Introduction: SDB in children may include a number of disorders as primary snoring, snoring with abnormalities of sleep architecture or oxygenation, obstructive sleep apnea syndrome (OSAS), central sleep apnea, respiratory failure. Habitual snoring may be associated with nocturnal oxygen desaturation events and daytime consequences. Aim of our study was to determine the prevalence of SDB and its possible association with risk factors such as parental smoking, adeno-tonsillar hypertrophy and obesity in a sample of 971 consecutive children aged 3 to 6 years.
Methods: We evaluated 524 children referred to our Pediatric clinic for suspected SDB (group A) and 447 children randomly selected from 8 kindergartens in Varese (North Italy) as control group (group B). This cross-sectional study was designed in two phases: a screening phase aimed to identify the symptoms and risk factors related to SDB by means of a structured clinical interview (questionnaire to parents), and an instrumental phase for the definition of SDB. An ODI (Oxygen Desaturation Index/per hour) > 5, SpO2 < 92% and snoring percentage > 30% were considered pathologic.All data were statistically evaluated by t-test Student, X2 test and logistic regression. The relationship between these two groups was examined by the odds ratio and the relative risk.
Results: In group A, 310 children were male (59%) and 214 female(41%) (mean age, 4.09; range 3 to 6 years); in group B, 243 were male (54%) and 204 female (46%) (mean age, 4.07, range 3 to 6 years). All children (n=971) underwent a cardiorespiratory recording at home. Cardiorespiratory results showed significantly different results in terms of snoring percentage, ODI and minimal SpO2 in the two groups: (group A vs group B: ODI 5.58 $\pm$ 7.44 vs 2.91 $\pm$ 5.27, p<.05, Minimal SpO2 84.3 $\pm$ 9.79 vs 89.4 $\pm$ 5.07, p<.05, % of snoring 48.3 $\pm$ 8.9 vs 18.4 $\pm$ 12.2. A total of 971 questionnaires were analysed. The following nocturnal symptoms were found: habitual snoring (group A 93%; groups B 34%), reported apnea (75% vs 19%), restless sleep (68% vs 42%). The prevalence of diurnal symptoms was also analysed: mouth breathing (82% vs 32%), hyperactivity (44% vs 29%), daytime somnolence (25% vs 14%). Moreover after an ENT evaluation 75% of the children in group A children resulted affected by adenotonsillar hypertrophy, 42% by ogival palate and 28% by dental malocclusion.
Conclusions: Our data demonstrated that adenotonsiilar hypertrophy increases SDB by 6 times. Parental smoking increases SDB of 4 times. No association was found with obesity.Cardiorespiratory monitoring as well as clinical, ENT and odontoiatric evaluation should always be carried out in children with a suspect of SDB.

0358.G

Drug History and Psychological Distress Affects Sleep and Daytime Sleepiness in Adolescents

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Introduction: The present report examines the relationships between sleep/daytime sleepiness with drug history and measures of psychological distress in adolescents with a history of substance abuse. This is part of a larger study to develop a treatment for sleep disturbance and daytime sleepiness as a means of reducing drug abuse relapse in adolescents. Only baseline measures are presented in this report.
Methods: Baseline measures were assessed for 15 participants, 5 females and 10 males between the ages of 14 to 17, who recently completed a two to four month outpatient substance abuse treatment program and who reported problems with sleep or sleepiness. Assessment instruments included the Global Assessment of Individual Needs: Substance Problem Index – Initial (GAIN-I), Epworth Sleepiness Scale, Penn State Worry Questionnaire, and a subjective daily sleep diary. Severity of drug problems and internal mental distress were assessed using the Substance Problem Index and the General Mental Distress Index of the GAIN-I. To reduce Type II error, results are reported for $p < .10$.
Results: Initial correlation analyses suggest that sleep and mental health are negatively impacted by drug use. Specifically, higher scores on the Substance Problem Index were marginally correlated with sleep efficiency ($r = -.45$, $p = .09$). High scores on the SPI represent greater severity of drug problems, as measured by physiological, psychological and social criteria, and are correlated with lower sleep efficiency which is determined by dividing the total sleep time by the actual time spent in bed. Prior preferred use of stimulants were associated with significantly higher scores on the SPI and marginally longer sleep onset latency than was preferred use of depressants (one-way ANOVA; $F = 4.8$, $p < .05$; $F = 3.5$, $p = .08$, respectively). The data also indicate that mental health distress affects normal sleep patterns. As mental health distress increases, sleep efficiency suffers ($r = -.45$, $p = .09$). Mental health distress was associated with a higher rating on the Penn State Worry Questionnaire ($r = .47$, $p = .08$). Overall, females had significantly lower sleep efficiency, longer sleep latency and were more likely to report lower sleep quality than males (one-way ANOVA; $F = 9.1$, $p < .05$; $F = 4.6$, $p = .05$; $F = 3.3$, $p = .09$, respectively).
Conclusions: The results suggest that drug use and mental health may affect normal sleep patterns. As scores increase on the Mental Distress Index and on the Substance Problem Index, sleep efficiency decreases. However, this is preliminary data and caution in drawing conclusions is warranted.

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0359.G

Cyclicity of Neonatal Sleep Behaviors at 25 to 30 Weeks Corrected Gestational Age

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Introduction: Sleep studies of extremely preterm neonates (< 28 weeks gestational age) suggest that coincidence among physiologic behaviors only is expressed only after 28 to 30 weeks gestational age. Studies of sleep state cyclicity of these behaviors at this age-range of prematurity have not been widely reported.

Methods: Our neonatal sleep consortium includes 350 neonates, with a subset of 33 extremely preterm infants who received their first of multiple EEG-sleep recordings beginning at corrected ages of 25 to 30 weeks. The entire cohort was comprised of both healthy and medically sick neonates recruited from the neonatal services in three obstetrical centers in Pittsburgh, Cleveland and North Carolina. One trained neonatal polysomnographer assigned EEG-sleep states (including epochs of discontinuous EEG), arousal durations and REM numbers over the 2 to 3 hours of each recording, which was entered into a relational database. Time intervals during which REM and epochs of EEG discontinuity were calculated, and these time durations were processed by an autocovariance function to estimate if a dominant periodic signal was expressed over the total recording time for each subject.
Results: A mean sleep cycle duration was estimated to be 68 minutes (+ 19 minutes, range 37 - 100 minutes) for the REM - EEG discontinuity for 24 neonates, beginning at 25 weeks corrected gestational age. The remaining nine neonates did not have sleep cyclicity either because they failed to express REM and/or EEG discontinuity, or expressed a chaotic sleep structure without reproducible intervals of REM - EEG discontinuity.
Conclusions: Sleep state cyclicity is expressed for a majority of neonates at 25 to 30 weeks corrected gestational age, reflecting an ultradian biologic rhythm of sleep in the immature brain. We are now investigating the presence of sleep state cyclicity in relationship to maternal-placental-fetal-and neonatal medical factors.

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0360.G

A Prospective Study on the Prevalence of Sleep Related Disorders in Children with Epilepsy

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Introduction: Sleep disorders in children are common, and are likely more common in children with neurologic disorders such as epilepsy. Obstructive sleep apnea has an incidence of approximately 1-3% in the pediatric population. This condition, as well as other conditions affecting sleep, such as, the upper airway resistance syndrome, periodic leg movements, insomnia, snoring, and excessive daytime sleepiness are believed to be under-diagnosed in the pediatric population. Prior outcome studies identified several unfavorable factors, such as, school failure, mental health conditions, hyperactivity, low IQ and other psychosocial pathologies in children with epilepsy. Sleep problems may also potentially adversely affect daytime behavior, attention and cognitive achievements. There is a clear reciprocal relationship between sleep and epilepsy. Adult studies have shown that treatment of SDB improves seizure control. There have been few studies documenting the incidence or prevalence of potentially treatable sleep disorders in children with epilepsy.
Methods: Children with Epilepsy between the ages of 2-18 years, who visited the Epilepsy Clinic at the Hospital for Sick Children (HSC), were screened using a validated Pediatric Sleep Questionnaire. This questionnaire is used to predict children at risk for chronic sleep disordered breathing (SDB), insomnia (INS), and periodic leg movements (PLMS) during sleep or excessive daytime sleepiness (EDS). The age of seizure onset, the frequency of seizures, the seizure type (partial vs. generalized), the number of anti-epileptic agents being taken at the time of evaluation, and the weight of the children were also requested. An attempt was then made to determine if there was a correlation between these factors and the sleep problems noted above.
Results: 73 questionnaires were filled out. Over 1/4 of the patients were at increased risk for SDB, and twice as many habitually snored. This increased risk was independent of age, age of seizure onset, frequency of seizures, and number of medications taken. A trend was however seen towards an increased risk for SDB in children on 3 or more antiepileptic agents and with more than 4 seizures per month. An overall increase in other sleep abnormalities was also found.
Conclusions: This study documents a clear relationship between epilepsy and sleep. Our results suggests that children with epilepsy are disproportionately affected with sleep related disorders (SRD). This is a significant finding, as prior studies have shown that treatment of problems affecting sleep can significantly improve grades and behavior. Detecting and treating SRD could therefore potentially improve cognitive and behavioral problems faced by children with epilepsy.

0361.G

Sleep Disordered Breathing (SDB) In Obese Children: The Southern Italy Experience

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Introduction: In adults, obesity is a strong, well-documented risk factor for sleep apnoea and those with a body mass index (BMI) greater than 28 are more likely to develop OSAS than those with a lower BMI. Although a similar experience has been recently published in childhood (Am J Respir Crit Care Med.1999;159:1527-32), obesity is still not widely considered as risk factor for sleep disordered breathing in this age group. We have conducted in a large cohort of Italian children, an epidemiological survey on the sleep related disorders aimed to the definition of the prevalence of, and risk factors for SDB.
Methods: 1207 pre-school aged children of Southern Italy were screened by a self-administered questionnaire aimed to select children with a history suggestive of sleep breathing anomalies. Questionnaires were scored allowing the classification of children in “non snores”, “occasional snorers”, and “habitual snorers”. All habitual snoring children underwent a polysomnographic home evaluation and those with an Oxygen Desaturation Index (ODI) greater than two were considered for Nocturnal Polygraphic Monitoring (NPM) allowing the diagnosis of Obstructive Sleep Apnea Syndrome (OSAS) (Apnea/Hypopnea index above 3). All children underwent an accurate nutritional assessment and were defined obese as the BMI exceeded the 95th percentile for age and sex reference values (Arch Pediatr Adolesc Med. 1991;145:259-63).
Results: 895 (74.2%) questionnaires were returned and we identified 710 children (79.3%) “non snores”, 141 (15.8%) “occasional snorers”, and 44 (4.9%) “habitual snorers”. Fourteen children were diagnosed as having OSAS by NPM and 70 subjects (7.8%) were obese. Among the obese children 52 (7.3%) were “non snores”, 16 (11.3%) were “occasional snorers” and 12 (27.2%) were “habitual snorers” (non snorers vs. habitual snorers: $p<0.0001$; occasional snorers vs. habitual snorers: $p<0.01$). Obesity increases the risk of habitual snoring of more than 4 times as compared to non-obese children (RR: 4,0; Odds Ratio: 4,7). Six out of 14 children with OSAS were obese as compared to 8 out of 30 who did not have OSAS (43% vs. 27%; $p<0.04$). Thus obesity increased the risk of having OSAS of almost five times (RR: 2,5; Odds Ratio: 4,8). We found no correlation between BMI and Apnea/Hypopnoea index.
Conclusions: Our data on a large cohort of children clearly demonstrate that being overweight does increase the risk of snoring and more importantly of having OSAS. Nowadays, the prevalence of obesity in children and adolescents is raising; implementing prevention programs for the treatment of obesity in youngsters is mandatory also because it may help to prevent SDB in childhood.

0362.G

Iron Deficient Anemic Infants Have Decreased Rapid Eye Movements Density In Active Sleep

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Introduction: Iron is critical for several brain functions involved in sleep regulation (neurotransmission systems, myelination, and neuronal metabolism), thus iron deficiency anemia (IDA) in infancy might alter sleep development (Peirano P et al: Interaction of iron deficiency anemia and neurofunctions in cognitive development. In: Nutrition and Brain, 2001,19–39). Since rapid eye movements (REMs) density within active sleep (AS) appears to correlate with cognitive development, a domain usually altered by early IDA, REMs density in AS could be particularly affected in IDA infants. Therefore, we assessed REMs density within AS in infants with IDA.
Methods: In a case-control study,polysomnographic recordings were performed in the laboratory during naturally occurring naps in a group of otherwise healthy 6-mo infants who presented IDA (n=21) or were nonanemic (controls, n=14). Both groups were comparable for known confounding variables such as socioeconomic and maternal characteristics, and home environment. Sleep-wake states were determined by combining usual behavioral and EEG, EOG and EMG criteria. The EOG signal during AS was processed off-line by an automated system in order to detect the beginning and end of each REM; the detection was then edited for visual confirmation. For each infant the following parameters were determined: (a) duration of AS episode; (b) index (number/min) of isolated and (c) non-isolated (at least 2 separated by no more than 0.5 sec) REMs; (d) mean duration of isolated and (e) non-isolated REMs; (f) mean number of REMs within non-isolated REMs episodes; (g) mean duration of non-isolated REMs episodes; and (h) percentage of AS time spent with REMs.
Results: The duration of AS episodes was similar in both groups. The indexes of isolated and non-isolated REMs were higher in controls than in IDA infants (18.2 vs 13.3, $p<0.01$, and 3.7 vs 2.7, $p<0.01$, respectively). There were no significant differences between groups with respect to durations of isolated and non-isolated REMs, number of REMs within non-isolated REMs episodes, and duration of non-isolated REMs episodes. The percentage of AS time spent with REMs showed a suggestive tendency ($p <.08$) to be lower in IDA infants relative to controls (5% vs 8% respectively).
Conclusions: Our results indicate that (a) the density of both isolated and non-isolated REMs within AS are decreased in IDA infants, and (b) iron is critical for the organization of this sleep state. We speculate that a reduction in REMs within AS may represent a contributing factor for altered cognitive development in IDA infants.

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0363.G

The Development of Diurnal Rhythmicity in Co-sleeping and Solitary-sleeping Infants

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Introduction: The purpose of this investigation was to examine the early development of diurnal rhythms in sleep and melatonin and how the environmental contexts of co-sleeping and solitary sleeping may influence these rhythms. It was hypothesized that co-sleeping infants would display rhythms earlier and/or stronger than solitary-sleeping infants. There is considerable evidence that mothers influence the diurnal rhythms of their offspring in non-human mammals, so it would not be surprising to find the same in humans.
Methods: Participants were 18 families (8 co-sleeping, 10 solitary sleeping). All infants were healthy at the time of study, were breastfed on demand, full-term, and had no pre or postnatal complications. Infants were studied for 72 continuous hours at 1 and 3 months of age. Sleep and wakefulness were measured through actigraphy, and the melatonin metabolite, aMT6s, was collected through diapers. Parents also filled out a sleep-wake diary and a light exposure questionnaire to get a rudimentary idea of how much light the baby had experienced since birth.
Results: All infants displayed a statistically significant sleep-wake rhythm at 1 and 3 months of age. In contrast, only 5 of the 18 (28%) infants displayed a significant melatonin rhythm at 1 month, but 14/18 (78%) had one by 3 months. Both the melatonin and sleep-wake rhythms significantly increased in robustness from 1 to 3 months of age. In addition, the 3 infants whose parents typically used a bright light source at night had significantly less robust melatonin rhythms at 1 month. (It should be noted that during the study period, parents were requested NOT to use a bright light so as not to suppress melatonin.) There was some indication that the sleep-wake rhythm also was less robust in these infants. There were no significant differences in diurnal rhythms between co-sleeping and solitary-sleeping infants, but the numbers were in the hypothesized direction for the sleep-wake cycle.
Conclusions: Although the main hypothesis was not confirmed, data were in the hypothesized direction. Statistically significant differences may not have been found due to the small sample size. The developmental increase in robustness of the melatonin and sleep-wake rhythms found in extant research was replicated. In addition, the data revealed some interesting results with regard to the effect of nighttime bright light on developing rhythmicity in early infancy. The results are compelling, and should be pursued with a larger sample size in future work.

0364.G

Impact of Behavioral Pediatric Sleep Interventions on Parental Stress and Consumer Satisfaction

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Introduction: Disturbed sleep has been consistently identified among the most common concerns presented in clinical settings for children. Anecdotal reports link ongoing struggles to resolve a child's sleep problem with increased stress, however, no study to date has directly measured the effects of interventions for children's sleep on parenting stress. The purpose of this study was to examine the impact of behavioral interventions for common sleep difficulties on parental stress levels and overall consumer satisfaction.
Methods: Participants included 35 parents and their children (24 male; 11 female: mean = 5.7 yrs; s.d. = 4.2) referred by their primary care physician for sleep disturbance. Top reasons for referral included night-waking (31%), disrupted sleep schedule (28%), bedtime resistance (17%), parasomnias (11%), and night fears (6%). Each participant completed a pre-treatment assessment packet prior to scheduling the intake appointment. The packet contained standardized behavioral and pediatric sleep scales, a sleep diary, and Parenting Stress Index-Short Form (PSI-SF). Upon discontinuation of services, each family completed a post-treatment packet on the child's sleep and behavior (to be reported in a separate study), parenting stress, and consumer satisfaction with the clinic. Empirically-supported behavioral interventions were individually tailored to the unique characteristics of the child's sleep disturbance in accordance with family-centered care. Typically, families met their treatment goals within two to three appointments unless additional mental health concerns were identified. The Parenting Stress Index-Short Form (PSI/SF) is a 36-item screening instrument with demonstrated validity and reliability in measuring sources of stress in parents with children

between 1 month and 12 years of age. The PSI-SF consists of a Total Stress score, a Defensive Responding score, and three subscale scores: Parental Distress, Parent-Child Dysfunctional Interaction, and Difficult Child. The Parent Consumer Satisfaction Questionnaire (PCSQ) has been used extensively in research on treatment satisfaction. The PCSQ consists of 15 items, with higher scores (range = 11 to 77) indicating greater satisfaction with the intervention procedures.
Results: Pre-treatment data for PSI-SF indicated that both the Difficult Child (Mean = 26.8) and Total Stress scores (Mean = 85.4) fell in the clinical range (> 85 percentile), indicating that parents of children referred for sleep disturbance show clinically elevated levels of parenting stress. Both scores dropped to within average range of parenting stress at post-treatment (t-tests; $p < .01$). Responses on the PCSQ indicated that parents endorsed high levels of consumer satisfaction with the behavioral interventions used to resolve their child's sleep disturbance (Mean score = 65.9; s.d. = 7.1). Comparatively, this mean score is slightly higher than parental satisfaction ratings of methylphenidate treatment for Attention Deficit Hyperactivity Disorder.
Conclusions: Parents attending a behavioral pediatric sleep clinic exhibited clinically elevated levels of parenting stress upon referral. Overall parenting stress was significantly reduced to within normal levels following the implementation of brief behavioral interventions to address the child's sleep disturbance. Parents also reported high levels of overall consumer satisfaction with the interventions employed.

0365.G

Association Between Aggressive Behavior and Sleep Disorders in Elementary School Brazilian Children

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Introduction: About 35 to 45% of school-aged children have sleep disorders according to questionnaire surveys obtained from a variety of population sample around the world. It is important to differentiate what is a normal behavior associated to sleep habits and abnormal phenomenon caused by sleep disorders. Many studies assess psychological and behavioral disturbance in the sleep disorders scenario, but we have few researches on specific emotional problems that could be associated to sleep disorders. Some children seem to be adapted to his/her sleep problems, but when we take a look over his/her behavior we can find problems mostly in the field of aggressive behavior, impulsive behavior, anxiety, mood disorders, attention disorders. Many studies have also reported sleep breathing disorders (SBD) in children to be associated to aggressive behavior. The goal of this study is to verify the association between general sleep disorders (GED) and aggressive behavior (AB) in the public elementary school in Brazil.
Methods: The sleep of 835 children of public schools of Sao Paulo City, Brazil, was evaluated throughout the sleep questionnaire adapted from Bruni et al (1996). The children were divided in groups: general sleep disorders (GSD) and normal sleep (control group - CG). The sleep disorders include: Disorder of Initiating and Maintaining Sleep, Sleep Breathing Disorder, Disorder of Arousal, Sleep Wake Transition Disorder, Disorder of Excessive Somnolence. The general emotional disorders (GED) were assessed throughout the Bender Gestalt Test. The data were analyzed for the association of GED and AB with GSD and SBD in relation to the CG, taking in account the age (8, 9 and 10 years). GED group consisted of all kind of ED detected in our sample, and because it is stressed in the literature, we pick up the AB subgroup for a specific analysis. We compared the results from GSD and SBD with the CG considering the presence or absence of GED and AB .
Results: The proportion of GED was similar between the two groups: GSD (98%) or SBD (98%) and CG (95%). Nine years old group showed a trend to have more children with GED (GSD: 97%; CG: 93%; p=0,08). The 10 years old children with GSD (52%) presented more AB than the CG children (52%, 34% respectively, p=0,009) but the children with SBD did not present more AB than CG (54%, 40% respectively, p=0,5).
Conclusions: The older children with GSD presented more AB than children of other ages, however when we considered only the group with SBD, the number of children with the AB did not differ from the CG. It is not possible to know, in this preliminary study, if the AB is caused by the GSD or the opposite, but we know for sure, based upon our data, that SBD and AB are not tied together in school aged children.

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0366.G

Children's Sleep Patterns At 8 Months Of Age: Actigraph Assessments, Parent Reports, And Associations With Maternal Characteristics

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Introduction: Objective data on children's sleep patterns during the first year of life are relatively rare, and have typically been collected on small samples. The introduction of actigraph technology for the assessment of sleep and wake states makes data collection in this age group more feasible. We examined 121 children at 8 months of age who were participating in a longitudinal study of maternal depression, parenting beliefs and practices, and children's development. Eight months of age was chosen as the first assessment point for actigraphy because it is believed to be a time when many children have consolidated their sleep into regular diurnal patterns with few night wakings, while other children maintain less organized patterns that are more disruptive of family life.
Methods: Pregnant women were identified prenatally, and evaluated for psychopathology. Mothers were queried about their own sleep habits and expectations regarding their soon-to-be-born child's sleep. At 4 months of age, mothers completed a sleep diary, a child sleep habits questionnaire, and a sleep expectations questionnaire. At 8 months of age, mothers again completed the sleep diary and sleep expectations questionnaire. Children were monitored for at least 1 week (and usually for 2 weeks) using Ambulatory Monitoring Systems actigraphs. Sleep and wake were scored using the infant algorithm developed by Sadeh – only children with at least 5 nights of scorable sleep were considered in this report. Children's temperament was measured by direct observation in the home on 8 separate occasions over a 2-week period, resulting in aggregate measures of mood, activity, intensity, and approach. Family functioning was assessed via structured interview and direct observation of family meals.
Results: Reliability of measures across the nights was variable (ICC for # sleep minutes was lowest at .34, sleep efficiency, # wake episodes, # wake minutes, longest sleep had ICC between .54-.71). Descriptive statistics: sleep minutes (M=596, SD=68, range 469-895); sleep efficiency (M=.94, SD=.03, range .86-1.0); # wake episodes (M=2.9, SD=1.23, range .69-8.1); # wake minutes (M=28, SD=17, range 4-104); longest sleep (M=279, SD=81, range 116-574). Sleep habits diaries and questionnaires were related in expected ways to actigraphy; correlations were typically .30-.50. Mother's negative expectations about children's sleep, even during the prenatal period, were associated with less organized sleep at 8 months of age. Children's temperament (activity only) was associated with longest sleep episode, but not with sleep efficiency or night waking. Family functioning was associated with higher longest sleep. Maternal depression was unrelated.
Conclusions: Infants' sleep at 8 months of age had a high degree of individual differences. Day-to-day stability of actigraph measures was generally moderate to high, with the exception of number of sleep minutes. Infant activity level was associated with the activity-based measures derived from actigraphy, but not in a manner that suggested a methodological confound. Family processes were associated with some sleep

parameters.

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0367.G

Prenatal Alcohol: Neonatal Sleep Organization And Spontaneous Movements

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Introduction: Pre-pregnancy levels of alcohol intake and years of alcohol use are associated with alcohol intake during pregnancy. In our previous study of this population of poor, white pregnant women from Northern Maine the prevalence of pre-pregnancy alcohol abuse was found to be 25% (Hayes et al., 2002). The hypothesis of the present study was that patterns of maternal alcohol use have neurotoxic effects that are revealed in the characteristics of sleep and spontaneous movements during the neonatal period and these results would concur with standard developmental assessments.
Methods: Pregnant women were recruited for a longitudinal follow-up study and interviewed for alcohol ingestion during the perinatal period using the quantity-frequency-variability method, Michigan Alcohol Screening Test (MAST) and TWEAK and T-ACE measures. Mother-infant dyads were examined on several measures postnatally during well-child checkups. Sleep and Movement Assessments. Infants are brought in for a scheduled nap conducted in our hospital laboratory. Sleep organization was measured using electroencephalography (EEG), actigraphy (10 mm x 10 mm x 10 mm piezoelectric sensor placed beneath the infant's body centered at the scapula and reaching from the lower head to the buttocks) and phase-locked, infrared videography. Infants were permitted to awaken from the nap spontaneously. Behavioral state was coded from the videography using standard methods.Movement Bout Analyses. The temporal structure of movement bouts was examined by three methods using the same algorithm. The absolute value of the digitized output was interpreted as indicative of movement and the mean movement change from zero was standardized for each subject separately. The data stream was binned into 6 sec, 12 sec or 1 min bins. The bout structure analysis yielded a measure of the number, average duration and maximum duration for each infant during the nap. Quiescence bout structure is analyzed in a mirror fashion. Developmental Assessments. Neonatal Behavior Assessment Scale was administered at 30 days. At 6 months the Bayley Scales of Infant Development-II was administered.
Results: Preliminary results of both pre-pregnancy and during-pregnancy estimates of alcohol use yielded significant associations with sleep and spontaneous movements parameters. Absolute alcohol per day (AA) and binge drinking (AA per drinking day) predicted less quiet sleep (QS), higher percent and number of epochs of active sleep (AS) and drowse (D), and more state transitions. Number of arousals and longer nap duration were increased in infants of mothers with a lifetime history of high alcohol use (MAST) and tolerance TWEAK ,T-ACE). Spontaneous movements analyses revealed disrupted movement bout structure characterized by shortened duration of quiescence periods.
Conclusions: Both dose-dependent exposure estimates and alcohol use history were found to modify neonatal sleep organization and spontaneous movements during daytime naps. The implications will be discussed in relationship to abnormal CNS development and relationship to NBAS and Bayley Scales developmental assessments.

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0368.G

Treating Sleep Problems of Adolescents with a History of Substance Abuse

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Introduction: This is the first report of outcomes from a project to develop a multicomponent, group treatment of sleep disturbance and daytime sleepiness for adolescents who have been in treatment for substance abuse. Sleep disturbance and daytime sleepiness are frequent consequences of both substance abuse and withdrawal from habitual substance use. This report focuses on sleep diary and questionnaire measures for the first 10 adolescents to complete the treatment program.
Methods: Ten adolescents (six males and four females) between the ages of 14 and 18 participated in six hour and a half, group treatment sessions over eight weeks. Participants kept daily sleep diaries and filled out questionnaires at baseline and post-therapy. The first session focused on sleep education. Subsequent sessions were divided with the first half focused on sleep and sleepiness strategies and the second half of mindfulness-based stress reduction (MBSR). The sleep intervention components included sleep hygiene education, attention to circadian rhythm problems (particularly phase delay), stimulus control instructions, cognitive restructuring, and relapse prevention. The MBSR component was modeled after a well-established stress reduction program, mindfulness-based stress reduction (MBSR), developed by Kabat-Zinn and colleagues at the University of Massachusetts Medical Center (Kabat-Zinn, 1982).
Results: Participants improved substantially on sleep diary measures telephoned daily into a voice mail system. This included improvement on sleep efficiency (pretest and posttest means of .873 and .912, p=.01), sleep onset latency (means of 34.01 and 19.4 min., p=.106), number of awakenings (means of 2.68 and 1.9, p=.025), total sleep (means of 433.7 and 501.3 min., p=.057), ratings of quality of sleep (means of 2.75 and 3.4, p=.003), and ratings of whether the night was better or worse than usual (means of 1.98 and 2.3, p=.046). There was no significant improvement on either the Penn State Worry Questionnaire or the Epworth Sleepiness Scale.
Conclusions: These results indicate that a multicomponent group intervention can produce substantial effects in improving sleep even with what might be considered a resistant population, adolescents who have been in treatment for substance abuse. Measures that will complement the above results, including actigraphy and dim-light-melatonin-onset have been collected, but not yet analyzed. In addition, data from three month and one year follow-ups will provide information about whether improvement in sleep lowers the risk for substance abuse recidivism.

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0369.G

Sleep-Breathing Disorders in Asthmatic Children Residents of Mexico City

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Introduction: It has been reported that there is a relationship between sleep-disordered breathing and respiratory daytime symptoms in children. Asthma prevalence is increasing in Mexico as it is in many other countries, and the associated sleep disorders in this group of patients is frequently under diagnosed. The aim of our study was to determine the

prevalence of snoring and sleep apnea in asthmatic children in Mexico City. We also wanted to explore if there was an association between asthma severity and nocturnal asthma, with the occurrence of breathing disorders during sleep.
Methods: This is a prospective, descriptive study which recruited 2-12 years old children with a established diagnosis of asthma. A questionnaire exploring respiratory symptoms, snoring and sleep habits was applied and answered by the parents. All subjects underwent an oral physical examination. Patients with a non-controlled systemic disease were excluded.
Results: The sample consisted in 193 questionnaires of children attending at least 6 months the Asthma Clinic of the Respiratory Diseases Hospital. 56.5% were boys, and 43.5% were girls. The mean age of the group was 6.9 ± 2.7 years. The mean weight was 28± 11.5 kg.Asthma severity was considered mild in 79.8%, and moderate to severe in 20.2%. With respect to sleep habits, 23.3% presented resistance to sleep at night. 27.5% experimented difficulties to awake. 15% were reported of being irritable during daytime. Oral breathing was reported in 19.7% of the sample. Tonsil's examination was divided according to size as follows: G0: 17 (8.8%), GI: 68 (35.2%), GII: 90 (46.6%), GIII: 18 (9.3%).Habitual snorers were 35 (18.1%), 12 of them (6.2%) were reported to have witnessed apneas. In this group a large proportion had asthma symptoms more than once a week, wheezing was reported in 57% and cough in 80%. Daily asthma related cough, was referred in 8.3% of the apneic group, 8.6% of the habitual snorers group, and in 2.2% in the non-snorers. Waking during the night because of asthma symptoms more than once per week, was reported in the habitual snorers group in 65.8%, in the apneic group in 75%; and in the non-snorers group in 48.3%. With respect to asthma severity and sleep habits, there was a mild correlation with irritability (0.2), difficulty to awake (0.2) and resistance to sleep (0.16). However, tonsil did not correlate with asthma severity.
Conclusions: Prevalences for habitual snoring (18.1%), and suspected apnea (6.2%), in this sample are higher than in general non asmathic population. There is a relationship between asthma severity and sleep-breathing disorders. Furthermore, nocturnal asthma and frequent awakenings appear to be associated with snoring and witnessed apneas, in a higher proportion than the observed in non-snorers. Asmathic children have disturbed sleep habits.

0370.G

Night Waking and Sleep Onset Patterns in Young Children: A Longitudinal Study

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Introduction: Several studies using parental self-report of a child's sleep patterns suggest considerable continuity in sleep problems in pediatric subjects. This has led many sleep clinicians to advocate strongly for certain practices without an understanding of the effect of parental concerns and developmental change in diagnosing and treating a sleep disorder. It is unclear whether an objective measure of a child's sleep in the first year of life or the practice of co-sleeping can predict the chronicity of a sleep problem. As part of a larger longitudinal study, we examined the potential predictors of sleep disturbances in early childhood. We revised an existing classification system to better account for individual variability and to align more closely with accepted criteria for functional impairment of sleep disorders in children. We hypothesized that the absence of self-soothing and the presence of co-sleeping at 12 months would be predictive of a sleep disorder at 2 and 3 years of age.
Methods: Video observations obtained at 12 months of age were coded for night awakenings and parental response to derive the self-soothing variable. Children who were co-sleeping at least half the night for 5 out of 7 nights a week were identified as "co-sleepers" at 12 months. At 2 years (T2) and 3 years (T3), a follow-up phone interview was conducted using an adapted version of the Sleep Habits Questionnaire. The children were identified as having a sleep onset disorder, night waking disorder, both, or no disorder. 83 families were initially enrolled in the study; 89% participated at 2 years and 82% at 3 years.
Results: A sleep onset disorder was present in 11% of the subjects at T2 and 9% at T3. Night waking disorders were equally prevalent at 2 years (12%) but declined to 3% at 3 years ($2 = 18.2$, $p < .01$). Very few children were reported to have both a night waking and a sleep onset disorder (2% at T2, 0 at T3). Surprisingly, neither co-sleeping nor the absence of self-soothing at 12 months was associated with a disorder at either follow-up assessment. Parental report of a sleep problem agreed with the classification system in 67% of the subjects at T2 but there was only a 25% agreement at T3. Considerable change was noted in the co-sleeping patterns of families over time. While 19% and 30% of the sample reported co-sleeping at 2 and 3 years, respectively, only 7% were continuous co-sleepers from 1 to 2 years, and 12% were identified as co-sleeping at 1 and 3 years.
Conclusions: The study findings indicate the importance of identifying and interpreting parental concerns, creating a more valid classification system to be used for a screening tool in pediatric care, and understanding the other factors that may contribute to maintaining a young child's sleep disorder.

0371.G

Sleep Disordered Breathing and Prevalence of Parasomnias in 6-12 Year Old Children-The Tucson Childrens Assessment of Sleep Apnea Study (TUCASA)

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Introduction: Sleep disordered breathing (SDB) in children can be associated with excessive daytime sleepiness (EDS), frequent snoring (SN), and neurocognitive deficit. However, the prevalence of parasomnias associated with RDI has not been evaluated in a community sample of children using full polysomnography (PSG). The TuCASA study utilizes home PSG to determine the relationship between SDB in children and symptoms, physiologic/anatomic risk factors, and performance on neurobehavioral measures.
Methods: Parents of all children in 14 Tucson elementary schools were asked to complete a 13-item survey inquiring about sleep symptoms attributable to SDB. On the survey, parents were asked whether their child snored loudly, was sleepy during the daytime, fell asleep at school or while watching television, or if their child had trouble staying awake during the day. SN or EDS was present if these symptoms occurred 'frequently' or 'almost always'. Parents of children who met the study criteria were asked if their child would permit an overnight, unattended recording of their sleep. Polysomnograms were obtained with the Compumedics PS-2 system and were scored according to recently published criteria. On the night of the PSG, a Sleep Habits Questionnaire (SHQ) was completed by parents which asked questions pertaining to parasomnias, such as frequency of bedwetting, frightening dreams, sleeptalking, and sleepwalking. Enuresis (EN) and sleeptalking (ST) were present if they occurred more than 5 times per month. Sleep terrors (TR) were present if the child awoke at night afraid and crying but did not remember a dream more than 5 times per month. Sleepwalking (SW) was present if it occurred more than 3 times per month. Respiratory Disturbance Index was defined as the number of apneas and hypopneas per hour of sleep with no associated oxygen desaturation.
Results: The survey response rate was 30.6%. Of the 363 subjects completing a PSG, 49.6% were males and 44.1% were Hispanic with a mean age of 8.8 years (range 6-12). The mean RDI was 5.4 (sd 4.9). The prevalence of EN, TR, SW, and ST was 7.2, 2.8, 2.5, and 11.3 percent

respectively. Children with SN were more likely to have report of EN (14.3% vs 5.8%, p<.03), TR (10.2 vs 1.6, p<.001), and ST (18.4% vs 10.2%, p<.09). EN, TR and SW were not associated with RDI, however, there was a significant association between RDI greater than 6 events per hour and ST (16.4% vs 8.9%, p<.04).
Conclusions: In this population based sample of children ages 6-12 years, frequent snoring is significantly associated with enuresis and sleep terrors. Children with an RDI of > 6 events per hour are more likely to report sleeptalking than children with and RDI<6.

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0372.G

Melatonin Improves Sleep-Wake Schedule, Social and Behavioral Manifestations in Young Healthy Children with Delayed Sleep Phase Syndrome (DSPS)

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Introduction: A substantial number of patients with delayed sleep phase syndrome (DSPS) reported that the onset of DSPS occurred in their early childhood or adolescence. It is widely accepted that DSPS patients respond favorably to melatonin therapy. Notwithstanding, there are no previous reports, to the best of our knowledge, concerning treatment of DSPS in otherwise healthy children with melatonin. The reports that exist deal only with disabled children such as those with severe psychomotor retardation or blind children. We present data regarding melatonin therapy in young children with DSPS who were otherwise healthy.
Methods: Between December 1st, 2001 and November 30th, 2002, 17 children, aged 5.3 to 11.8 years (8.9 $\pm$ 2.2 years), 8 boys and 9 girls, form the Institute for Fatigue and Sleep Medicine, Sheba Medical Center, Israel, were suspected on clinical grounds as having DSPS and were referred for actigraphy of one week duration with non-restricted schedule.
Results: All 17 children (100%) were reported to have difficulty in falling asleep, 13 children (76%) had difficulty waking up. 15 children (88%) manifested excessive daytime somnolence that affected their achievements in the kindergarten and school. 12 children (71%) were having attention deficit, hyperactivity or behavioral difficulties that affected their social status among peers. 12 children (71%) were under professional supervision of pediatric neurologist, psychiatrist or psychologist. 15 children (88%) performed actigraphy, all of them (100%) had results compatible with DSPS. They fell asleep at 24.8 $\pm$ 1.7 o'clock and woke up at 9.6 $\pm$ 2.1 o'clock, requiring an average of 9.1 $\pm$ 0.7 hours of sleep. Melatonin therapy was prescribed to all 15 patients, however, only 11 children (73%) complied, taking either 3 or 5 mg per day. Melatonin was taken for 2.6 $\pm$ 1 months. 10 out of the 11 children (91%) responded favorably to melatonin, sleep-wake schedule became organized and educational, behavioral and social problems resolved, according to parents' reports. No side effects were reported.
Conclusions: The diagnosis of DSPS should be considered in children with day time somnolence, social, educational and behavioral difficulties. Clinical diagnosis of DSPS in children can be quite accurate, and actigraphy helps in establishing the exact schedule and assessing the specific child's sleep requirements. Melatonin seems to be efficacious and safe in treating DSPS in young children.

0373.G

Age-related Changes in Sleep/Wake Patterns of Korean Adolescents

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Introduction: Adolescents go through various biological and psychosocial changes which influence many aspects of sleep. In Korea, adolescents are under great academic pressure related to college entrance examination, thereby possibly making them seriously sleep-deprived. The present study aimed to investigate age-related changes in sleep/wake patterns of Korean adolescents.
Methods: A School Sleep Habits Survey (a modified version of Carskadon¡¯s survey) was administered in homeroom classes to 1,457 Korean students (male 52.9%, female 47.1%) ranging from 5 to 12 grade (aged 10-17 years). The survey included items regarding sleep/wake patterns (both on school days and weekends) as well as various scales (such as daytime sleepiness scale, sleep/wake problems behavior scale, depressed mood scale and morningness/eveningness scale). The subjects were selected by two-way stratification sampling method.
Results: The higher the grade, the later the bedtime on school days (p<.001), whereas bedtime on weekends remained relatively constant across grades. Parental control over bedtime decreased with grade (p<.0001). For wake-up time, the higher the grade, the earlier on school days (p<.0001) and the later on weekends (p<.0001). Total sleep time decreased by about 3 hours (school nights, p<.0001) and 1 hour (weekend night, p<.01) across grades. Especially, 10-12 graders were severely sleep-deprived. Total sleep time (school days) for 10-12 graders was 6.02hr, 5.62hr and 4.86hr, respectively. Higher graders left for school earlier (p<.0001) and showed increased daytime sleepiness(p<.0001). However, there was no significant difference in sleep latency across grades. Higher graders showed more tendency of sleep phase delay (p<.0001), more sleep/wake problems (p<.0001), and more depressed mood (p<0.0001). The main reasons our subjects blamed for their sleep deprivation were different across grades: academic demand and entertainments (such as the Internet and TV) in 5-6 graders; entertainments and then academic demand in 7-9 graders; early school start time and academic demand in 10-12 graders (p<.0001).
Conclusions: The present study clearly showed that most of the Korean adolescents surveyed did not get enough sleep and their sleep hygiene (described by most self-reported sleep related variables) deteriorated with grades. When we compare our results with previous studies in western countries, Korean adolescents are even more severely sleep deprived. Our 10-12 graders¡¯ total sleep time on school days was about 1 hr 30 min shorter than the American counterparts (Wolfson & Carskadon, 1998). The present survey demonstrated that academic demand/stress and early school start time were the most important contributing factors for Korean adolescents¡¯ sleep deprivation. It seems imperative to promote an awareness of the adolescents¡¯sleep deprivation and its detrimental effects in our society.

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0374.H

Edema, Obesity and Obstructive Sleep Apnea: A Cross Sectional Study

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Introduction: Previous research has identified associations among bilateral leg edema, obesity and obstructive sleep apnea (OSA). The present study was undertaken to clarify whether bilateral leg edema is a marker for underlying OSA, independent of level of obesity, in patients with normal left ventricular function.
Methods: Sixty-one ambulatory, obese adults were enrolled, 33 with bilateral, pitting edema, and 28 without edema. Edematous subjects, but not non-edematous subjects, underwent echocardiographic evaluation to ensure that left ventricular function was normal. Spirometry, pulse oximetry on room air, and polysomnography were obtained for each subject.
Results: For most of the subjects with edema, the edema was mild, usu-

ally 1+ or 2+ pitting. Compared to the non-edematous subjects, the edematous subjects were more obese (body mass index = 41.0 ± 9.8 kg/m2 versus 35.7 ± 4.5 kg/m2, p = 0.007), were more likely to use diuretic medication (42% versus 11%, p = 0.006, and had more daytime somnolence (Epworth sleepiness scale = 11.3 ± 5.6 versus 5.6 ± 3.5, p < 0.001). Edema was associated with the severity of obesity, the more obese subjects being more likely to have edema (p = 0.025). Using an apnea-hypopnea index (AHI) > 15 as the criteria for diagnosing OSA, there was no relationship between edema and OSA. Using an AHI or a rapid eye movement AHI > 20 as the criteria for diagnosing OSA, and adjusting for body mass, edematous women were more likely to have OSA than non-edematous women (72% versus 26%, p = 0.005).
Conclusions: If the results of this study are generalizable, for subjects with normal left ventricular function, bilateral leg edema is associated with severity of obesity. In addition, bilateral leg edema may be a marker for OSA in women, but not men.

0375.H

Restricting Time in Bed to 8 Hours Improves Sleep Consolidation in Older Adults

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Introduction: Further research is needed to resolve the discrepancy between the idea that people need at least 8 hours of sleep and evidence that sleeping over 7 hours is associated with increased mortality. We examined the influence of moderate sleep restriction or extension on sleep and mood.
Methods: Volunteers (ages 60-79 years, n=72) were selected for depressive symptoms and/or insomnia and were assessed for one week in their usual environment. Sleep-wake was recorded with actigraphy. Depression was assessed with the Center for Epidemiologic Studies Depression (CESD) scale. Following home recording, volunteers spent 5 nights and 4 days in the laboratory. Time in bed (TIB) was fixed at 8 hours. In the laboratory, actigraphic data provided the most valid comparison to home actigraphic data, but polysomnograms were also recorded. CESD assessments were repeated. At 4 times per day, several 100 mm visual analogue mood scales were assessed including: sadness, sleepiness, alertness, weariness, effort to do anything, and overall mood.
Results: The fixed 8-hour laboratory TIB enabled us to assess the actigraphic sleep changes in subjects whose home TIB was shortened (n=41 with home TIB >8 hr.) or lengthened (n=29 with home TIB <8 hr.). TIB differed 1.75 hours between groups but TST differed by only 19 minutes. There were no significant differences between those with longer and shorter home TIB in subjective sleep quality or depression measured in the home.Long home TIB was reduced by a mean 52 minutes in the laboratory, resulting in a decrease in TST of only 3 minutes. Actigraphic wake after sleep onset (WASO) was decreased by 29 minutes and sleep onset latency (SOL) was decreased by 9 minutes. The reduction of TIB was accompanied by significantly reduced CESD-depression. Visual-analogue scale ratings between laboratory day 1 and day 4 revealed significant improvements in sleepiness, weariness, sadness, tenseness and overall mood in volunteers with long home TIB.In those with short home TIB, a 52 minute increase in TIB in the laboratory resulted in only a 22 minute increase in TST. Actigraphic WASO increased by 16 minutes. Thus, only about 40% of the additional TIB was spent asleep. CESD levels decreased significantly, but the lengthening of TIB resulted in no significant changes in any of the visual-analogue scales. The fixed 8-hour laboratory sleep period produced no differences in actigraphically-recorded sleep between groups whose habitual TIB varied by 1:44. Similarly, there were no polysomnographic differences between those with long and short home TIB in PSG SOL, TST, WASO, SWS, stage 1 or stage 2 sleep.
Conclusions: Much of the TIB in those with long TIB was not necessary for sleep; the restriction resulted in a consolidation of sleep, and did not impair the volunteers in any way. Indeed, TIB restriction produced more improvement in overall mood and sleepiness than laboratory sleep extension.

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0376.H

Melatonin Offset Delayed After Wake in Aging Subjects

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Introduction: In order to compare their circadian phase adjustment, subjects ages 60-79 years with sleep and minor mood complaints were compared with adults ages 20-40 years selected for absence of sleep problems.
Methods: Using Actillume I, wrist activity was recorded at home for a week to infer sleep/wake timing. Then, for 72 hours in the laboratory, subjects underwent an ultra-short sleep-wake cycle of 60 minutes wake (in 50 lux) and 30 min for sleep (lights out in-bed). Samples were collected every 90 min. for salivary melatonin, urinary aMT6s (the 6-sulfatoxymelatonin metabolite), and urinary free cortisol. Circadian phase was estimated from least-squares cosine fits.
Results: Preliminary results are available for 18 adults ages 20-40 and 54 adults ages 60-79. The acrophase timing of home sleep for the younger adults was 04:26 and for older adults 02:52 ($p<0.001$). As anticipated, the younger subjects had higher fitted mean (mesor) salivary melatonin ($p<0.001$) and higher aMT6s ($p=0.06$) as contrasted to older adults. The rhythm amplitudes were highly correlated with the mesors, $r=0.96$ and $r=0.97$ respectively, and showed similar trends.The acrophase (fitted peak) timing of salivary melatonin correlated $r=0.74$ ($p<0.001$) with the acrophase of urinary aMT6s, indicating that both are reasonably reliable phase markers. Moreover, excellent acrophase repeatability was found for separate laboratory studies of subjects 60-79 years, who returned to the laboratory a second time after an average of 5.7 months. Acrophase repeatability was $r=0.91$ ($p<0.001$) for salivary melatonin, $r=0.83$ ($p<0.001$) for aMT6s, and $r=0.80$ ($p=0.002$) for cortisol. This suggests that these are accurate and reliable phase markers. The acrophase of the urinary metabolite aMT6s lags the salivary melatonin acrophase by about 1.55 hours both in subjects ages 20-40 years and ages 60-79, indicating the expected lag for urinary excretion.
As anticipated, nocturnal home midsleep and the acrophases of sleep and cortisol were significantly earlier among the older subjects; however, salivary melatonin and aMT6s did not differ significantly in acrophase by age. As a consequence, both the salivary melatonin and aMT6s acrophases were relatively late (2 hours delayed) in the older subjects, as referenced to cortisol ($p=0.002$) or to sleep.
Conclusions: These are consistent with other data from several laboratories suggesting that with aging, the nightly melatonin elevation is relatively delayed with respect to sleep. One possibility is that the circadian rhythm of the SCN, and its control of pineal melatonin synthesis (SynOff), is not delayed with aging, but delayed metabolism prolongs the morning decline in melatonin receptor occupancy. This could be one cause for development of longer and more fragmented sleep with aging.

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0377.H

Night-to-Night Variability Does not Differ Between Elderly African-Americans and Caucasians

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Introduction: Previous research has suggested that African-Americans have fewer sleep complaints than Caucasians, but that sleep disordered breathing (SDB) may be more prevalent in African-Americans. Other studies have suggested that sleep architecture might differ between races. In order to determine if gender or race would have an influence on night-to-night variability, the present study compared night-to-night variability of sleep and respiratory parameters in elderly Caucasian and African-American men and women.

Methods: As part of a larger study, 56 African-American adults (mean age 74.4, SD=6.5; range=65-89) and 71 age and gender-matched Caucasian adults (mean age 73.9, SD=5.8, range=65-93), with complaints of snoring or excessive sleepiness were recruited. Each had their sleep recorded for two nights with the modified Respitrace/Medilog portable recording system which recorded thoracic and abdominal respiration, tibialis EMG and wrist movement. Sleep was scored for total sleep time (TST), number of awakenings, wake after sleep onset (WASO), number of apneas, number of hypopneas and number of leg jerks. Apnea index (AI) and respiratory disturbance index (RDI) were computed. Two-tailed Pearson correlations were computed to determine the relationship in sleep and respiratory variables, between the two nights. Analyses of variance were computed on the change scores to examine for gender and race main effects.

Results: For all subjects, night 1 sleep and respiratory variables were all significantly correlated to the night 2 variables ($p<0.0001$). Analyses of variance resulted in a gender main effect for AI ($p=0.022$), RDI ($p=0.050$) and number of apneas ($p=0.033$) with men, more than women, showing a significantly greater absolute numbers and a greater change from night to night in all three variables. There were no race main effects.

Conclusions: These results suggest that there is little variability in sleep architecture or in respiratory variables from night-to-night in older adults. There were no differences in night-to-night variability by race. This reinforces that it may be sufficiently reliable to record just one night of sleep when studying sleep disorders in older adults. This may be particularly important for older adults who are less likely to agree to multiple nights of recordings.

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0378.H

Treating Sleep Disturbances in Community Dwelling Alzheimer's Disease Patients: The NITE-AD Study

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Introduction: There is considerable evidence that non-pharmacological interventions can improve the sleep quality of older adult insomniacs. However, there are no controlled trials examining the efficacy of behavioral interventions for reducing sleep problems in community dwelling Alzheimer's disease (AD) patients.

Methods: Subjects were 24 AD patients randomly assigned into either an active treatment or a control condition (mean age = 76.7 years; mean dementia duration = 5.1 years; 54% male; mean MMSE score = 12.0). Subjects had at least one sleep problem on the Neuropsychiatric Inventory (NPI) Nighttime Behavior scale occurring three or more times per week (mean = 3.8 problems). Sleep estimates for patients and their family caregivers (mean age = 63.1 years; 83% female; mean PSQI score = 8.2) were inferred over one week at baseline and again at 2-month post-test using an Actillume Sleep Watch. All subjects completed six one-hour in-home treatment sessions, and received written educational materials describing standard principles of good sleep hygiene. Active treatment subjects were also assisted in developing and implementing a personal sleep hygiene plan, and were placed on a daily walking (30 minutes/day) and timed light exposure (1 hour/day; SunRay light box) program. Control subjects received general dementia education and caregiver support, but no individualized sleep hygiene, walking, or light exposure recommendations or assistance with implementation.

Results: Findings from this ongoing study indicate that active treatment subjects fully complied with sleep scheduling, daily walking, and light box recommendations 90%, 54%, and 71% of the assigned days, respectively. At post-test, active treatment patients had fewer nighttime awakenings (7.9 vs. 10.1), higher circadian quotient of sleep scores (0.73 vs. 0.58), and fewer hours of daytime sleep (1.3 vs. 1.8) than control subjects, although these differences were not significant. Active treatment subjects increased their daytime lux levels 51% at post-test compared to 7% decreases in controls. Active treatment subjects with more disturbed baseline sleep (sleep efficiency .85) showed the greatest post-test improvements in sleep quality. Caregivers in active treatment also self-reported significantly (p .05) lower levels of depression and stress at post-test than controls. The majority of active treatment subjects maintained daily walking and light box use during four months of post-treatment followup, supporting the feasibility of these interventions with dementia populations.

Conclusions: The study provides evidence that nonpharmacological interventions for sleep disturbances with community-dwelling AD patients are possible to implement and may have positive treatment effects on both patients and their caregivers.

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0379.H

The Relationship Between Sleep And Physical And Mental Health In the Elderly

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Introduction: Previous studies indicate that 40-50% of the elderly report symptoms of insomnia and that disturbed sleep is often accompanied by physical and mental illnesses in this population. Therefore, it is important to understand the implications of sleep disturbances on the physical and mental functional status in the elderly.

Methods: 1503 participants were obtained from 10 primary care sites in Illinois primarily serving elderly patients (6 Chicago, 4 outside Chicago metropolitan area). The mean age of participants was 75.5 (±6.8, range 62-100) years, 62% female and a diverse ethnic background. Subjects were interviewed and completed questionnaires including 5 sleep related questions and the SF12 questionnaire. In addition, a systematic chart review was carried out. Based on weighted formula, a Physical Component Summary (PCS12) and Mental Component Summary (MCS12) score were calculated. To maintain consistency with sleep items and scales, PCS12 and MCS12 scales were converted to z-scores based on normative mean and standard deviation.

Results: Approximately 70% of the participants responded positively to at least one of the sleep questions and 40% to two or more. Participants most commonly reported a positive response (45%) to a question about

the "difficulty falling asleep, staying asleep, or being able to sleep". When examined separately both PCS12 and MCS12 status significantly predicted the number and/or type of sleep problems reported. Even if a respondent answered yes to only one sleep problem they were more likely to have a higher PCS12 and MCS12 score. In order to determine what question sequence most efficiently predicted physical and mental health status a forward entry regression model was used. The question that best predicted both PCS12 (R2=0.46, F=72.16, p<0.001) and MCS12 (R2=0.35, F=54.8, p<0.001) was item one "Do you feel excessively sleepy during the day?". Chart review determined that in patients responding positively to 1-5 sleep questions, that a sleep complaint was reported in the chart only 9.2-19.2% of the time. Such that when a patient responded positively to all 5-sleep questions, a sleep complaint was only reported in the chart 19.2% of the time.

Conclusions: In conclusion, this study indicates that when elicited, sleep complaints predict general physical and mental health status in the elderly. However, even for the patients with the most prominent sleep complaints, primary care health professionals rarely identified the sleep problem. Therefore, educational interventions aimed to increase awareness of the importance of sleep in the primary care practice and the need to include questions about sleep in a medical history are essential for improving the health of older adults.

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0380.H

Differences In Sleep Between Older African-Americans and Caucasians

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Introduction: Previous research has suggested that there are differences in sleep variables between young-middle aged African Americans and age-matched Caucasians, with African-Americans sleeping longer and having less fragmented sleep. The present study explored differences in sleep between elder African-Americans and Caucasians at risk for sleep disordered breathing (SDB).

Methods: 70 African-American men and women (mean age=73.69, SD=6.38, range =65-88) and 69 age and gender-matched Caucasians (mean age=73.27, SD=5.71, range =65-93) with complaints of loud snoring and/or excessive daytime sleepiness participated in the study. Sleep was recorded with the modified Respitrace/Medilog portable recording system (thoracic and abdominal respiration, tibialis EMG, and wrist actigraphy). Total sleep time (TST), wake after sleep onset (WASO), and number of wakes (Wakes) were measured controlling for the apnea-hypopnea index (AHI), the oxygen desaturation index (ODI), the body mass index (BMI), and the periodic leg movements in sleep index (PLMSI).

Results: A regression analysis was performed to investigate the relationship between race and TST, WASO, and Wakes, controlling for AHI, ODI, BMI, and PLMSI. The results showed that there were no significant differences in TST between races. However, African-Americans spent more time awake (mean WASO=114.00, SD=65.16, range=6.00-317.45) than Caucasians (mean=95.94, SD=61.45, range=14.35-316.70; F=6.165, p=.014), while Caucasians showed a tendency to have more awakenings (mean=53.90 , SD=39.77, range=11.00-234.50) than African-Americans (mean=45.03, SD=29.23, range=5.00-141.00; F=3.538, p=.062). All differences were independent of the covariates.

Conclusions: The results of this study suggest differences in sleep between older adults of different races vary from that seen in younger adults. It was interesting to note that although Caucasians woke up more frequently during the night, the African-Americans spent more time awake suggesting their awakenings were on average longer. Although all subjects had complaints suggestive of sleep apnea and many had a diagnosis of SDB and/or PLMS, the differences in sleep were independent of these covariates. We continue to examine these data to try to determine what might explain the differences in sleep between the two races.

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0381.H

Subjective Sleep Quality of Caregivers of SDB/Alzheimer's Patients

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Introduction: Sleep disordered breathing (SDB) is more prevalent in Alzheimer's patients than the typical elderly population. With both of these diseases the patient's caregivers often experience sleep problems. As part of a larger protocol, this study examined whether treating sleep apnea in the patient with Alzheimer's disease (AD) would also improve the sleep of the caregiver.

Methods: Nine patients with a diagnosis of AD were recruited to the study. Each had an over-night sleep study for evaluation of SDB and was randomly assigned to either six weeks of CPAP or three weeks of placebo CPAP followed by three weeks of real CPAP. Subjective reports of sleep were evaluated with the Pittsburgh Sleep Quality Index (PSQI) at baseline (pre-CPAP), three weeks and six weeks. The PSQI has a maximum score of 21 with lower scores suggesting better sleep. PSQI was compared at baseline for all caregivers with the PSQI administered after three weeks of real CPAP (week three for the real CPAP group and week 6 for the placebo CPAP group).

Results: In this small, preliminary sample, there was a trend for PSQI scores to be reduced from a mean of 6.8 (SD=2.72, range=3-7) at baseline to a mean of 5.3 (SD=6.31, range=2-12) after three weeks of CPAP (p=0.063).

Conclusions: The data suggest that treating the sleep disordered breathing of the Alzheimer's patients may result in significant improvement in sleep quality of the caregiver. Dealing with the stress of caring for an Alzheimer's patient can be hard to handle and improving the sleep of the caregiver may be beneficial to their overall sense of well-being. Nursing home placement for AD patients often occurs when the caregiver's sleep is so disturbed by the patient that they cannot handle caring for the patient at home any longer. The ability to help improve caregivers sleep efficiently may greatly encourage the use of CPAP, when possible, in patients with AD and SDB. We continue to explore this question.

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0382.H

Sleep Quality Among Peri-menopausal Women: The Relative Contribution Of Hot Flashes, Mood, And Dysfunctional Beliefs And Attitudes About Sleep

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Introduction: Sleep patterns unique to women have been relatively understudied and warrant theoretical and clinical attention. Approximately 40-60% of peri- and post- menopausal women report sleep disruption, however, the nature and etiology of these symptoms are not clearly delineated. While hormonal fluctuations (e.g., hot flashes) may partially explain the difficulties that women experience during this tran-

sition, the contribution of psychological factors are not well understood. We sought to identify the relationship between these psychological factors and sleep quality in order to obtain a biopsychosocial understanding of potential causes and consequences of sleep quality among women, particularly as they approach menopause.
Methods: A mail-in survey study of peri-menopausal women was undertaken to determine the relative contribution of psychological factors compared to physiological complaints (e.g., hot flashes) in predicting sleep quality. Women responded to advertisements placed in local newspapers from a large metropolitan area and were screened by telephone to determine peri-menopausal status. Eligible participants were mailed a packet of questionnaires containing the following measures: Beck Depression Inventory-II (BDI -II), State-Trait Anxiety Inventory (STAI), Dysfunctional Beliefs and Attitudes about Sleep (DBAS), the Women's Health Questionnaire (WHQ), the Pittsburgh Sleep Quality Inventory (PSQI) and a comprehensive form measuring sleep-related difficulties and behaviors, as well as descriptive information. Participants received $20.00 for returning their completed packets. Our final sample included 168 women (88% response rate), whose demographics were comparable to the 2000 census for this area.
Results: Sixty-six per cent of women reported difficulty sleeping for 6 months or more. Ethnicity, age (albeit a limited range), education, and marital status did not differentiate sleep quality, all p's > .05, whereas, employment status and income did differentiate sleep quality, $F(6, 131) = 6.15$, $p < .01$, and $F(5, 132) = 3.39$, $p < .01$, respectively. "Flashers"(women reporting hot flashes) reported significantly worse sleep quality compared to "non-flashers" $F(1, 142) = 10.09$, $p < .002$. Stepwise regression revealed that the BDI-II, DBAS, and "flasher" status uniquely predict PSQI ratings, R square = .40, $F(3, 117) = 26.02$, $p < .001$. A separate stepwise regression revealed that Trait Anxiety, the DBAS, and "flasher" status uniquely predict PSQI ratings, R square = .37, $F(3, 128) = 25.34$, $p < .001$.
Conclusions: These data reveal significant relationships between depression, anxiety, and dysfunctional beliefs and attitudes and sleep quality, above and beyond what hot flashes alone would predict, during the peri-menopausal transition. While this study is limited by self-report and would benefit from polysomnography, it highlights the importance of psychological factors that are associated with sleep quality during menopause. In light of difficult decision-making around HRT, it is imperative that we address women's sleep from a multidisciplinary perspective.

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0383.H

CPAP Compliance in Mild-Moderate Alzheimer's Patients with SDB

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Introduction: Sleep disordered breathing (SDB) is very common in patients with Alzheimer's disease (AD), yet these patients are often not treated as it is believed that they will not tolerate CPAP. Even in sleep disorders clinics, CPAP compliance is often low as patients may find CPAP uncomfortable to wear. In clinic samples, CPAP compliance often averages around five hours a night. As part of a larger study, this study examined CPAP compliance in patents with mild/moderate AD and SDB.
Methods: Nine patients with mild/moderate AD and SDB were randomized to either six weeks of CPAP (n=4) or three weeks of placebo CPAP followed by 3 weeks of real CPAP (n=5). Respironics Remstar Pro CPAP with Profile Lite masks were used. Each machine was equipped with a compliance meter that recorded number of hours that the machine was used at the set pressure. Results are available for eight patients as compliance data were lost for one patient.
Results: On average, patients in the real CPAP group used the CPAP for 5.36 hours per night (SD=2.81). Patients in the placebo CPAP group used the placebo CPAP for a mean of 7.15 hours per night (SD=9.7) and real CPAP for a mean of 5.44 hours per night (SD=5.2).
Conclusions: With education and a good caregiver, patients with mild/moderate AD are able to tolerate CPAP to the same extent as sleep disorders clinic patients. The patients were called daily and when necessary, frequent evening visits were made to ensure that the patient and the patient's caregiver were setting up the CPAP properly and using it nightly. Although more labor intensive, the benefits of treating the sleep apnea will likely outweigh the extra attention needed.

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0384.H

Long-Term Growth Hormone Releasing Hormone Administration Does Not Improve The Sleep Quality Of Healthy Older Men And Women

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Introduction: As much as 50% of the older population suffers from and complains of fragmented sleep and poor sleep quality, more than any other age group. The public health burden associated with sleep disturbances in the elderly is considerable and pharmacological interventions other than traditional hypnotics would potentially be of great benefit to this population. One such intervention may be augmentation of the somatotrophic or growth hormone (GH) axis. There is a considerable literature suggesting growth hormone releasing hormone (GHRH) is involved in the regulation of NREM sleep. Here we report the results of a randomized, placebo-controlled trial of long-term GHRH treatment on the sleep quality of health, non-complaining older men and women.
Methods: 89 carefully screened, community-recruited, healthy older (60-85 yrs.) men and women were randomized to either placebo or GHRH treatment conditions. Subjects underwent baseline (T1) and five month / treatment (T2) polysomnography on the second and third nights of two 72 hour stays at the UWMC GCRC. The third night of each stay included periodic (20-min) blood sampling via an indwelling catheter. Subjects self-injected GHRH (1-29) NH2 (sermorelin acetate, GEREF, donated by Serono Laboratories Inc.) or placebo subcutaneously prebedtime each evening for five months including during the T2 assessment.
Results: GHRH treatment resulted in a doubling ($p<.001$) of integrated 24 hr GH secretion, resulting from a single large pulse of GH secretion. Late-night GH was not stimulated; indeed there was a trend toward inhibition of endogenous late-night GH secretion. IGF-I levels rose significantly ($p<.001$) ~35%. There were also significant ($p<.001$)increases in lean body mass (~2%) and significant decreases in body fat (~6%), particularly intra-abdominal fat (~12%). Despite these previously reported GHRH-induced endocrine and somatic changes, no significant changes were seen on any measure of sleep quality (e.g., sleep latency, total sleep time, measures of nighttime wakefulness, sleep efficiency, measures of SWS and REM, or DELTA QEEG) on either normal (i.e., undisturbed) or catheter nights with GHRH treatment. Finally, no changes in any of the above endocrine, somatic or sleep measures were observed for the placebo group.
Conclusions: The lack of an observed beneficial effect of GHRH upon sleep may be related to the short duration of action (minutes) of the GHRH formulation used and/or its pre-bedtime injection (~30 minutes).

Studies that previously reported a beneficial GHRH effect typically employed bolus intravenous injections during sleep. As such intra-sleep GHRH administration is impractical for general use, the true test of GHRH as an agent to improve sleep quality will have to await development and testing of longer acting agents, which may be taken at bedtime and which result in longer duration of action at the medial preoptic area where the impact of GHRH on NREM sleep is most likely mediated.

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0385.H

Post-Treatment Effects Of Bright Light Exposure In Demented Nursing Home Patients

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Introduction: Bright light treatment is reported to reduce nocturnal sleep fragmentation in aged individuals with dementia. Post-treatment duration of bright light treatment effect is commonly believed to be short acting. No studies, however, have exclusively investigated the duration of bright light effect after treatment termination. Investigation of post-treatment effects of bright light exposure is important for the management of sleep disorders among demented elderly and for the design of future studies. The present study investigates the duration of sleep-improving effects after termination of bright light exposure.
Methods: Eleven long-term nursing home patients with insomnia, defined as < 85% actigraphically scored sleep efficiency, were included. Mean MMS was 11.7 (SD = 4.2, range = 6-18). No subjects showed signs of depression. After a two-week baseline period, subjects received two weeks of bright light treatment for two hours/day within the period 08:00 – 11:00. Sleep and waking were actigraphically measured 4, 8, 12 and 16 weeks after treatment termination. Based on individual rising and bed times several actigraphical parameters were calculated: Sleep efficiency (percent sleep of total bed-time), total sleep time, total wake time, number of awakenings, length of each awakening, sleep onset latency, wake after sleep onset and early morning awakening. SPSS-software was used for statistical analysis. Sleep/wake activity was recorded with an Actiwatch portable recorder (Cambridge Neurotechnology Ltd, UK), with sensitivity set to medium.
Results: Bright light treatment produced significant ($P<0.05$) improvement in all parameters compared to baseline. The improved sleep parameters gradually returned to baseline, and after 16 weeks there were no significant difference from baseline for any variable. Actigraphically measured sleep efficiency differed significantly from baseline values at 4 weeks post-treatment, and sleep onset latency remained statistically reduced for 12 weeks post-treatment. Analysis for overall effect showed that treatment increased sleep efficiency ($F_{5,50} = 3.95$, $p = 0.004$) and light/dark-ratio ($F_{5,50} = 3.18$, $p = 0.014$). Treatment reduced total wake time ($F_{5,50} = 4.80$, $p = 0.001$), sleep onset latency ($F_{5,50} = 3.38$, $p = 0.010$) and early morning awakening ($F_{5,50} = 2.83$, $p = 0.025$). Treatment failed to produce any overall significant changes in wake after sleep onset ($F_{5,50} = 1.42$, $p = 0.233$), total sleep time ($F_{5,50} = 1.23$, $p = 0.308$) or time in bed ($F_{5,50} = 1.86$, $p = 0.119$).
Conclusions: These data suggest that the positive effects of morning bright light treatment for sleep disturbances among demented institutionalised elderly extend further in the post-treatment period than previously assumed. The most persistent change was seen in sleep onset latency, which remained significantly reduced 12 weeks post-treatment. At 16 weeks all parameters were back to baseline. These findings imply that bright light treatment schedules for demented elderly could be flexible, for example with alternating light treatment periods, and yet effective. Furthermore, the present data suggest that a washout period of more than 12 weeks is necessary in future crossover-designed studies.

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0386.H

Daytime Sleepiness Increases With Age More in Alzheimer's than Normals

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Introduction: Patients with Alzheimer's disease (AD) have very disrupted sleep at night and exhibit daytime sleepiness. AD patients with more severe dementia are sleepier than those with mild-moderate dementia both during the day and during the night. Few studies have had the opportunity to examine the progression of sleep disturbances from pre-diagnosis to post-diagnosis of the dementia. This study looked at a sub-group from a large population of elderly who were tested approximately every five years for the last thirty years.
Methods: 78 men and 94 women (mean age 75.7 years, SD=6.4) were studied. As part of a larger study, questions on hours spent napping during the day and total sleep time (hours) at night were collected from subjects interviewed between 1984-1987. Between 1990-1993 subjects were tested for AD and a diagnosis was made. Between 1992-1995 subjects were again asked questions on hours spent napping during the day and total sleep time at night. Analysis of variance was used to look at the relationship between the diagnosis of AD and change in the reported sleep variables. Diagnosis was defined as AD (n=46), borderline AD (n=11) or no dementia (n=115).
Results: There was a greater increase in the amount of reported napping in the borderline and AD groups compared to the no dementia group ($p<0.0001$). For the AD group, reported hours napping pre- to post-diagnosis were 0.19 (SD=0.32) to 0.88 (SD=0.79); borderline group was 0.51 (SD=0.48) to 1.61 (SD=1.34) and the no dementia group was 0.23 (SD=0.40) to 0.60 (SD=0.67). There was no significant change in total sleep time at night (pre-diagnosis to post-diagnosis: AD 7.20 (SD=1.15) hours to7.54 (SD=1.34) hours; borderline 7.55 (SD=0.93) hours to 7.64 (SD=1.00) hours; no dementia 7.23 (SD=1.01) hours to 7.35 (SD=1.10) hours).
Conclusions: This study supports the finding that patients with Alzheimer's disease report being sleepier during the day than those with no dementia and this increase in daytime sleepiness is likely to be a function of the dementia itself. It was surprising to find that there were no differences in reported nighttime sleep between the groups. Additional research will help clarify which other attributes might be contributing to the daytime sleepiness.

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0387.H

Old Rats Sleep Less After Adenosine Stimulation

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Introduction: There are significant changes in sleep with age. Old rats have less sleep rebound in response to 12h-prolonged wakefulness (W) indicating a reduction in sleep drive with age (5). This decline cannot be attributed to loss of neurons implicated in sleep since the numbers of cells in the VLPO is similar between young (3.5 mos) and old (21.5 mos)

rats. Nevertheless, old rats have less c-Fos and DNA binding activity in response to 12h-prolonged W (1). One possibility for the reduced sleep with age is that there is a decline in endogenous sleep factors such as adenosine (AD). However, at last year's APSS meeting we presented data that AD levels were higher in old rats after 6h-prolonged W. At last year's meeting Mackiewicz et al (4) also showed that the enzymes involved in AD synthesis are higher in old rats. If old rats accumulate more AD then why don't they have more sleep? We now investigate whether the sensitivity of the AD receptor is decreased in old rats. We investigate this through the infusion of AD as well as A1 receptor agonist cyclohexyladenosine (CHA).

Methods: Young (3 months, n=5) and old (21 month, n= 3) F344 rats were implanted with sleep recording electrodes and a guide cannulae (IC guide, BAS) placed into the basal forebrain cholinergic neurons (MCPO; A= -.35; L= 2.0; H= 8.5). Animals were housed at constant temperature (21 $\pm$ 1oC) and under a controlled light-dark cycle (12:12 L-D). Food and water were provided ad lib. AD (300 and 900 uM) and CHA (10, 25, 50 and 100 uM) were infused through a microdialysis probe (BAS 1mm of length; flow rate= 0.25ul/min). Drugs were injected during 2h at the starting of the lights-off period. The EEG data recordings were scored manually on a computer (Icelus software) in 12-s epochs for W, SWS and REM sleep.

Results: Infusion of AD increased SWS in young but not old rats. CHA (50 and 100 uM) enhanced SWS in young rats. In old rats, only the higher dose of CHA (100 muM) increased SWS.

Conclusions: We found that young rats responded to AD while old rats did not. In old rats, only the higher dose of CHA (100 uM) increased SWS. This suggests that in old rats there might be less number of AD receptors or less affinity to the ligand. A1 receptors are less in old rats (3) and affinity is also decreased (2). Such a change at the AD receptor level might transduce a weaker intracellular signal in old rats. Indeed, c-fos and AP-1 binding are decreased in old rats (1). We conclude that a reduction in sensitivity of the AD system fails to adequately inhibit wake-active BF neurons so that old rats wake up more frequently and have less sleep after prolonged W.

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0388.H

Relationships of Ambient Illumination to Depressed Mood: Contribution of Ophthalmic Diseases

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Introduction: Population-based data have shown an association between low ambient illumination levels and depressed mood. A concern has arisen that individuals with ophthalmic diseases might require greater illumination to achieve circadian entrainment because ocular pathology could reduce light transmission to the suprachiasmatic nucleus (SCN). Of note, a bright light study found improvement of circadian rhythm functions only among patients with intact vision, but not in visually impaired patients. Additionally, UCSD research has shown that older adults may exhibit resistance to light treatments. These findings have suggested that the biologic effects of ambient illumination may be attenuated by ophthalmic diseases. This study investigated the relationships of ambient illumination to depressed moods and the contribution of eye diseases as an explanatory factor.

Methods: Seventy Black (59%) and White (41%) Americans participated in the study; 73% were women and 27%, men. Their average age and BMI were 68.27 „b 5.97 years and 27.68 „b 5.72 kg/m2. Baseline measures included physical health (Comprehensive Assessment and Referral Examination), depressed mood (Geriatric Depression Scale), and sleep quality (Pittsburgh Sleep Quality Index). Participants also provided sociodemographic data. Participants who met study criteria underwent an eye exam at SUNY Downstate, providing data on visual acuity, visual field defects, intraocular pressure, cup-to-disk ratio, and nerve fiber layer thickness. Eye diagnoses were rendered using medical and ophthalmic data. During the week that followed eye exams, participants wore an actigraph (Actiwatch-L) at home to monitor ambient illumination levels. Cosine analyses were performed on the logarithm of measured illumination, yielding average daily illumination levels and acrophase timings. Internal Review Boards at UCSD and SUNY approved the study.

Results: Of the sample, 46% reported visual impairment, but 85% reported being in good to excellent health. None of the volunteers were legally blind, but 27% were visually impaired. Of the sample, 5.8% received a diagnosis of glaucoma; 7.2% cataract; and 7.2%, ocular hypertension. The median daily illumination for this sample was 518 lux, with acrophase timing averaging 14:30 „b 1:29 hours. Partial correlation analyses showed an inverse correlation between daily illumination levels and depressed mood [$r_p = -0.34$, $p < 0.05$]; age, sex, ethnicity, BMI, and education were controlled. With further control for visual acuity, intraocular pressure, visual field mean deviation, cup-to-disk ratio, nerve fiber layer thickness, and diagnosis, the magnitude and significance of the correlation diminished [$r_p = -0.21$, NS]. Individuals receiving daily illumination later in the day were characterized by more depressed mood [$r_p = 0.34$, $p < 0.05$]; this correlation was, however, not significant after control for ophthalmic covariates [$r_p = 0.09$, NS].

Conclusions: The present findings support our previous observation of depressed mood among older San Diegans experiencing low ambient illumination, although illumination in the present sample was relatively greater. This suggests that ambient illumination has a similar antidepressant effect in differing geographic locations and among individuals of different sociodemographic characteristics. It remains unclear how differing eye diseases might differentially compromise retinal input to the SCN, although one might conjecture that individuals with glaucomatous retinopathies may be at increased risks for circadian malsynchronization. It is believed that the peripheral ganglion cell damage noted in glaucoma might be particularly harmful to the melanopsin cells, which are the hypothesized circadian photopigment transducing environmental light cues to the SCN via the retinohypothalamic tract.

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0389.H

The Impact of Psychosocial Factors on Sleep Quality in two Elderly Groups of Widowed Women (Jewish and Arab)

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Introduction: The aging process is associated with subjective and objective changes in the quality and quantity of sleep. Complaints of difficulty in initiating and maintaining sleep and daytime drowsiness, are more prevalent among the elderly than in any other group. People over 65 years of age are disproportionately affected by insomnia: whereas just 9% of patients aged 20-30 years old complain of insomnia, between 35%-50% of patients older than 65 years lodge the same complaint. It is generally accepted that sleep disturbances figure as one of the most ubiquitous health problems in elderly persons. Multiple age-related factors may contribute to sleep disturbances in elderly people. Beyond the normal neurobiological aging process, empirical evidences suggest that psy-

chosocial factors help perpetuate chronic insomnia in the elderly. The purpose of this study was to examine the impact of psychosocial factors on sleep quality in two groups of Israeli elderly widows: Arab and Jewish. Likewise in the Jewish community a comparison was made between the city and the kibbutz.

Methods: The study population comprised three groups: forty-four Jewish elderly widows who were Kibbutz members, aged 65-94 (78.8±8.0 years), forty Jewish urban elderly widows, aged 66-85 (73.8±5.6 years), and forty-six Arab urban elderly widows aged 65-85 (71.6±6.4 years). All subjects were living independently in the community, and were in good clinical condition. Participants completed the Life Satisfaction Index (LSIA), Social Support Scale (SSS), and the Self-Esteem Scale (SES). Sleep was assessed using Mini Sleep Questionnaire (MSQ).

Results: Significant differences were found between the three groups in life satisfaction ($F(2,127)=7.5$, $p<.001$), social support ($F(2,127)=9.5$, $p<.0001$), and self-esteem ($F(2,127)=7.0$, $p<.001$). Likewise, a significant difference was found between the three groups in sleep efficiency ($F(2,127)=6.0$, $p<.003$).Post-hoc analysis revealed that the Kibbutz widows reported significant higher sleep efficiency, higher Life Satisfaction, higher Social Support, and higher Self-Esteem compared to the Jewish urban widows, and compared to the Arab urban widows. Pearson correlation showed that sleep efficiency correlated with life satisfaction ($r=0.2$, $p<. 01$) and with self-esteem ($r=0.3$, $p<. 0001$).

Conclusions: These data suggest that insomnia in ageing women is responsive not only to the physiological process of aging, but also to psychosocial factors.

0390.H

Elderly With and Without Insomnia: A Comparison of Visual Perception of Global and Local Aspects

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Introduction: Disturbed sleep, an important cause of human misery at any stage of life, exacerbates with advancing age. Complaints of difficulty in initiating and maintaining sleep and daytime drowsiness are more prevalent among the elderly than in any other group. Likewise, aging is associated with a decline in many aspects of visual perception including changes in global-local processing. However, little is known about the interaction between sleep disturbances and visual processing of global and local aspects among elderly people. This study aims to assess whether insomnia is associated with age-related changes in global-local processing.

Methods: The study population comprised three groups: twenty-one young adults without sleep disorders (mean age=23.8, SD=0.4; mean sleep efficiency=93.2%, SD=0.8), nine elderly who were free of sleep disorders (mean age=72, SD=1.9; mean sleep efficiency=92.2%, SD=0.6), and thirteen elderly who suffered from chronic insomnia (mean age=70.9, SD=1.2; mean sleep efficiency=68.2%, SD=4.0). All subjects were living independently in the community, and were in good clinical condition. Participants completed the Mini Sleep Questionnaire (MSQ), the Mini-Mental State Examination and the Geriatric Depression Scale. None met any criteria for dementia or depression according to the Mini-Mental State Examination and the Geriatric Depression Scale. Subject's sleep was continuously monitored for one week with a wrist actigraph (Ambulatory Monitoring, Inc.). Visual processing of global and local aspects was evaluated employing the Global/Local Paradigm.

Results: A four-way mixed design ANOVA revealed a significant interaction between task, congruency and age $F(1,41)=6.69$, $p<0.02$, and an interaction between task, congruency and insomnia $F(1,41)=4.28$, $p<0.05$. Further analyses, conducted within each age group, showed that the global and the local structures were equally manifested in young adults. For elders, however, the pattern of results showed a processing advantage, though not significant, for the local aspects, suggesting a relative impairment in the elders' ability to process global structure compared with local features. For Elderly Insomniacs, a two-factor (task X congruency) repeated measures ANOVA revealed a significant effect of task $F(1,11)=9.34$, $p<0.01$, which interacted significantly with congruency $F(1,11)=11.34$, $p<0.006$. Reaction time for the local features was significantly faster (633 msec) than for the global structure (733 msec). Moreover, the amount of interference caused by the incongruent local features was significantly larger (83 msec) than the amount of interference caused by global information (23 msec). Taken together, the pattern of results showed overall age-related differences in processing speed, and a disproportionate deterioration of the global processing in elders. Furthermore, elderly subjects with insomnia showed a substantial advantage for the local features and an asymmetric local-to-global interference, suggesting that the ability to integrate individual elements into a coherent pattern deteriorates with age, and becomes substantially impaired among elderly insomniacs.

Conclusions: The findings of this study imply that, at least in some aspects, sleep disturbances may account for the decline of visual perception in the elderly.

0391.H

The Timing of Activity Rhythms in Patients with Dementia is Related to Survival

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Introduction: Older adults with dementia often have disruptions in circadian rhythms, including disruptions of the rest/activity and sleep/wake cycles. These disruptions are a product of internal neuronal activity and external environmental influences, both of which are deficient in dementia. However, the consequences of disturbed rhythms are unknown. This study examined the relationship between rest/activity rhythms and mortality in patients with dementia.

Methods: The sample included 150 subjects with a mean age of 84.1 years (SD=7.8; range=60-100), with 105 women and 45 men. The Mini Mental State Examination (MMSE) was used to assess dementia severity (mean= 8.5; SD=7.6; range=0-27). Public records were searched to determine which subjects were deceased. Death certificates were found for 121 subjects (81.2%), 9 subjects (6.0%) were confirmed alive, and 19 subjects (12.8%) were lost to follow up. Rest/activity patterns were monitored for three days using an Actillume recorder (Ambulatory Monitoring, Inc., Ardsley, NY). Rest/activity data were modeled using an extended cosinor model which allows the shape of the waveform to be non-sinusoidal. The traditional cosinor parameters were computed along with two additional variables that relate to the steepness of the curve as well as the width of the peak. Based on previous research an additional variable was computed as the difference in hours between each subject's acrophase and the mean acrophase of a similarly-aged, non-demented comparison group. Cox proportional hazards models were used to determine which aspects of rest/activity rhythms were related to survival while controlling for the effects of potential confounding variables: age, gender, ambulatory status, medical burden, use of sedating medications, and bright light exposure.

Results: Mean survival was 2.3 years (SD=2.0, range=0.05 to 10.4). Longer survival was associated with having a higher MMSE (i.e., being more cognitively intact), female gender, and being ambulatory compared to being confined to a wheelchair (all $p<0.05$). Subjects with an acrophase closer to that of the non-demented comparison group ($c2(1)=9.01$, $p=.003$) and those with steeper rhythms ($c2(1)=4.88$, $p=.027$) had longer survival.

Conclusions: Although the overall strength of rest/activity rhythms was not related to survival, the timing of the rhythm was important. Patients with dementia appear to develop an abnormal timing of their rhythms, which is predictive of shorter survival. It is not clear from these data whether abnormal timing leads to death or whether it is a marker of pathologic processes. It may be possible to intervene in patients with dementia to correct the timing of their rest/activity rhythms and possibly prolong life.

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0392.H

The Relationship Between Dementia Severity And Rest/Activity Circadian Rhythms

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Introduction: There is a growing body of literature documenting disturbed circadian rhythms in patients with dementia. There is also much evidence of impairment in endogenous generation of rhythms as well as evidence of deficient environmental cues in this population. However, little is known about the progression of rhythm disturbance as an individual's dementia progresses. The aim of this study was to examine patterns of change in rest/activity rhythms as they relate to dementia severity.

Methods: The sample consisted of 150 subjects with a mean age of 84.1 years (SD=7.8; range=60-100) and contained 105 women and 45 men. Dementia severity was estimated with the Mini Mental State Examination (MMSE) with a mean for the sample of 8.5 (SD=7.6; range=0-27). Three days of rest/activity patterns were collected using the Actillume (Ambulatory Monitoring, Inc., Ardsley, NY). The rest/activity data were modeled using an extension of the cosinor approach which allows the shape of the waveform to be non-sinusoidal. In addition to the traditional parameters, two additional variables are computed that relate to the steepness of the curve as well as the width of the peak. The relationship between the computed rhythm parameters and dementia severity was then examined while controlling for the effects of the following factors: age, gender, ambulatory status, medical burden, use of sedating medications, and bright light exposure.

Results: Rest/activity rhythms were affected by age, gender, bright light, sedating medications and medical burden (all $p<0.10$). After controlling for these factors, MMSE was not related to rhythms. When the sample was split according to the strength of their rhythms, interesting relationships emerged. In the half with less robust rhythms (n=75), those with stronger rhythms had less severe dementia ($F(2,68)=5.10$, $p=.009$). In the half with more robust rhythms (n=75), milder dementia was associated with having an earlier acrophase ($F(2,68)=3.53$, $p=.035$) and narrower peak of the rhythm ($F(2,68)=4.21$, $p=.019$).

Conclusions: These results indicated that the relationship between rest/activity rhythms and dementia severity is complex and may change over the course of the illness. Inconsistent results in other studies may have been the result of failing to control for factors that can influence rhythms. A three-stage model can be used to explain the results of this study. In the first stage there is a rapid decline in rhythmicity as there is damage to the endogenous pacemaker. This is followed by a slight return to stronger rhythms as dementia progresses and environmental cues play a stronger role. In the later stages of dementia, rhythms decline even further.

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0393.H

Randomized Controlled Trial of Nonpharmacological Interventions on Sleep in Nursing Home Residents

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Introduction: Many older people will spend time in a nursing home (NH). Sleep impairment is more common and more severe among NH residents than expected based on increased age alone. Prior research suggests that lifestyle and environmental factors in the NH contribute to poor sleep, including excessive time in bed, little or no bright light exposure, lack of social cues to structure the day/night sleeping cycle and a noisy nighttime environment. The purpose of this study was to examine the effects on nighttime sleep of a multidimensional non-pharmacological intervention to improve these factors in the NH setting.

Methods: This was a randomized controlled trial targeting residents from 4 community NHs who had both daytime sleepiness and nighttime wakefulness. Participants randomized to the intervention received 5 consecutive days and nights of: 1) efforts to decrease time spent in bed during the day, 2) 30 minutes or more of sunlight exposure, 3) increased daytime physical activity, 4) improved nighttime sleep hygiene, and 5) efforts to decrease nighttime noise and light. The intervention was provided by research staff. Control subjects received usual care. Activity and sleep/wake patterns were estimated by wrist actigraphy (Actillume, Ambulatory Monitoring, Inc., Action3 software) at baseline and follow-up for 72 consecutive hours. Actigraphy variables reported here include: mean minutes exposed to light >1000 lux, nighttime total sleep (in min), nighttime percent sleep (time asleep over time monitored at night), number of nighttime awakenings and mean nighttime awakening length (in min). Split-plot (time X treatment group) ANOVAs were performed with normal scores transformation of data. Descriptives are presented as raw values.

Results: 121 people participated in the study (76% female, mean age 86.9 years, 90% non-Hispanic white). Mean minutes per day of light exposure > 1000 lux increased from 12.3 min at baseline to 65.3 min at follow-up in the intervention group, with no change in controls (13.9 min at baseline, 16.9 min at follow-up)($F= 43.722$, $P<.0005$). There was a modest decrease in the mean duration of nighttime awakenings in intervention participants (9.4 min at baseline, 9.0 min at follow-up) versus an increase in controls (7.9 min at baseline, 12.2 at follow-up)($F=4.938$, $P=.029$). There was a trend towards increased nighttime percent sleep in intervention (83.1% at baseline, 84.5% at follow-up) versus controls (84.8% at baseline, 79.3% at follow-up) ($F=3.858$, $P=.052$). There were no significant differences between groups in nighttime sleep minutes or number of awakenings.

Conclusions: We implemented an intensive, non-pharmacological intervention to address multiple factors that likely contribute to sleep impairment among NH residents. This intervention resulted in a modest decrease in the duration of awakenings at night, as estimated by wrist actigraphy. Further work is needed to determine whether more stringent targeting would identify NH residents likely to show a more pronounced response, and to assess the clinical signficance versus staffing implications of instituting such interventions given these modest improvements in sleep.

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0394.H

Eye Movement Density in Normal Elderly Subjects is Substantially and Significantly Lower than in Young Normals

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Introduction: Studies comparing eye movement density (EMD) in young and elderly normal (YN and EN) subjects (Ss) have thus far been based on categorical visual ratings. These studies have not shown clear age differences. Here we examined computer-quantified eye movement potentials in ENs and YNs who participated in a study of the effects of naps on post-nap sleep. In addition to testing for mean age differences in EMD we compared the EMD trends across cycles in the two groups. Last, we tested for correlations between NREM delta and EMD in baseline sleep and whether the reduced delta on the post-nap night was associated with a significant increase in EMD in either group.
Methods: YN Ss (N=19, mean (sd) age=22.4 (1.4)) and EN Ss (N=19, 71.4 (4.9)) underwent four separate sleep recording sessions consisting of a baseline night, nap, and post-nap night. Nap times were 09:00, 12:00, 15:00 and 18:00. EMD was measured with PASS PLUS (Delta Software, St. Louis) period-amplitude (PA) analysis as described by Tan and colleagues in this laboratory. A smoothing constant of 50mv was applied and the following variables were measured in 0.3-2 Hz for each 20 sec epoch of stage REM: integrated amplitude (IA), curve length (CL- peak-trough amplitude) halfwaves (HW), IA/HW and CL/HW. Age group differences in the baseline night EMD were examined with a t-test. EMD differences between baseline and post-nap sleep and changes in EMD across successive sleep cycles in baseline nights were evaluated with repeated measures ANOVA.
Results: ENs had significantly lower EMD than YNs in baseline sleep (56.0 vs. 91.6 mvsec/20 sec epoch, p=0.0002). Sleep cycle patterns for EMD also differed significantly (p<0.0001). YN Ss exhibited significantly lower EMD in cycle 1 compared to cycles 2, 3, and 4. EN Ss showed significant differences only between cycle 1 and cycle 4. EMD was not correlated with delta power in either group's baseline night. EMD on the post-nap night was also unchanged from baseline, both for the entire night and in cycle 1 alone. The reduction in delta power on the post-nap night was not correlated with EMD changes.
Conclusions: The main positive finding in this study is a highly significant reduction in EMD in the normal elderly. The clinical and basic significance of this result requires further study. The main negative finding is the absence of a correlation between EMD and NREM delta in baseline and post-nap sleep. This result suggests that the decreased EMD following sleep deprivation is not a simple function of increased delta. Brain arousal level, which is only indirectly related to delta, is more likely to be the operative variable.

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0395.H

Sleep of Caregivers of Patients with Alzheimer's Disease

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Introduction: Alzheimer's disease (AD) is the most prevalent form of irreversible dementia, affecting approximately four million patients in the U.S. Caring for a relative with AD is an enormous burden. Our group has shown that sleep in Alzheimer's patients is severely fragmented, which may in turn disturb the sleep of the caregiver. The purpose of this study was to examine sleep patterns of a sample of spousal caregivers of AD patients.
Methods: 8 men and 19 women who were spousal caregivers of patients with Alzheimer's disease (mean age=74.5 years, SD=9.0, range=52 to 88) and 8 control men and 35 control women (mean age =68.0 years, SD=7.6, range=55 to 86) were recruited. The Clinical Dementia Rating scale (CDR) was administered in an interview format to the caregiver or control. AD patient CDR ratings were moderate (n=15) or severe (n=12); all control spouses were normal. Each caregiver and control spouse wore an actigraph (Sleep Watch-L, Ambulatory Monitoring, Inc) for three consecutive 24-hour periods. Action-W was used to score the sleep/wake activity data for day and night percent sleep and percent wake as well as for number of and mean duration of nighttime awakenings and number of daytime naps.
Results: During the day, caregivers spent significantly less time awake (813 min, SD=146 vs. 898 min, SD=125; p=0.01) with lower mean percent time awake (86%, SD=11.5 vs. 92%, SD=7.6; p=0.037). Number of minutes asleep during the day was greater in caregivers (129 min, SD=107 vs. 79 min, SD= 70; p=0.041) as was the percent time asleep (13.7%, SD=11.5 vs. 8.3%, SD=7.6; p=0.037) during the day. Although there were no significant differences in the number of daytime naps, the caregivers were awake for shorter time periods between naps (95 min, SD=81.8 vs. 143 min, SD=108; p=0.050). There were no significant differences in nighttime values, with caregivers sleeping an average of 415 minutes and controls sleeping an average of 405 minutes.
Conclusions: Caregivers with spouses with AD were sleepier during the day than controls, although there were no differences in the amount of sleep at night nor in the number of sleep disturbances at night. One explanation may be that caregivers take naps with their spouses, as patients with AD often nap during the day. As additional data are collected, we will examine this question with polysomnographic data as well additional actigraphy data and try to determine what other physiological and psychological factors may be contributing to the daytime sleepiness seen in this group of elderly caregivers.

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0396.H

Naps and Circadian Rhythms in Postmenopausal Women

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Introduction: Increasing attention is paid to out-of-bed naps in relation to nocturnal sleep and circadian rhythms. Evening napping in older adults, which has been reported by our laboratory, should be interesting, since it is characteristic of aging and might be explained in terms of changes of circadian rhythms in aging. We wanted to explore napping patterns of postmenopausal women. Relationships between naps, circadian rhythms, and nocturnal sleep were also evaluated.
Methods: Postmenopausal women ages 50-81 years (67.8 $\pm$ 7.9) were analyzed. All 436 subjects were living independently in the community. Each subject wore an Actillume® wrist-activity monitor and kept a sleep diary for one week. The major urinary melatonin metabolite (6-sulfatoxymelatonin, aMT6s) was measured for two 24-h periods at home. Bedtime and wake-up time were determined from illumination, activity, and sleep diaries. Other sleep parameters such as sleep latency (SL), total sleep time (TST), wake time after sleep onset (WASO), and sleep efficiency (SE) were estimated from actigraphic algorithms previously validated. Out-of-bed naps were analyzed in reference to each day's wake-up time and the following bedtime. Acrophases, amplitudes, and mesors (24-hr-cosine mean) of aMT6s excretion were estimated from 24-hr-cosine fits to aMT6s data. Onsets and offsets of aMT6s were estimated as upward and downward crossings of the mesor levels, respectively.
Results: In the nap analysis, three peaks were observed. The highest

peak was around 1 hr before bedtime, the second highest was around 8 hr after wake-up time, and the smallest was around 2 hr after wake-up time. Evening naps were defined as out-of-bed sleep from 2 hrs to just before bedtime. There were significant correlations between age and all-day nap duration (r=0.169, p<0.01), and evening nap duration (r=0.123, p<0.05). Significant inverse correlation was observed between evening nap duration and wake-up time (r= -0.118, p<0.05), but not between all-day nap duration and wake-up time. In partial correlations controlled for age, diagnosis, and race, there were significant associations between evening nap duration and melatonin acrophase (r= -0.115, p<0.05), and the phase angle (i.e., time interval from melatonin onset to bedtime) (r=0.133, p<0.05). Decreased WASO, increased SE, and increased napping at other times than evening were observed in evening nappers (N=176) compared to non-evening nappers (N=260) (all, p<0.01). Melatonin onset time was advanced by 32 min in evening nappers (p<0.05).
Conclusions: Late evening was the most characteristic time of napping in these postmenopausal women. Evening napping could be in part explained by an advance of circadian rhythms in this age group. Relationships between evening napping and earlier wake-up time, though weak, might be a common manifestation of advanced circadian rhythms or a homeostatic effect. Increased napping at other times than evening and less nocturnal waking of evening-nappers suggest that they might have higher sleep need.

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0397.H

Fatigue, Sleepiness, and Sleep Quality in Healthy Older Adults
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Introduction: The relationship between fatigue and sleepiness is not well established in older, healthy populations. Previous research in college samples found that people with differing levels of fatigue (measured by the 10-item Fatigue Impact Scale, FIS-10) did not significantly differ in amount of sleep, but more fatigued people expressed greater sleep dissatisfaction. This study examined the FIS-10 in an older, healthy sample, and examine relationships between perceived fatigue, sleepiness, and sleep quality.
Methods: Participants ages 55 and older in two randomized clinical trials of exercise adoption were contacted by mail to complete a cross-sectional survey. In one study (CHAT), participants were sedentary, older adults without major health complaints. In the second study (RTC), participants were sedentary older adults with mild-to-moderate sleep complaints. Participants completed the FIS-10, Epworth Sleepiness Scale, 3 Pittsburgh Sleep Quality Index subscales (PSQI subjective sleep quality, sleep medication use, and daytime dysfunction), and questions about the average hours of nightly sleep obtained, hours of sleep desired each night, general sleep satisfaction, daily coffee and tea consumption, and weekly alcohol consumption. T-tests and Pearson correlations were performed to explore potential confounders of fatigue (i.e., study, gender, age, caffeine or alcohol intake). Pearson correlations and T-tests were also used to examine cross-sectional associations between the FIS-10 and sleep variables.
Results: Of 284 surveys mailed, 157 were returned, resulting in a 55% return rate. The sample included 103 women and 54 men, average age was 64 years (SD = 9.68). Data for 2 subjects were incomplete; therefore, analyses were performed on 155 surveys. Internal consistency of the FIS-10 was good (Cronbach alpha = .93). Age, gender, caffeine and alcohol intake, and study assignment were not related to fatigue (p > .05). Higher fatigue was associated with fewer hours of sleep (r=-.23, p<.003) higher Epworth scores (r=.44, p<.001), greater PSQI daytime dysfunction (r=.58, p<.0001), and poorer sleep satisfaction (r=.50, p <. 0001). Participants in the RTC study reported poorer PSQI sleep quality; after removing the effect of study assignment in a partial correlation, greater fatigue was still associated with poorer PSQI sleep quality (r=.48, p<.0001).
Conclusions: In this first use of the FIS-10 in an older sample, the FIS-10 remained an internally valid measure. More fatigue was negatively related to a variety of indicators of sleep quantity and quality. Similar to previous research, fatigue, sleep satisfaction, and daytime dysfunction were closely related. However, contrary to previous findings in younger samples where sleep patterns were similar regardless of fatigue level, more fatigued older adults obtained fewer hours of sleep. Also, in college samples, more fatigued students consumed more caffeine, whereas in the older sample this relationship was not present. These results reveal that the nature of the relationship between fatigue, sleepiness, and sleep quality appears to change with age.

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0398.H

Melatonin as Treatment for Sleep Disturbances during Menopause
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Introduction: Up to half of all women going through menopause report significant sleep disturbance, mainly attributable to hormonal imbalance and hot flashes (HFs). Previous work has indicated that not only low levels of sex steroids but also the marked increase of gonadotropins during the menopause transition may contribute to disturbed sleep. Our studies have shown that elevated levels of luteinizing hormone (LH) or a low estradiol-to-LH ratio were associated with low sleep efficiency in postmenopausal women. The aim of this study is to investigate whether exogenous melatonin decreases LH levels and in so doing, increases sleep quality. Furthermore, we hypothesize that melatonin will reduce severity and number of HFs by virtue of its temperature-lowering effect, thereby reducing number of HF-related awakenings and improving sleep.
Methods: Peri- or postmenopausal women (45-58yrs) ingested 3mg melatonin or placebo daily at bedtime over 14 days. Each subject underwent both conditions. During treatment, subjects wore wrist activity monitors with event markers to record rest-activity patterns and HFs. Subjective sleep quality, menopausal symptoms, and mood were also assessed. At the end of each treatment arm, subjects spent two consecutive nights in the sleep laboratory. Polysomnographic (PSG) variables and core body temperature were recorded continuously. HFs were assessed by measuring skin conductance and temperature. Over-night urine samples were collected to assess LH levels. Variables were compared across conditions using paired t-tests.
Results: To date, 6 women (53.8$\pm$2.9 yrs) completed the study. Urine samples of four subjects were analyzed. Results demonstrated significantly lower LH levels during melatonin treatment than during placebo administration. The mean total amount of LH excreted overnight during melatonin treatment was 21.7$\pm$20.9 IU while it was 32.9$\pm$17.5 IU during placebo intake (p<0.05). No significant differences between the two treatments were observed regarding actigraphy-derived sleep data or number of nocturnal HFs, e.g. the average sleep efficiency across the 14 days was 86.1$\pm$2.7 with melatonin vs. 86.9$\pm$3.8 with placebo, and the number of nocturnal HFs was 2.2$\pm$1.7 vs. 2.0$\pm$1.1. PSG data revealed a significantly longer total sleep time with melatonin 401.5$\pm$65.3 min than with placebo 346.1$\pm$54.6 min. No other significant differences were observed. Sleep efficiency was 86.9$\pm$6.4 with melatonin vs. 82.1$\pm$14.2 with placebo, sleep latency was 9.3$\pm$8.3 min vs. 22.4$\pm$33.0 min, WASO 65$\pm$25.4 min vs. 93$\pm$60.2 min, and number of awakenings

31±9.5 vs. 26±7.4. No subjective improvement of sleep quality, menopausal symptoms or mood was observed with melatonin.
Conclusions: This study indicates that low-dose melatonin significantly suppresses LH levels in peri- and postmenopausal women. Melatonin did not improve subjective sleep quality or reduce the number of hot flashes, but PSG measures suggested improvement in several measures. Data from additional subjects is being collected.

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0399.H

Menopausal Sleep Disturbance
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Introduction: Some epidemiologic studies have found increased reports of poor sleep at menopause. It is generally believed that hot flashes (HFs) cause increased awakenings, which contribute to these reports. However, few studies have tested these relationships in the laboratory.
Methods: We studied 3 age-matched (45-51) groups of women: those with regular menstrual cycles (CY, n=6), postmenopausal women with HFs (FL, n=12), and postmenopausal women without HFs(NF, n=6). Postmenopausal was defined as amenorrheic > 1 year and plasma estradiol < 20 pg/ml. CY women were run during the follicular phase, when estrogen levels are lowest. All subjects were screened to be healthy, drug-free, have no sleep or major psychiatric disorder, and have a BMI < 30. They were run for 3 consecutive nights at 23 degrees C with 8 h recordings of PSG, and objective HF markers (sternal skin conductance, 4 site skin temperature). Following night 2 they received the MSLT, PVT and divided attention tasks, the POMS, and fatigue and EDS questionnaires.
Results: Ten women were screened out for the following reasons: 5 failed the drug screen, 2 had PLMs and apnea, and 3 NF had HFs in the lab. There were no significant group differences in age, BMI, or skinfold thickness. An average of 5.2 ± 2.9 SD (range = 1-18) HFs occurred in FL. There were none in NF or CY. Of HFs occurring within 2 min. of an arousal, 46% occurred before, 48% after, and 6% simultaneous with the arousal. CY had significantly ($p<.05$) fewer awakenings, 2.9 ± 1.7 SD/night compared to FL (6.6 ± 2.1) and NF (6.7 ± 4.6). There were no other significant group differences on any other sleep stage measure, analyzed as the means of nights 2 and 3. For example, for CY vs. FL vs. NF: total sleep time, 6.8 ± .9 SD hours, 7.0 ± .4, 7.0 ± .6; sleep efficiency, 86.5 ± 10.4%, 87.6 ± 5.7%, 88.1 ± 7.0%, # stage changes, 135.3 ± 32.8, 154.1 ± 33.9, 140.6 ± 34.3; entrances to awakening, 36.7 ± 9.9, 38.2 ± 12.0, 38.2 ± 12.7; MSLT latency, 11.5 ± 8.5 min, 8.2 ± 6.0, 11.6 ± 3.5. There were no significant differences on performance tests, EDS, or fatigue questionnaires.
Conclusions: We found little evidence of sleep disturbance in FL subjects as evidenced by PSG, MSLT, performance, and questionnaire data. Both FL and NF had significantly more awakenings than CL. This cannot be attributed to HFs, but possibly to menopause, per se. The majority of arousals were not preceded by HFs. The lack of sleep disturbance found in our postmenopausal women may be due to the fact that they were prescreened to eliminate those with drug use, obesity, and other sleep, medical, and psychiatric disorders.

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0400.H

Prefrontal Cortex – Associations Between <1Hz Sleep EEG and Waking Neuropsychological Performance in Healthy, Older People
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Introduction: Low frequency delta (<1Hz) in sleep is of increasing interest as it indicates cortical re-organisation, especially in the prefrontal cortex (PFC). Other research shows that delta power in sleep is positively linked to waking metabolic rate, with stronger links for the PFC. Such findings suggest a possible association between waking PFC function and low frequency delta in this region.
Methods: 24 right-handed, healthy, older adults (mean 67.9y ± 0.7y SEM, range 61-75y) were screened to ensure they were healthy 8h (±1h) sleepers without daytime sleepiness (<2naps/month and KSS screening over 3 days). Home sleep EEGs were recorded for two nights. A neuropsychological test battery oriented to the left PFC (e.g. non-verbal planning [NVP], verbal fluency [VF]) was administered late morning (i.e. high alertness) on another day. Power spectra (8 x 0.5Hz bins, from 0.5-4.5Hz) were computed for four bipolar derivations (Fps1s-Fs3s; Fps2s-Fs4s; Os1s-Ps3s; Os2s-Ps4s) and standardised to control for individual differences.
Results: No associations between neuropsychological test performance and total (0.5-4.5Hz) power were found. However, for the first non-REM period (only), 0.5-1Hz power in the frontal channels was associated with neuropsychological performance, more so for the left side: NVPT (Left: r = -0.60 [df 22] $p<0.002$; Right: r = -0.46 [df 22] $p<0.03$) and VF (Left: r = 0.57 [df 14] $p<0.02$; Right: r = 0.50 [df 14] $p<0.05$). All associations remained significant after age was partialled out. No such associations were found for parietal regions and/or tests non-specific to the PFC (e.g. Reaction Time), nor were there any significant associations between neuropsychological test performance and activity above 1Hz
Conclusions: PFC delta <1Hz activity in the first non-REM period was linked to waking performance at tasks known predominately to activate this region, especially the left PFC. That is, healthy, older people having more <1Hz activity during the first non-REM period, from the PFC, perform better at tasks known to activate this region. Such findings may reflect the role <1Hz activity may have in the localised function of sleep.

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0401.H

Rapid Eye Movements Activity In REM Episodes Preceding The Awakening In The Elderly
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Introduction: In young adults, eye movements activity during the REM episode preceding awakening was shown to be more intense than in other REM phases and might reflect a higher probability to transit from sleep to wakefulness (Barbato et al., 1994).This study is intended to assess whether the characteristics of rapid eye movements during the REM episodes followed by an awakening (REM-W) are different relative to those followed by a transition to NREM sleep (REM-S) also in the healthy elderly . The clustering into REM bursts, which in the past has been shown to be deeply modified in the elderly (Ficca et al., 1999; Vegni et al., 2001), will be evaluated besides the global quantitative aspects of REMs (number of REMs, REM density).
Methods: Night polysomnography (EEG, EOG, EMG) was performed on three age groups of healthy subjects (Young (Y): 19-23 yrs., n=16; Old (O) : 67-74 yrs, n=9, Old Old (OO): 76-98 yrs, n=10). REM phases were identified through conventional scoring (Rechtschaffen and Kales,

1968). For each REM episode, we calculated: absolute number of REMs, REM density (number of REMs/min) and, according to the methodology described by Ktonas et al. (1990), all second-order parameters (i.e., absolute number and percentage of REMs in the burst mode, duration of REM bursts). Two-way ANOVAs were performed having "age" and "sequence" as factors, and each eye movement parameter as dependent variable.When an effect of age was found, post-hoc contrasts allowed the comparisons between age groups in pairs.
Results: The duration of REM episodes was not significantly different either amongst age groups (F=1.5) or amongst sequences (F=0.76).Age significantly affects all REMs parameters (absolute number of REMs, F=7.5, p<0.001; REM density F=19.6, p<0.001; number of REMs in burst, F=7.7, p<0.001; percentage of REMs in burst, F=42.8, p<0.0001; duration of REM bursts, F=30.5, p<0.0001)Instead, sequence affects only REM density (F=5.58, p<0.05) with a strong interaction between the two main factors (F=4.9, p<0.01). Between-group analysis shows that in group Y, REM-W show significantly higher density than REM-S (p<0.001), whereas no significant difference is found between REM-W and REM-S in group O and OO.
Conclusions: The present data confirm previous observations of our group (Ficca et al., 1999; Vegni et al., 2001) about an impairment of the organization of REM activity across aging. However, neither in the young adults nor in the elderly do the organizational aspects change as a function of the following state.Only REM density in young subjects seems to change as a function of what follows REM sleep, with REM-W characterised by a higher density than REM-S. Interestingly, this difference is not present any longer in elderly subjects, possibly reflecting what we showed in past studies about the lose of the gating role of REM toward awakening (Salzarulo et al., 1999).

0402.H

Associations Between Physical Fitness And Sleep In Older Adults
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Introduction: Given that sleep complaints increase with age while physical fitness tends to decrease, this study examined the associations between these two factors in adults 55 years and older.
Methods: Sixty-four sedentary adults (35% men, 65% women), aged 55 to 79 years with moderate sleep complaints (Pittsburgh Sleep Quality Index [PSQI] Global mean score = 7.7 $\pm$ 3.1) participated in this study. Subjects were excluded for sleep apnea using pulse oximetry (Desaturation Index <10, multi-variable apnea prediction score < 0.8). Participants underwent three consecutive nights of home polysomnography (HPSG) with self-report sleep logs followed by a clinic visit which included the following fitness assessments: 7-day physical activity recall (PAR), body mass index (BMI), waist circumference, and peak oxygen consumption (pVOs2s). Sleep quality was measured via self-report PSQI, Epworth Sleepiness Scale (ESS), and HPSG-determined variables: total sleep time (TST), percent time in stage 1 sleep (STG1%), stage 2 sleep (STG2%), slow wave sleep (SWS%), and REM sleep (REM%), and sleep efficiency (SE%). Associations between fitness parameters and sleep variables were determined using Pearson partial correlation coefficients, controlling for age, gender, and sleep medication usage.
Results: The average peak VOs2s was 24.2 (SD = 4.4 ml/kg/min), indicative of a "poor to fair" level of fitness. Peak VOs2s was positively associated with TST (mean = 366.1 $\pm$ 68.5 min, r = 0.28, p = 0.05). No fitness parameters were associated with STG1%, STG2%, REM%, SWS% or SE%. The PAR was not related to any sleep parameters. While BMI and waist circumference were associated with somewhat better sleep quality measured via self-report, they were not associated with any HPSG variables.
Conclusions: In this moderately sleep impaired sample, higher physical fitness levels were associated with longer PSG-measured total sleep time. Proposed relationships between fitness and sleep parameters such as SWS% or sleep efficiency were not observed, although these results may be limited by the fact that the sample was reasonably homogenous, sedentary, and relatively unfit. Further research is needed to determine if improvements in physical fitness will produce changes in total sleep quality or increases in total sleep time in older adults with moderate sleep complaints.

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0403.H

Averaged Evoked K-complex Amplitude Correlates With Aging Over The Adult Life-span
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Introduction: Aging is associated with reductions in the amount and amplitude of delta activity seen during non-REM sleep. We have recently shown that relative to healthy young adults, healthy elderly have fewer spontaneous and evoked K-complexes and diminished amplitude of the negative component in the average of the evoked K-complexes. In these experiments, extreme groups of healthy young and old subjects were compared. Given that cortical gray matter volume decreases over the adult life span in a linear manner, and that gray matter plays a role in determining the amplitude of K-complexes, we hypothesized that K-complex amplitude would also display a linear decreases across the adult life span.
Methods: Data were combined from three recently published studies to provide a sample that ranged in age from 18 to 80 years. After investigating subject characteristics, an additional 11 subjects were studied to fill gaps in the age distributions for each sex. The final subjects numbers were 24 women aged 18 to 80 and 24 men aged 19 to 77. In the older subjects, hearing was verified using an audiometer to be within 15dB ISO at 1000Hz. EEG was recorded from either Grass gold-cup electrodes placed according to the International 10-20 system at Fz, FCz, Cz, CPz, Pz and O2, or tin electrodes in an electrode cap (Quickcap) and referenced to linked ears. A Neuroscan system continuously recorded all EEG at a sampling rate of 1000Hz.. Auditory stimuli (52 ms 1000Hz tone pips at 80dB) were presented binaurally via E-A-RTONETM 3A insert earphones. All tones presented in stage 2 sleep were analyzed to determine whether a K-complex was produced. Averaged waveforms were constructed, and K-complex elicitation probabilities determined. The peak-to-peak amplitude of the negative component of the averaged K-complex was subjected to linear regression analysis with age as the independent variable. Data from men and women were analyzed separately.
Results: In women K-complex amplitude ranged from -16.73 to -162.65 microvolts. In men it ranged from -38.75 to -174.16 microvolts. The linear regression analysis between K-complex amplitude and age indicated a significant correlation r =-0.77, F(1,46)=67.6, p <.0001 (r square = 0.595). For women the correlation was r = -0.71, F(1,22) =22.9, p < .0001 (r square = .49). For men it was r = -0.81, F(1,22)=22.9, p < .0001, (r square = .65). There was no significant difference in the slopes of the data from men and women (F(1,44) =0.55, n.s.).
Conclusions: The amplitude of the averaged K-complex is a measure of the extent to which the frontal cortex can produce a synchronized delta frequency EEG response. There are a number of elements underlying this measure: the number of neurons available to be synchronized, the extent of their dendritic arborization impacting on local synchronization ability and the extent to which they are connected to the thalamus to

enable synchronization to occur. Strong linear relationships between averaged K-complex amplitude and age, accounting for 59% of the variance in the group, indicate that at least one of these features shows a steady decline over the adult lifespan.

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0404.H

Waking Up Comfortably from an Afternoon Short Nap: the Application of the Self-Awakening Method to the Elderly People

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Introduction: Self-awakening is defined as the awakening upon a time designated before sleep. Our previous study (Kaida et al. 2002) suggests that self-awakening produced comfortable feelings and high alertness after awakening from a afternoon short nap. In the present study, we tested whether this hypothesis holds also true for the elderly people. Since, the elderly people take a nap more often than young people, it is worth examining how they wake up more comfortably.
Methods: Healthy nine participants (74.1 } 5.01 years old: 3 females, 6 males) accepted and signed to the informed consent. Electroencephalogram and polysomnogram was measured using a portable recording device (Polymate AP1000, TEAC Instruments, CO., LTD, Japan). The participants took part in three experimental conditions in different days: (1) the self-awakening condition in which the participants awoke by themselves after 20 } 5 min from lights off, (2) the forced-awakening condition in which the participants were unexpectedly awaken by the the experimenter fs calling after 20 min from lights off, and (3) the control rest condition in which the participants read a newspaper for 20 min instead of taking a nap. The orders of conditions were counterbalanced across participants. Each condition began from 14:00. Before the sleep or the rest period, the participants carried out a task session consisting of a visual analogue scale on subjective fatigue (1 min) and an auditory oddball detection task (4 min) with 1200 Hz targets (p = .2) and 1000 Hz standards (p = .8). After the sleep or the rest period they performed the same task session six times (post nap sessions: 30 min). The amplitude of the P300 event-related potential was calculated as a mean voltage between 400 to 500 ms after the target stimulus onset.
Results: Sleep variables did not differ significantly among the conditions. Stage REM was not observed in any conditions. In the self-awakening condition, the subjective fatigue was lower than in the forced-awakening condition at the post nap session 1 (VAS score: 33.9 } 7.95 vs. 45.4 } 9.14, P < .05). At the midline frontal site, P300 amplitude was larger in the self-awakening than in the forced-awakening condition [F(1, 6) = 8.45, P < .05].
Conclusions: The present study showed that subjective fatigue was reduced and P300 amplitude was increased after self-awakening than forced-awakening in the elderly people. Previous studies recommended the intake of caffeine to prevent sleep inertia after awakening from a short nap. However, there are people who do not like to take caffeine. The self-awakening method would be an alternative way to wake up comfortably from a short nap.

0405.H

Medications and Sleep in Nursing Home Residents with Dementia

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Introduction: Sleep disturbance is a highly prevalent, disabling symptom in persons with dementia, particularly those in nursing homes. Their nocturnal sleep is light and fragmented with frequent awakenings. Persistent short napping episodes interfere with daytime functioning and nighttime sleep. Current interventions consist primarily of pharmacologic agents, but provider practice patterns for prescribing these medications in nursing home residents with dementia and their effectiveness in this difficult to treat population are unclear.
Methods: We examined prescribing practices for common classes of medications affecting sleep including novel antipsychotics and serotonin selective reuptake inhibitors (SSRIs), and for specific medications including trazodone and zolpidem in 221 persons with dementia who resided in 9 nursing homes. We also analyzed how receiving these medications affected nighttime and daytime sleep. Data were obtained using actigraphy and review of medication records. Participants wore actigraphs on their wrists continuously for five days and nights. We analyzed the data using descriptive statistics and t-tests.
Results: The mean age of the participants was 80.2 years. There were 107 females and 114 males. Most were severely cognitively impaired, as indicated by a mean Mini-Mental State Examination score of 8.6 (s.d. 6.97). Mean time slept during 24 hours was 504.8 minutes, but only 70% (355.6 minutes) of sleep occurred at night. 49 participants (22%) received a novel antipsychotic (risperidone, olanzapine, or quetiapine). Residents on novel a antipsychotic slept more at night (370.2 minutes) and slightly more in the daytime (103.3 minutes) than those not on a novel antipsychotic (night sleep = 353.2 minutes; day sleep = 96.9 minutes), but these differences were not statistically significant. 46 residents received an SSRI (sertraline, bupropion, fluoxetine, or paroxetine). Those on an SSRI slept less at night (324.0 minutes) than those not on an SSRI (370.4 minutes), and they slept more in the daytime (on SSRI = 167.2 minutes, not on SSRI = 137.2 minutes. Residents on trazodone (n = 23) slept more at night than those not on trazodone (on trazodone = 394.1 minutes; not on trazodone = 353.2 minutes) and trazodone did not lead to increased daytime sleep (daytime sleep on trazodone = 101.3 minutes; not on trazodone = 151.2 minutes). There was a significant (p£.05) improvement in percent of 24 hour sleep that occurred at night in the trazodone group (trazodone = 77%; not on trazodone = 69%). Only 5 residents received zolpidem.
Conclusions: The residents slept more than 8 hours during a 24-hour period, but almost 1/3 of their sleep occurred in the daytime. Excessive daytime sleep interferes with daytime functioning and quality of life. Novel antipsychotics were mildly sedating during both day and night. SSRIs decreased nighttime sleep by 46 minutes and increased daytime sleep by 30 minutes, but these differences were not statistically significant. Trazodone improved nighttime sleep and did not lead to daytime sedation. Although zolpidem may be beneficial for sleep onset insomnia in older persons, it was rarely prescribed for residents of nursing homes with dementia.

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0406.H

Challenging the Sleep-Wake Cycle in Aging: the Effects of 200 mg of Caffeine During the Evening in Young and Middle Aged Moderate Caffeine Consumers

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Introduction: The effects of caffeine on sleep of young subjects have been studied extensively. Studies have shown longer sleep latencies, decreased sleep consolidation and reduced amount of slow wave sleep following caffeine ingestion. Important modifications of the sleep-wake cycle appear between the ages of 20 and 60 years, which may make the sleep of the middle-aged population particularly sensitive to challenges. The aim of this study was to evaluate age-related effects of caffeine on

sleep. It was hypothesised that middle aged subjects would be more sensitive to the effects of caffeine compared to young subjects.
Methods: 23 healthy subjects, all moderate caffeine consumers (1-3 cups of coffee/day), were studied. They were separated into two groups according to their age; young (10 subjects, 20-30 y, mean: 23y, 6W, 4M) and middle-aged (13 subjects, 40-60 y, mean:49y, 4 pre-menopausal W, 2 post-menopausal W, 7 M). All subjects were submitted to both a caffeine (200 mg) and a placebo (200 mg of lactose) condition in a double blind cross over design, separated by one week. They received one capsule containing caffeine (100 mg) or placebo (100 mg) three hours prior to their habitual bed time and the remaining dose (100 mg), one hour before bedtime. All night polysomnography was recorded. Two-way factorial ANOVAs on sleep parameters were used with one Group factor and one repeated factor (Condition). Simple main effect analyses were used to decompose the interaction effect.
Results: Compared to the placebo condition, sleep latency was lengthened (19.6 min vs 8.2 min; p=0.01), sleep efficiency was reduced (89.3 % vs 92.7 %; p=0.01) and sleep duration was decreased (403.20 min vs 430.23 min; p=0.01) following caffeine administration. Also, caffeine decreases the amount of stage 2 sleep (258 min vs 284.6 min; p=0.00), stage 3 sleep (11.33 min vs 14.33 min; p=0.01) and a significant interaction between Group and Condition for the total amount of stage 4 sleep (p=0.05) was found. Young subjects showed a significant decrease of stage 4 in the caffeine condition compared to placebo (5.43 min vs 3.0 min; p=0.01) and middle-aged stayed stable across both conditions (0.4 min vs 0.3 min; ns). No other effects of Condition or Group X Condition interaction were found.
Conclusions: Administration of 200 mg of caffeine during the evening increased sleep latency and reduced sleep consolidation, sleep duration and the amount of stages 2 and 3, with no differential effect between young and middle-aged subjects. The differential decrease of stage 4 sleep may be explained by a floor effect since middle aged subjects exhibit very low values of stage 4 sleep in the placebo condition. Quantitative sleep EEG analyses will allow to determine if middle-aged subject show a more pronounced reduction of slow-wake activity compared to the young. The possibility that middle-aged subjects who are more sensitive to the effects of caffeine have stopped consuming it with advancing age to avoid it's adverse effects may explain the lack of differential effects between young and middle-aged subjects. A study evaluating the effects of caffeine on sleep in young and middle-aged subjects who do not consume caffeine is under way.

0407.H

Heart Rate Changes Associated with Microarousals During Sleep in Pre and Postmenopausal Women

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Introduction: Micro-arousals (MA) are defined as abrupt shifts in EEG frequency, which may include theta, alpha and/or frequencies greater than 16Hz. It has been found that MA were associated with a tachycardia followed by a bradycardia. Recently, an age-related reduction in the amplitude of both tachycardia and bradycardia was observed. Menopause is known to increase the risk in cardiovascular diseases and it is not clear if hormone replacement therapy can improve cardiovascular health. Therefore, the aim of this study was to investigate the impact of menopause and hormone replacement therapy (HRT) on the heart rate (HR) associated with MA.
Methods: Twenty women were divided into 2 groups according to their menopausal status (premenopausal and postmenopausal women). Postmenopausal women were recorded at baseline and after 6 months of treatment (estrogen and progesterone). MA were scored according to ASDA criteria. The R-R interval was calculated for 16 heartbeats before and 20 heartbeats after the onset of MA. The mean of the 10 R-R intervals prior to MA was considered as baseline and was subtracted from all R-R intervals. Values were then converted in beats per minute.
Results: No between-group difference was observed for mean MA index. The change in HR associated with MA was characterized by a tachycardia followed by a bradycardia and was observed in the 3 groups. No difference was seen for MA-related HR changes between pre and postmenopausal women. However, the amplitude of bradycardia was lower in postmenopausal women, but the difference was not statistically significant ($p = 0.1$). A delay in HR increase, leading to a reduction in the duration of tachycardia, was observed in postmenopausal women with HRT in comparison with the two other groups ($p < 0.05$).
Conclusions: As in previous studies, these results showed that EKG changes associated with MA are characterized by a tachycardia followed by a bradycardia in middle-aged women. Menopause does not induce any significant changes in tachycardia or bradycardia associated with MA during sleep. HRT produces a delay in the tachycardia and therefore, enhances the changes observed with normal aging.

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0408.H

Elderly Males with Mild Nocturnal Oxygen Desaturation Exhibit Reduced Cognitive Performance

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Introduction: Decrements in executive functioning in the non-demented elderly are often noted frequently but poorly understood. To probe for potential mechanisms, we assessed physiological and neuropsychological traits of a non-clinically derived group of elderly caucasian subjects (Bay Area Sleep Cohort, BASC).
Methods: Two consecutive nights of in-lab PSG used standard configurations for EEG, EOG, and EMG. Thoracic and abdominal excursion was determined with inductance plethysmography, oronasal airflow with thermistry, and arterial oxygen saturation with continuous pulse oximetry. A neuropsychological test battery comprised of the Wisconsin Card Sorting Test (WCST), Folstein Mini-Mental Sate Examination (MMSE), Geriatric Depression Scale (GDS), Raven Colored Progressive Matrices, Peabody Picture Vocabulary Test, Finger tapping, Trailmaking Test, verbal List Learning (Buschke procedure), and the Benton Visual Retention Test was administered the morning following the first night of PSG. In the AM, all subjects also underwent arterial blood gas (ABG) analyses followed by pulmonary function testing (PFT's). The ABGs were analyzed for values of pH, partial pressure of oxygen (Pa02) and carbon dioxide (PaC02), and sodium bicarbonate (Hc0-3). PFTs generated data on forced expiratory volumes during the first second of expiration (FEV1) and were derived from the best of three maneuvers. Present analyses are derived from 51 males aged 64.7 ± 9.6 years who were split into two groups based on an SaO2 Index (number of desaturations > 4% per sleep hour) of < 10 (n = 44) vs > 10 (n = 7).
Results: By definition, the desaturation index was different across groups (17.7 ± 10.8 vs 0.8 ± 1.2, $p < 0.001$), as was the RDI (44.9 ± 15.6 vs 8.9 ± 11.1, $p < 0.001$). Desaturators also had more Stage 1 (28.9 ± 13.3 vs 14.4 ± 7.9 %, p=0.03), less Stage 3/4 (0.7 ± 1.2 vs 3.1 ± 5.3, p=0.01) and less REM (12.4 ± 3.9 vs 18.5 ? 6.0, p=0.01) sleep. They were also older (77 ± 6.1 vs 62.8 ± 8.6, $p< 0.001$). There were no differences in daytime ABG's, PFT's, levels of education, MMSE (27.7 ± 1.8 vs 28.0 ± 2.1), or GDS (6.7 ± 6.2 vs 4.3 ± 3.7) between desaturating and non-desaturating subjects. Most metrics of neuropsychological performance were similar between groups. However, desaturating subjects made more total errors (25.6 ± 11.2 vs 17.0 ± 10.6, $p = 0.05$) and

more perseverative errors (14.7 ± 9.1 vs 8.8 ± 7.5, p=0.06) during the WCST than non-desaturating subjects.
Conclusions: Lower WCST performances are typically ascribed to impairment in executive functions. Our data suggest that nocturnal, but not daytime, hypoxia may be associated with such decrements within the elderly non-institutionalized population. Future studies are required to determine whether hypoxia accompanying sleep disordered breathing, or the sleep fragmentation and disrupted sleep architecture observed in individuals, best accounts for these observations.

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0409.H

The Influence of Naturalistic Diurnal Behaviours on Sleep in the Healthy Aged

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Introduction: One of the causes of insomnia in aged persons may be changes to the circadian regulation of sleep. Sleep/wake dysfunction in the healthy aged potentially emerges from (i) a weakened ability to generate a 24 hour circadian signal (ii) a weakened ability to utilise zeitgebers and/or (iii) fewer or weaker zeitgebers acting on the individual. Improvements in the functioning of the circadian system should result in improved quality of night time sleep. This study set out to explore which factors may be good predictors of sleep quality in the health aged and included, not only a range of physical and psychological variables (personality, mood, physical and mental health, social and emotional functioning), but also variables that influence the circadian system. In particular daytime activity (objectively determined), exposure to naturalistic daylight (measured in lux), self report measures of the strength of their daily social routines and morningness-eveningness were included as circadian measures. Sleep quality was measured both objectively (via actigraphy) and subjectively.
Methods: The participants were 11 men and 22 women aged between 65 and 85 years old (mean =74.18) who were in good health, living independently, physically mobile and reporting good sleep habits. Participants were screened to exclude those with conditions (and/or taking medications) known to disturb sleep, depression or cognitive dysfunction. All participants completed a range of personality, mood and health status questionnaires, a morningness scale and the Social Rhythm Metric. Subjective measures of sleep wake behaviour were the Pittsburg Subjective Sleep Quality Index (PSQI) and a sleep diary over 3 days (yielding Diary Sleep Efficiency). Sleep quality was objectively determined using Minimitter wrist actigraphy, with a focus on the Nocturnal Immobility actigraphic variable. Ambient light was measured in lux using the actigraph with a lapel sensor. Daytime activity level was determined by actigraphic measures.
Results: Sleep quality variables, derived from nocturnal actigraphy, the PSQI and Diary Sleep Efficiency, were found to be poorly correlated and thus separate linear regressions (stepwise) were performed. The only model of note to emerge was with Nocturnal Immobility as the dependent variable, and four variables entered the model (Daytime Extended Immobility, Daytime Movement Average, Minutes light >3000 lux, Bodily Pain). These four variables together accounted for 57.5% of the total variation in the Nocturnal Immobility data. The first three of these four variables were measured objectively. A factor analysis showed that the daytime activity variables and bright light made independent contributions to objective sleep quality.
Conclusions: The naturalistic behaviours of daytime activity, exposure to bright light over 3000 lux and the self-report of bodily pain were the best predictors of objective sleep quality in the healthy aged and were more important than a wide range of self reported physical and psychological health variables. No variables were important in predicting subjective sleep quality. It is proposed that behaviours that increase activity levels and light exposure enhance the functioning of the circadian system and this results in improved sleep quality.

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0410.H

Role of Sleep Complaints in Initiation of Hormone Replacement Therapy

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Introduction: Observational studies have not consistently shown that objective or subjective sleep is better in menopausal women who use hormone replacement therapy (HRT), compared with those who do not. One explanation for the discrepancy is that women with poor quality sleep, compared to those without sleep problems, are more likely to seek HRT. Our aim was to investigate sleep problem frequency prior to initiation of HRT with prospective data.
Methods: Sleep problems, use of HRT, and other data have been recorded daily by a sample of midlife women enrolled in the Wisconsin Sleep Cohort Study. Out of the women enrolled in this study, 34 began HRT after entering the study. These women (users) were matched by age with 34 women who did not begin HRT (nonusers). The 3-month period before HRT initiation for the users and the same time period for her matched control were examined for the occurrence of the following sleep complaints: restless sleep, trouble getting to sleep, trouble staying asleep and nightmares. Two outcomes were computed for these sleep complaints: 1) the average number of days with sleep complaints in the 3 month exposure period and 2) whether or not at least two months with 5 or more days of trouble getting to or maintaining sleep or restless sleep was reported. We used t-tests to compare the mean number of days of each sleep complaint and Chi-square tests to compare whether or not women reported at least two months with 5 or more days of sleep complaints between those who did and did not initiate HRT.
Results: Women did not differ in their average number of days with sleep complaints or the percentage reporting at least two months with 5 or more days of sleep complaints in the previous three months given their HRT initiation status. On average (se), women who initiated HRT reported 0.7 (1.1), 2.6 (0.9), 0.6 (0.4), and 1.7 (0.4) days of trouble getting to sleep, trouble maintaining sleep, nightmares, and restless sleep, respectively. This is compared to women who did not initiate HRT who reported 1.0 (1.8), 3.0 (1.1), 0.4 (0.2), and 1.9 (0.5) days of trouble getting to sleep, trouble maintaining sleep, nightmares, and restless sleep, respectively. Additionally, 30% of women who initiated HRT reported at least two months with 5 days or more of trouble getting to or maintaining sleep or restless sleep out of the previous 3 months. This is no different from women who did not initiate HRT, of whom 29.4% reported at least two months with 5 or more days of trouble getting to or maintaining sleep or restless sleep out of the previous 3 months.
Conclusions: Our data did not suggest a role of sleep complaints in the initiation of hormone replacement therapy in midlife women.

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0411.H

The Relationship Of Sleep Quality And Memory Function In Taiwanese American Older Adults

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Introduction: Older adults often complain of increased sleep onset latency, middle-of-the-night or early-morning awakenings, and decreased sleep satisfaction. When sleep is disturbed, people are less

able to concentrate or remember things. Memory failure is another of the most common complaints of the elderly. This study was conducted to examine the relationship of sleep quality and everyday memory in Taiwanese American older adults.

Methods: A cross-sectional design was used in this study. Forty-seven women and 53 men with ages ranging from 60 to 89 living in the community were recruited from a Taiwan Center in a northeast American city. Sleep quality was measured by the Pittsburgh Sleep Quality Index (PSQI), which includes sleep latency, duration, efficiency, disturbance, sleep medication use, and daytime dysfunction. Everyday memory function was measured by the Extended Rivermead Behavioral Memory Test (ERBMT), which includes immediate and delayed memory of story, picture, face, route, appointment, belongings, and message. Data was collected through face-to-face interviews.

Results: The global PSQI score indicated that 37% of subjects had poor sleep quality (M = 6.0, SD ¡Ó 4.3). Among the subjects, 22% rated their sleep quality bad or very bad, 27% took longer than 15 minutes to fall asleep, 78% slept for less than 7 hours per night, 21% had a sleep efficiency of less than 75%, 83% awakened in the middle of night, 9% used sleep medication, and 29% had daytime sleepiness. With regard to memory, 88% of the subjects complained that their memory had declined. According to the ERBMT score, Taiwanese American older adults were very good at remembering picture, route, and message; 70% obtained perfect score on these subscales. Story, face, name, and appointment tasks seemed to be more difficult for the subjects. Pearson¡¦s correlation analysis found that the global PSQI score correlated significantly with immediate and delayed story recall (r = -.28, p<.01). Sleep latency correlated with immediate story recall (r = -.27, p<.01), delayed story recall (r = -.20, p<.05), immediate route recall (r = -.21, p<.05), appointment (r = -.25, p<.05), name (r = -.28, p<.01), and total ERBMT score (r = -.26, p<.01). Sleep efficiency correlated with total ERBMT (r = -.28, p<.01) and awakening at night correlated with total ERBMT (r = -.24, p<.05) as well.

Conclusions: The study results indicate that sleep quality is significantly correlated with the everyday memory function of Taiwanese American older adults. With a higher prevalence of older adults voicing complaints about their sleep satisfaction, health care providers need to be more aware of sleep problems in this population. Improving the sleep quality of older adults will enhance not only their quality of life, but possibly their memory function as well.

0412.H

The Effects of REM-Sleep Deprivation and REM-Sleep Augmentation on Learning and Memory in Healthy Older Adults

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Introduction: It has been known for a long time that it is more favorable to sleep after learning than to stay awake for an equally long period in order to promote memory performance. In this context, results of various studies suggest that REM-sleep deprivation has a negative impact on learning and memory. Furthermore, previous studies suggest a stronger relationship of REM-sleep deprivation with procedural than with declarative learning. However, findings regarding these effects in older adults or regarding the effects of REM-sleep augmentation have been rare so far. Therefore, the present study investigates: 1) possible age effects in the study of REM-sleep and learning, 2) the effects of REM-sleep augmentation on learning as opposed to the effects of REM-sleep deprivation on learning and 3) the differential effect of REM-sleep manipulation on declarative and procedural learning. As the study is still in progress, this abstract presents only an excerpt of results which will be extended by further data acquisition and analysis.

Methods: Participants - aged 60 to 85 years - are randomly assigned to five different groups with a target n of 20 per group and spend one adaptation night in our sleep laboratory before the subsequent study night. During the study night the first group is deprived of REM-sleep by being woken whenever REM-sleep sets in. The second group is matched with group one in terms of frequency of awakenings but in contrast is woken during NREM2-sleep. REM-sleep augmentation is achieved physiologically through REM-rebound after a night of REM-sleep deprivation in the third group and pharmacologically by an AChE inhibitor in the fourth group. A fifth group is administered a placebo in a double-blind design. Performance in a procedural (mirror tracing) as well as declarative (paired-associate list) learning task are investigated before and after the study night.

Results: Preliminary results indicate that the percentage of REM-sleep during the study night only predicts memory performance in the morning in the declarative learning task (ß=.32; [Delta]R^2=.10; p<.05; N=18) but not in the procedural one after statistically controlling for learning performance in the evening.

Conclusions: Contrary to findings in young adults, the results of this study suggest a stronger relationship of REM-sleep with declarative than with procedural learning in older adults. These results may be seen as indicative of older adults showing different result patterns in the context of REM-sleep and learning and question previous findings of stronger associations of REM-sleep with procedural learning than with declarative learning. As the study progresses, further analysis of the data will be needed to confirm these preliminary results and to elucidate the influence of age in the context of REM-sleep and learning as well as the role of REM-sleep augmentation in learning.

0413.H

Sleep in Postmenopausal Women: Different Response to Hormone Replacement Therapy Between Short-Term and Long-Term Menopause

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Introduction: The menopause is the cessation of cyclic ovarian function as manifested by the occurence of the final menstrual period. Women typically live over one-third of their life after the onset of the climateric and he occurence of menopause wherein they may suffer from a number of symptoms. The symptoms are thought to be due to decreased levels of circulating estrogem and progesterone. These symptoms which are variably present frequently include alterations in sleep such as insomnia and night sweats and a number of non-sleep related symptoms including: hot flushes paresthesias, vaginal dryness, dyspareunia, urinary frequency, palpitations, headache, vertigo, anxiety,and so on. There were no studies comparing early and late postmenopause and their responses to hormone therapy as far as sleep is concerned. The aim of this survey was to study the sleep in post menopause: to see if there were any differences on sleep when using hormone replacement therapy between early and late postmenopausal women.

Methods: Thirty-three women in postmenopause were selected to join the group, None of them had any contraindications for the use of hormone therapy. They were not using either hormone therapy or hypnotic drugs. All of them had a basal polisomnography and answered a questionnaire about sleep after what they had been divided in two similar groups. Fourteen women formed our tested group (Group A), subdivided in early and late postmenopause. Nineteen women joined our control group (Group B), subdivided in early and late postmenopause. The pacients from Group A received estrogen whereas those from Group B receveid placebo. Pacients of both groups had another polisomnography and answered again the sleep questionnaire after three months of drug administration. Then Group B used estrogen plus progesteron and Group A placebo plus progesterone for three months and all of then did the final polisomnography and the sleep questionnaire for the last time.

Results: Both early and delayed postmenopausal women were benefit by hormone therapy in clinical complaints of insomnia. Nevertheless there was a significantly reduction in the sleep latency in the subgroup of delayed postmenopause when using the medroxiprogesterone acetate (p=0,008). Nor the polisomnography neither the sleep questionnaire exhibit differences between the subgroups when evaluating PLM. There was a decrease in the complaint of snoring, especially in subgroups of delayed postmenopause using either estrogen isolated (p=0,02)or combined with medroxiprogesterone (p=0,02).
Conclusions: Estrogen with or without the medroxyprogesterone acetate reduced the incidence of snoring in the delayed postmenopausal womenThe sleep latency was reduced by medroxyprogesterone in the delayed postmenopausal women.

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0414.H

A Comparison of Actigraphy and Polysomnography in Assessing Sleep Among Nursing Home Residents

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Introduction: The relative accuracy of actigraphic measurements of sleep relative to polysomnography (PSG) among frail elderly nursing home (NH) residents remains controversial. Actigraphy is simple to use and minimally intrusive, making it attractive for use in the NH population. This study examined the correlation between simultaneously performed actigraphy and PSG among frail and demented NH residents
Methods: Participants were a convenience sample of 37 nursing home residents who generated 52 nights of simultaneous actigraphy and PSG. We employed the Actillume recorder and the Action 3 (version 3.15) scoring algorithm to record and score the actigraphy data. PSG was performed using the SensorMedics (Yorba Linda, California) SomnoStar 4100 digital acquisition system. Actillume recordings were truncated to match the "light off" and "light on" times of the PSG. PSG was scored by an R.PSG.T blinded to the actigraphic data. Spearman's rank order correlations were used for data analyses.
Results: The mean (SD) age of the 37 patients was 82.5 (8.7) years; 78.4% were female.The mean (SD) Charlson comorbidity index was 3.0 (1.9). The mean (SD) MMSE was 11.7 (10.2), with 85.3% of subjects having MMSE < 23. The subjects were severely mobility impaired; 36 subjects were unable to transfer from bed without assistance. The mean (SD) total sleep time (TST) were 329.8 (145.6) and 288.0 (129.1) minutes for actigraphy and PSG, respectively (Spearman correlation = 0.46, p = 0.001). The mean (SD) sleep latencies were 15.8 (50.3) and 59.0 (63.1) minutes for actigraphy and PSG, respectively (Spearman correlation = –0.05, p = 0.73). The mean (SD) sleep efficiencies were 68.3 (27.1) and 59.1 (23.4) percent for actigraphy and PSG respectively (Spearman correlation = 0.42, p = .002). The mean (SD) of wake time after sleep onset (WASO) were 121.0 (115.2) and 143.7 (90.8) minutes for the actigraphy and PSG, respectively (Spearman correlation = 0.26, p = 0.068). The differences between mean values for actigraphy and PSG were 41.8 minutes for TST, 43.2 minutes for SL, 22.7 minutes for WASO and 9.2% for sleep efficiency.
Conclusions: In this study, actigraphy underestimated sleep latency and WASO while overestimating TST and sleep efficiency relative to PSG. Even though actigraphy may be attractive for use in frail, demented nursing home residents, these limitations may have to be taken into consideration while interpreting the actigraphy results.

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0415.H

Ambulatory PSG First Night Effects in Community-dwelling Sleep Impaired Older Adults

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Introduction: Substantial data suggest that laboratory polysomnographic (LPSG) studies in normal sleepers and insomniacs are associated with first night effects (FNEs), i.e., a relative disruption in sleep on the first night of a series of PSG recordings. As a result, researchers have relied heavily upon LPSG data from the second and third nights, while often ignoring the first night. Home-based polysomnography (HPSG) may allow an objective evaluation of sleep quality in a manner that is more acceptable and less burdensome to participants than measurement in a sleep laboratory. HPSG may thus decrease the incidence of FNEs, allowing the researcher to utilize first night data along with subsequent nights. Limited data exist with regard to FNE in the home setting, particularly in older adults, who often experience poor sleep. We used 3 consecutive HPSG recordings to evaluate FNEs in older adults with moderate sleep complaints.
Methods: Thirty (24 women, 6 men) sedentary older adults (mean age = 62 $\pm$ 7 yrs) with moderate sleep complaints (mean score = 7.7 $\pm$ 3.1) on the Pittsburgh Sleep Quality Global Index (PSQI), underwent 3 consecutive nights of HPSG. Participants had no evidence of clinical sleep disorders or health problems linked to their sleep complaints. All had a Desaturation Index of < 10 events per hour, and a multi-variable apnea prediction score < 0.8. Participants were instructed to follow their usual bedtime routines and sleep schedules. The following variables were measured in the participant's home using 15-channel polysomnography: total sleep time (minutes) (TST), percent time in stage 1 sleep (STG1%), stage 2 sleep (STG2%), slow wave sleep (SWS%), time in REM sleep (REM%), total arousals per hour (TA), and sleep efficiency (SE%). Paired comparison t-tests were used to compare variables measured during PSG night 1 with the means of nights 2 and 3.
Results: There were no statistically significant differences between data collected from the first HPSG night (HPSG1) and averaged values for the second (HPSG2) and third (HPSG3) nights for the following variables: TST (t = -1.29, p = 0.21), STG2% (t = -0.58, p = 0.57), SWS% (t = 1.18, p = 0.25), REM% (t = -0.30, p = 0.77), TA (t = 1.17, p = 0.25), and SE% (t = -0.18, p = 0.86). STG1% approached statistical significance (t = 1.96, p = 0.06; means = 9.7 vs 7.7), with a slightly greater percentage of time spent in stage 1 sleep on HPSG1 versus the average STG1% of HPSG2 and HPSG3.
Conclusions: These findings suggest that home-based polysomnography may minimize the incidence of relative sleep disruption on the first night in sleep-impaired older adults. This is in contrast to FNE results that have been reported with laboratory-based polysomnography.

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0416.H

Relation Between Sleep Efficiency and Waking Vigilance in the Elderly

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Introduction: A good night's sleep is one factor that affects daytime vigilance and performance. Normal aging is accompanied by sleep disturbances that can have a negative impact on both subjective well-being and objective health status. Exactly how and why these sleep-related changes affect daytime performance is still unclear and some researchers

have argued that the elderly are generally not as sensitive to degradation in sleep quality as younger populations. We present preliminary results from an ongoing study on the relationship between sleep quality and level of daytime vigilance in a population of healthy elderly subjects.
Methods: Participants were fourteen healthy elderly (9 women, 5 men), aged 60 to76 (mean age 67 ± 5.3). Participants were well educated with a mean number of 11.6 ± 3.9 years of schooling. All were in good health and none suffered from a medical condition that could affect either sleep or daytime vigilance (e.g., primary sleep disorder, dementia, head trauma, epilepsy, cerebrovascular accident, depression) and all were free of medication that could adversely affect sleep and/or daytime vigilance. Exclusion criteria included scores of 24 or less on the Folstein Mini-Mental Scale, scores of 19 or more on the Beck Depression Inventory-II, and scores of 15 or more on the Beck Anxiety Inventory. Participants were investigated in the sleep laboratory for two consecutive nights. They were also required to perform a time reaction task (Four Choice Reaction Time Test or FCRTT) at regular intervals the day following their second night in the laboratory. The FCRTT trials took place at 10:00, 12:00, 14:00 and 16:00. Subjective sleep quality was assessed by the Pittsburgh Sleep Quality Index (PSQI) and subjective level of daytime vigilance with the Epworth Sleepiness Scale. Participants also had to indicate their level of subjective alertness on a visual analog scale (VAS) before each FCRTT trail.
Results: Scores on the PSQI were within normal limits (mean 3.9 ± 2.6) as were those on the Epworth (mean 5.9 ± 3.5). Sleep efficiency ranged from 65% to 95% with a mean of 87.2 ± 9.1. Scores on the PSQI, the Epworth, and VAS were not significantly correlated with performance at any time on the FCRTT (ps>0.05). On the other hand, sleep efficiency was positively correlated with FCRTT performance on all 4 trials (r = .71, .68, .72, and .84, ps<0.05).
Conclusions: The data indicate that among healthy elderly who are free of sleep complaints, sleep efficiency is nevertheless related to daytime performance on a vigilance task. Furthermore, the results underscore the importance of assessing objective measures of sleep quality and not only subjective ones when investigating the impact of sleep on daytime vigilance.

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0417.H

Driving Simulation (DS) Performance Deteriorates in the Elderly with Mild Cognitive Impairment
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Introduction: Objectively measuring driving performance should help isolate factors contributing to driving problems in the elderly population. Factors contributing to driving problems may include changes in vigilance, motor skills, visual and auditory acuity and cognition. In this study, we examined the effects of mild cognitive changes.
Methods: Inclusion criteria: age > 70 years, a valid drivers license, and normal or vision corrected to normal. Exclusion criteria: 1) dementia (determined by a clock draw test and MMSE <23); 2) symptoms of a significant sleep disorder; 3) a significant medical disorder; 4) alcohol abuse; 5) consumption of more than five caffeine beverages/day; 6) smoking more than ½ pack of cigarettes per day; and 7) use of sedative or stimulant substances (including caffeine or cigarettes) within 3 hours of the task. Eight men and ten women (71 to 85 years old; mean = 78.8 + 3.9) were tested after providing informed consent. We divided them into those with normal (N) Mental Mini Status Examination (MMSE) scores of 29 - 30 (n = 10) and those with low normal (LN) scores of 27 - 28 (n = 8). Following a ten-minutes practice "city drive", subjects completed a 60-minute task designed to replicate highway driving with long wide curves and an oncoming vehicle every ten minutes. We used a System Technology simulator. The PC based driving simulator had a steering wheel, gas and brake pedals, and sound. The simulator continuously sampled performance and grouped data into six 10-minute time blocks. Subjects were instructed to maintain a speed of 55 mph during the 60-minute task.
Results: Examination of lane position variability (using an analysis of variance with repeated measures on the six ten-minutes bocks and a between subjects analysis for the two MMSE groups), indicated that performance deteriorated during the drive (p = 0.002). The greatest increase in lane variability occurred in the LN group (p = 0.011). Their lane variability increased from 1.1 + 0.2 ft during the first 10 minutes to 1.5 + 0.3 ft during the last 10 minutes of the drive. The normal MMSE group's lane variability was 1.1 + 0.4 ft during the first and during the last 10-minute blocks.
Conclusions: Performance of elderly subjects in the LN group deteriorated during a one-hour drive more so than those with higher cognitive functioning. In other DS studies, subjects with excessive daytime sleepiness also have increasing lane variability during the drive while normals have stable lane variability with lane variability increasing to > 2 feet in apnea patients (e.g., Risser et al., 2000). These data suggest that daytime sleepiness contributes to the poor DS performance in the elderly with mild cognitive impairment. Possibly sleepiness contributes to poor performance on the MMSE. Follow-up measures of sleepiness are needed in these groups.

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0418.H

Older Adults' Attitudes Towards Sleep Disorders
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Introduction: There is a high prevalence of sleep disorders among the elderly, with more than half reporting sleep complaints such as trouble falling asleep or daytime sleepiness. However, Haponik et al found that most physicians either rarely or never order sleep studies to evaluate sleep complaints in their patients, despite the fact that many physicians were aware that sleep disorders carry a significant morbidity. It is thus conceivable that other factors, such as the patient's own cognitive beliefs, may also mediate the undertreatment of sleep disorders. To explore this further, we decided to characterize the significance of various patient beliefs on the decision to seek evaluation/treatment of sleep disorders.
Methods: A questionnaire was developed to evaluate sleep complaints and the willingness to pursue an evaluation of those complaints. The first half consisted of the Pittsburgh Sleep Quality Index, and the second half contained additional questions and response options derived from interviews with patients attending a nearby geriatrics clinic. The finalized questionnaire consisted of 39 items and took approximately 10-15 minutes to complete. It was mailed to a population-based cohort of older adults (age>65) living in the greater Philadelphia metropolitan area.
Results: A total of 220 subjects completed and returned the questionnaires (response rate of 72%). Of these, 50.9% (95% C.I.: 44.1 - 57.7) complained of either taking >30 minutes to fall asleep, or waking up in the middle of the night/early morning, three or more times a week. 15% (95% C.I.: 10.6 - 20.4) had difficulty breathing, coughing or snoring three or more times a week suggesting possible sleep apnea. Of those subjects with sleep complaints, 55.4% (95% C.I.: 45.7 - 64.8) had not spoken to their doctor about it. When asked why, 34.8% (95% C.I.: 27.5 - 42.6) stated that sleep problems are a normal part of getting older. Other common reasons chosen included "My doctor never asks me about it" and "I do not want my doctor to prescribe any medicines to help me sleep", both of which were cited by 18.9% (95% C.I.: 13.2 -

25.8) of the subjects. These three responses were chosen with a frequency that was significantly higher than the others (chi-square test, df=9, p<0.001). Subjects with complaints suggestive of sleep apnea did not differ significantly from those with insomnia complaints in their rates of endorsement (chi-square test for trend, df=9, p=0.9).
Conclusions: The results of this survey suggest that many older adults with sleep complaints do not discuss them with their health care provider. A lack of inquiry by the health care provider was a factor in many cases, but a more common reason was the perception that sleep complaints are a natural occurrence with aging. Efforts to increase the awareness of sleep disorder-related morbidity may help prompt more older adults to seek potentially beneficial treatment

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0419.H

Effectiveness Of The Global Sleep Assessment Questionnaire In Distinguishing Two Older Community-Dwelling Groups

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Introduction: Recently, Roth et al. validated the short, user-friendly Global Sleep Assessment Questionnaire (GSAQ), designed to aid in screening for sleep disorders. The authors validated the instrument in a large sample of sleep center and primary care clinic patients (N=212, mean age 45 yrs, 6% with no sleep disorders). Given the high prevalence of sleep disorders among the elderly, we tested the effectiveness of the GSAQ in detecting the presence of sleep disorders in older subjects. Our approach was to compare the scores of a sample of older primary insomnia research subjects with those of asymptomatic, community-dwelling, older adults.
Methods: The GSAQ contains 11 items with 4 response choices (never, sometimes, usually, and always). The items were designed to screen for insomnia, insomnia associated with a mental disorder, obstructive sleep apnea, restless legs syndrome, periodic limb movement, parasomnia, and shiftwork sleep. We compared self-rated responses from two groups: 1) Applicants for a behavioral treatments for insomnia research project (N=18, mean age=63.3 yrs, SD 8.8, 13 female) screened by clinical interview, questionnaire responses, sleep logs, and overnight ambulatory monitoring for sleep apnea to meet criteria for primary insomnia. 2) A sample of convenience of 35 respondents (mean age=65.4, SD 7.5, 19 female) asymptomatic for insomnia recruited for a study of morningness/eveningness tendencies. We compared the responses of the two groups on an item-by-item basis, using the Mann Whitney test. Our hypothesis was that the two samples would differ on their responses to two GSAQ items relating specifically to insomnia; with the treatment group having higher scores than the non-complaining group.
Results: There were no differences between groups on the 9 non-insomnia GSAQ items; however, as expected, the insomniacs scored significantly higher (p<.05) on the two insomnia items rated for the past month: Item 1) “Did you have difficulty falling asleep, staying asleep, or feeling poorly rested in the morning?”: Insomniacs, mean=2.1, SD 0.8, versus Normals, mean=0.8, SD 0.7. Item 3) “Did sleep difficulties or daytime sleepiness interfere with your daily activities?”: Insomniacs, mean=0.7, SD 0.7, versus Normals, mean=0.3, SD 0.4.
Conclusions: The questionnaire distinguished older subjects with an insomnia complaint severe enough to seek treatment from a sample of asymptomatic elderly on the two insomnia-related items. In further support of the discriminative value of the instrument, the two samples (one screened to meet primary insomnia criteria and the other expected to be healthy and free of sleep disorders) did not differ on any other sleep disorder items. However, larger, more representative clinical samples, and screening using the gold standard, polysomnography, would be required to determine the validity of the GSAQ for detecting sleep disorders in elderly clinical populations.

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0420.H

Minute by Minute Probability of Transition from Sleep to Wake: A New Measure of Homeostatic Sleep Drive

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Introduction: Laboratory studies show that a conventional bedrest episode is fragmented into Sleep and Wake bouts. Using a criterion that requires a minimum bout to have one consolidated minute for which the polysomnogram is scored either as Wake or Sleep (of any stage, including REM), approximately 10 Sleep or Wake bouts per episode are observed [Lo C-C, et al. Europhys.Lett. 2002;57:625-31].Transitions from Sleep to Wake exhibit the character of a random semi-Markov process in which transition rate is a varying function within bedrest. This transition rate is also known as the “hazard function”(h), a name derived from medical applications. The inverse of h,(h-1) has the units of time and can be thought of as the expected duration of a sleep bout centered at the time the hazard is evaluated. This inverse, h-1, is a quantitative measure of the drive to maintain Sleep.
Methods: We apply the concept of inverse hazard as a measure of sleep drive to data generated in a Forced Desynchrony protocol in younger and older human volunteers [Dijk D-J, Duffy JF, Czeisler CA. Sleep 2001;24(5):565-82.] In this protocol, all circadian phases are sampled equally. Here we average over all circadian phases, retain the age groupings of Older and Younger subjects and examine cohorts of Sleep bouts originating in successive bedrest bins of 100 minute width.
Results: For Sleep bouts ³ 8 minutes, the hazard changes extremely slowly within a 100 minute width bin (~ a pure Markov process). For bouts < 8 minutes, the hazard increases sharply for shorter bouts, indicating a different underlying statistical process. Since bouts < 8 minutes comprise less than 10% of cumulative sleep time, we exclude them here.At the start of a bedrest episode, sleep drive (h-1) is highest and declines exponentially toward baseline, with a decay constant of ~100-120 minutes for both Older and Younger subjects. The strength of the initial excess sleep drive is much larger for Younger than for Older subjects: ~6.4 times versus ~1.3 times baseline values, respectively. The time constant with which h-1 decays after sleep onset is very close to the value of 100 minutes indicated for “Process S” in simulations based on measured Slow Wave Activity (SWA) [Achermann P et al. Brain Res.Bull. 1993;31:97-113.]. For both Older and Younger subjects, h-1 is essentially constant over the last half of bedrest episode: h-1 is ~20 minutes for Older and ~40 minutes for Younger subjects.
Conclusions: The inverse hazard function affords a quantitative measure of sleep drive across a bedrest episode and between different populations.

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0421.H

Spectral Analysis And The Electrophysiological Characteristics Of Sleep In Ageing People With Down Syndrome

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Introduction: Down syndrome (DS) people are known to have a precocious ageing. Research has demonstrated that ageing people with DS are predisposed to Alzheimer's disease (AD). By the age of 40 virtually all of them have the neuropathology of the disease. In the early stages of AD, alterations to the sleep architecture are observed. It is known that the EEG during REM sleep is affected by the deterioration of the CNS caused by AD. The aim of this study was to examine the effects of ageing on the sleep architecture of people with DS and to verify if the sleep architecture and the different REM sleep components are similar to those observed in normal ageing or in AD.
Methods: Ten people with DS with a moderate to severe level of functioning, at a mean age of 46.3 participated in the study. The subjects slept in the sleep laboratory for one night. Subjects using anxiolytics or hypnotics were excluded from the study. The presence of sleep apnea and PLMS were eliminated. Cerebral activity for the spectral analysis was recorded during both wakefulness and sleep at sites F3-C3, F4-C4, T3-T5, T4-T6, P3-O1 and P4-O2.
Results: The results of the sleep architecture variables showed that the DS patients had a sleep efficiency of 61.3% (SD=7.5). The mean percentage of time spent in the different stages of sleep was 17.2% (SD=8.4) for stage 1; 52.9% (SD=10.3) for stage 2; 6.7% (SD=6.1) for SWS and 13.5% (SD=4.5) for REM sleep. The different REM sleep parameters revealed a mean number of REM periods of 3.7 (SD=0.8) and an overall REM sleep efficiency of 67.3% (SD=14.4). For the spectral analysis of the EEG, a global cortical slowing was calculated [slow (delta + theta) / fast (alpha + beta) ratio] for wakefulness and REM sleep. The result revealed a significant difference (p=0.008) between wakefulness and REM sleep with a respective ratio of 1.31 (SD=0.6) and 3.2 (SD=0.7). No differences was observed in the cortical slowing for the different cerebral regions recorded.
Conclusions: Compared to the young adults with DS (Clausen et al., 1977; Castaldo et al., 1974), we obtained a decrease in sleep efficiency, a lower percentage of SWS and a decrease REM sleep. The decrease in REM sleep could be attributed to the neuronal degeration observed in AD and in people with DS over the age of 40. The EEG ratios we reported for global cortical slowing were similar to those reported in previous studies for AD patients for both wakefulness and REM sleep (Petit et al., 1992; Prinz et al., 1992). Several studies have reported EEG slowing during REM sleep in AD, which is more prominent in the temporal area (Petit et al., 1992; Prinz et al., 1982). We did not observe any significant difference in EEG slowing between the cortical areas we examined. A possible explanation for this could be that ageing people with DS have a more global cerebral deterioration than AD patients.

0422.I

The Disconnected Brain Stem Does Not Support Rapid Eye Movement Sleep Rebound Following Selective Deprivation

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Introduction: Following deprivation there is an increase in sleep duration, called sleep rebound, while during the deprivation period there are more attempts at transition into sleep, called sleep pressure. Here we address the question of whether the brain stem can independently support these two processes for rapid eye movement (REM sleep).
Methods: We used cats with a long-standing brain stem separation from the forebrain and compared their response to REM sleep deprivation to that of intact subjects. The animals sustained a mesencephalic transection and implantation of electrodes and the experiments began 3-4 weeks later, when the cats displayed all the previously reported polygraphic and behavioral manifestations of sleep-wakefulness (S-W). A 24 hr undisturbed S-W recording session was first performed, and the next days a similar session started with a 6 hr deprivation period which was followed by 18 hr of undisturbed sleep. Six-hour blocks were used for comparisons of percent time spent in the different S-W states.
Results: During the baseline session REM sleep features were similar in both animal groups except that no signs of REM sleep were seen in the isolated forebrain of the transected cats. Deprivation produced respective 90.1% and 87.8 % losses of REM sleep in intact and decerebrate cats. However, no significant changes in non rapid eye movement (NREM) sleep, drowsiness, and waking time percentages were seen in either group of animals for the four time-blocks of the deprivation session versus the corresponding baseline time-blocks, indicating selective deprivation of REM sleep. During the 6 hr block following deprivation, REM sleep increased significantly (34.6%) in the intact cats while, in contrast, there was no sleep rebound in the decerebrate animals. The rebound in the intact acts was accounted for by minor increases in both number and duration of REM sleep episodes. There were no significant animal group differences between the two remaining time-blocks. The number of aborted episodes of REM sleep during deprivation exceeded the number of episodes during the same time period of the baseline day by 3 and 5 folds in intact and decerebrate cats, respectively, indicating a pronounced increase for REM sleep pressure, but without significant between groups differences.
Conclusions: The data showed that rebound of REM sleep can not be sustained by the brain stem alone. In contrast, REM sleep pressure persisted in the decerebrate cat thereby showing that it does not dependent on forebrain influences. Therefore, rebound and pressure are two different aspects of the REM sleep recovery process and they are controlled by two different mechanisms We propose that the rebound depends on a permissive control descending from the hypothalamus, while pressure is generated in the pons, and involves the ventral pontine reticular nucleus. This also shows that occurrence of REM sleep pressure does not need to be preceded by NREM sleep.

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0423.I

Inhibition of NF-Nuclear Translocation Prevents Sleep Deprivation-Induced Increase in As1s adenosine Receptor mRNA

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Introduction: Previously we had shown that 3h of sleep deprivation not only increased the levels of extracellular adenosine but also the levels of As1s receptor mRNA and the DNA binding activity of NF-(Basheer et al.,2001a and b). Recently, using acute brain slices, we demonstrated adenosine-mediated activation of a signal transduction pathway that could potentially lead to the activation of the transcription factor NF-in basal forebrain cholinergic neurons(Basheer et al.,2002). Together these results led to the hypothesis that sleep deprivation-induced extracellular adenosine may increase the levels of As1s adenosine receptor transcription by activation of NF-, which in turn increases As1s transcription by acting on As1s promoter region. To test this hypothesis, we examined the effect of blocking nuclear translocation of NF-by targeted microinjection of an inhibitor peptide, SN50, into basal forebrain prior to three hours of sleep deprivation.
Methods: Male Long-Evans rats (250-300g) housed in 12 hr light/dark cycle (lights on 7:00 A.M. to 7:00 P.M.) at a constant temperature (23±10C) with access to food and water *ad libitum* . The microinjec-

tions were performed at 7:00AM. Under general anesthesia, the cell-permeable NF-inhibitor peptide, SN 50 or control peptide, SN 50M (Calbiochem, San Diego, CA) prepared in ACSF were microinjected unilaterally (0.5 µl of the freshly prepared 30mM solution at the rate of 0.1µl/min) into cholinergic zone of basal forebrain (Bregma coordinates: AP -0.30, ML -2.2, DV –8). The animals were allowed to recover from anesthesia (approximately 20-30 min) and kept awake for three hours by gentle handling. At the end of 3h of sleep deprivation the rats were either 1)anaesthetized, transcardially perfused and brain sections (40mm) were double labeled for ChAT and NF-immunohistochemistry, or 2) basal forebrain tissue was collected for real time RT-PCR for As1s receptor mRNA levels. The As1s mRNA levels were normalized using the ratios of CsTs values for As1s receptor and 18S RNA.

Results: Double labeling immunohistochemistry showed an absence of nuclear translocation of NF-in basal forebrain cholinergic neurons in rats that were injected with the inhibitor peptide, SN50, whereas the control peptide, SN50M, did not prevent sleep deprivation-induced nuclear translocation of NF-. Furthermore, the levels of As1s receptor mRNA, determined by real-time RT-PCR, were significantly lower (-18.97$\pm$0.3% control,N=4, p> 0.01) in inhibitor peptide injected rats when compared to rats that were injected with control peptide.

Conclusions: These results suggest that sleep deprivation-induced increase in As1s mRNA may be dependent on the activation of NF-in basal forebrain of rats.

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0424.I

Further Analyses on Event-Related Potential Measures of Frontal Lobe Activity: Sleep Deprivation Versus Post-Recovery Sleep

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Introduction: Increasing evidence suggests that frontal lobes are particularly vulnerable to the effects of sleep deprivation (SD). Unfortunately, it is not clear whether this phenomenon is due to frontal lobe impairment or to task complexity. Detection of novelty, a non-complex behavior, involves frontal lobes. Event-related potentials (ERP) can be employed to monitor the activity of various brain regions. If subjects are presented with rare, highly novel stimuli, a positive wave called P3a is elicited, which maximizes over anterior regions of the scalp. It has been shown to be smaller in frontal regions following sleep deprivation (SD). However, the reversibility of this phenomenon following recovery sleep (RS) has yet to be explored. The aim of the present study was to compare P3a amplitude during SD and after RS to determine if the smaller P3a amplitude observed in frontal lobes during SD will come back to baseline values following RS.

Methods: Three men and 8 women (age range 18 to 26) were sleep deprived for 38 h. They were tested after 36 h of waking and re-tested after 10 h of RS. A control group of four men and 8 women (age range 18 to 25) were tested after 12 h of waking. EEG was recorded from Fz, Cz and Pz. EOG was also recorded to monitor blink artifacts. An auditory oddball task was administered at 8 pm for both groups and at 8 am, after RS, for the SD group only. Subjects were asked to detect (button press) rare high pitch tones (p=0.10) that occurred among frequently presented low pitch tones (p=0.80). Unexpected environmental sounds (p=0.10) were also presented at random. Participants were told to ignore the unexpected (novel) stimuli. ERPs were averaged separately for each stimulus type.

Results: The auditory novel stimuli elicited a positive wave that ranged in latency from 250-375 ms. A Time (36 h SD vs. post RS) X Electrode (Fz, Cz, Pz) repeated measures ANOVA revealed a significant interaction ($F(2,20)=8.35$, $p=0.002$): Following RS, participants showed larger P3a amplitude at Fz (p=0.03) and Cz (0.004) but no significant difference at Pz (p=0.88) when compared to 36 h of SD. Additionally, a Group (post-RS vs. controls) X Electrode (Fz, Cz, Pz) ANOVA did not show any interaction ($F(2,42)=2.58$, $p=0.09$) or any significant Group effect ($F(1,21)=0.02$, $p=0.89$): Following RS, the SD participant's P3a amplitude was no different from the control group's P3a amplitude at any electrode site.

Conclusions: Commensurate with observations of frontal lobe injury patients, a previous study revealed that P3a amplitude was reduced in frontal regions after SD. This phenomenon is reversible, however, because the P3a returns to its baseline value following RS. Nevertheless, the results following RS were measured at a different circadian moment. This could also have influenced the observed P3a amplitude increase. Further studies are needed to increase our understanding of this phenomenon.

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0425.I

The Effect of Education about the Consequences of Sleep Deprivation and Driving

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Introduction: Sleepiness, the second major cause of vehicle accidents and responsible for approximately 100,000 accidents annually in the United States has only recently been considered a significant risk factor. Consequently, the dangers of sleep deprivation and driving are underrecognized. And it is important that the public is educated on this matter. Evidence from drinking and driving advertisements indicates that messages containing both the negative consequences and preventative strategies relevant to a situation, rather than negative consequences only are more effective at changing existing beliefs and behaviours. Further evidence indicates that messages presented in an audio-visual format are more understandable and more likely to capture the audience's attention than messages in a printed format. The aim of this study was to investigate the effectiveness of different methods of education on participants' ratings of driver culpability in a sleep-related accident and on their ability to suggest suitable preventive strategies.

Methods: 300 undergraduate students (mean age 19.7) who gave their informed consent were randomly assigned to either a control condition or one of four experimental conditions created by the factorial combination of message content (negative; negative with preventative strategies) and method of delivery (text; video). Following education, participants read a motor vehicle accident scenario and rated the culpability of the driver. Beliefs and behaviours relevant to the effects of sleepiness on driving were assessed before and after education. The data were analysed by analysis of variance.

Results: Participants in the strategies condition felt they had learned more than participants in the negative conditions ($p < .005$) and reported more preventative strategies than participants in the negative conditions ($p < .005$). Participants in the video conditions did not feel that they had learned more about the consequences of sleep deprivation and driving than those in the text conditions ($p > .10$) but did report more preventative strategies than participants in the text conditions ($p < .05$) and in the control group ($p < .05$).

Conclusions: In general, people feel that they have learned the most information when they receive a message containing both the negative consequences of sleep deprivation and driving and possible preventative strategies. Further, people are more knowledgeable about the preventative strategies for sleepiness and driving when they receive a message in the form of a video, and when the message contains information regarding both the negative consequences of sleep deprivation and driving and the preventative strategies. If organizations can make use of these findings in their campaigns for public awareness on sleep deprivation and

driving, then perhaps motor vehicle accidents related to sleepiness will start to decrease.

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0426.I

Visual Neglect in 26 hours of Continuous Wakefulness Demonstrates Patterns Consistent with Prefrontal and Biparietal Brain Impairment

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Introduction: We hypothesized that visual neglect would occur with less than 24 hours of continuous wakefulness and in a pattern representative of the hypometabolism observed in fdg-PET scans of continuous wakefulness. We hypothesized that peripheral visual neglect and simultanagnosia would occur, representing dysfunction in the biparietal regions. In a study testing these hypotheses, we implemented a visual field task designed to assess awareness of visual stimuli during cognitive loading in U.S. Air Force pilots over 26 hours of wakefulness using a high fidelity jet simulator. In this abstract we report patterns of visual neglect and correlation of neglect with an operational measure.
Methods: Eight U.S. Air Force pilots (male, RH, 25 - 52 years) certified in air refueling were studied. Tasks: The Air Refueling Partial Task Trainer (ARPTT), McGuire Air Force Base, simulated a C-141 aircraft in the task of air refueling from a KC-135 tanker. The visual testing device (LVFT) was mounted onto the dashboard, just below the simulated horizon. The LVFT presented 150 sequential single or double white light stimuli, each 0.25 second duration at random intervals over a 20 minute period while the pilot maintained a position approximately 50 feet behind and below the tanker with an air speed of approximately 400 mph (275 knots). Stimuli spanned 75-degrees-left to 75-degrees-right of center at 15 degrees intervals. The pilot responded verbally to the stimuli. On study Day 1 the subjects re-familiarized in the simulator, trained on the LVFT, and was allowed 6 hours of time-in-bed overnight. On study Day 2 subjects remained active throughout the day and at 8pm began a 12.5-hour overnight simulated flight. 15 LVFT trials were presented on Day 2. Preliminary analyses are presented.
Results: Analyses include all omissions of single stimulus and double stimuli. Omissions occurred with all stimulus types. When compared to baseline, performance on the LVFT showed response omissions that achieved significance beginning at 19 hours continuous wakefulness (Trial 10, $p<0.05$, n=8), and continued through the end of the study period. Of the double simultaneous stimuli, that is when a center light was presented simultaneously with either a left or right light, right omissions were missed significantly more often than center, than left, or both ($t=-3.08$, $p=0.008$). One pilot showed a pattern of significant peripheral visual neglect, with nearly equivalent omissions of stimuli at left-75 and right-75 ($p<0.05$). Correlation with simulator shutdowns was $r=.948$, $p<0.0001$.
Conclusions: Impairments in responses to visual stimuli presented along the horizontal meridian using the LVFT began after 19 hours of sleep deprivation. Omissions included all stimulus types, reflecting a pattern of prefrontal attention neglect, and included omissions of one of two stimuli and of peripheral stimuli, reflecting biparietal lobe dysfunction. These findings support our hypothesis that transient visual performance impairments occur with less than 24 hours of sleep deprivation. Correlation of visual neglect with simulator shutdowns is high.

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0427.I

Increased Serum Antibodies Induced by Sleep Deprivation in Rats

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Introduction: The goal of this research is to elucidate the health effects of inadequate sleep through comparative research. The earliest clinically meaningful sign so far identified in laboratory rats is translocation of gut bacteria and survival in extraintestinal tissues, considered diagnostic of immunosuppression. Different mechanisms of immunity are now being studied to determine whether their responses to sleep deprivation indicate immunodeficiency or compensation. The present investigation focused on humoral immunity by studying serum immunoglobulin concentrations.
Methods: Total and partial sleep deprivation by the Bergmann-Rechtshaffen method was continued for 5, 10, 15, and 20 days in rats operated for EEG monitoring, and according to established procedures. In brief, total sleep deprivation (SD) of each rat was produced by motor locomotion of short duration (6 sec) upon sleep onset without interference with other behaviors. Partial sleep deprivation of a paired rat, a.k.a. the yoked condition (YC), was produced by the same brief locomotion, which frequently disrupted sleep. Baseline controls (BC) were permitted to sleep normally. Five animals per group were studied at each time point. Serum specimens obtained by cardiac puncture were assayed by radial immunodiffusion for IgA, IgM, IgG, and subclasses IgG1, IgG2a, IgG2b, and IgG2c. SD and YC data were compared for significant differences ($P<0.05$) by two-way ANOVA, and compared with BC data by one-tailed t test.
Results: IgM, IgG, IgA, and IgG2a increased with differing time courses in both SD and YC groups. All three classes of immunoglobulin (IgA, IgM, IgG) and one subtype, IgG1, were significantly greater in the SD group compared with the YC group. Progressive increases in IgM by 5 days and IgG by 10 days were significantly different from BC values in SD, but not in YC rats (mean ± stdev, IgM: SD 807 ± 121, BC 702 ± 54 mg/l; IgG: SD 476 ± 180, BC 259 ± 119 mg/dl). Group differences in other immunoglobulins occurred later.
Conclusions: Early, moderate increases in serum antibodies in sleep-deprived rats indicate spontaneous stimulation of B lymphocyte and plasma cells. IgM is the first immunoglobulin to increase in response to a threat to host defenses, typically peaking within the first 3 to 4 days. IgG increases next, usually after 5 or more days. Thus, humoral immune responses require time. The present results show IgM and IgG responses by Days 5 and 10, indicating an early inception during sleep deprivation. The specificity of the antibody response requires future study, but the results are consistent with antigenic challenge. For example, one main effector function of IgG1 is activation of microbicidal mechanisms and toxin neutralization. A hint that B lymphocyte functions are affected by 64 hours of sleep deprivation in humans is indicated by a shift in DNA synthesis toward cell mitosis (Dinges et al., 1994). Blood phagocyte cell numbers increase progressively during sleep deprivation in both humans and laboratory rats, perhaps reflecting effector functions that lead to stimulation of humoral immunity.

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0428.I

The Effect Of REM Sleep Deprivation On Acquisition And Maintenance Of Food Reward In An Operant Task

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Introduction: Sleep deprivation causes a significant increase in feeding in rats and humans, but the neural mechanism(s) behind this relationship

are still unclear. We have previously shown that short-term REM sleep deprivation (RSD) by the "flower-pot" method is sufficient to produce increased feeding. In this experiment, we sought to determine whether sleep deprivation-induced feeding was related to changes in motivation for food reward in an operant task.
Methods: Sleep Deprivation: The multiple platform method was used to deprive rats of REM sleep (D rats). They were compared to large platform controls (C rats) and home cage control group (H rats). Operant Training: Animals habituated to sugar pellets and the operant chambers were exposed to 15 min sessions each day. During acquisition, rats were food deprived to maintain 85% of free-feeding weight. A lever press resulted in delivery of a sugar pellet on a FR1 schedule for the first 50 presses and a VR2 schedule for the remaining lever presses. Three experiments were performed to assess the effects of sleep deprivation on the following parameters: 1. Acquisition of responding: After two days of lever exposure, rats were assigned to D, C and H groups. Acquisition of the operant task was measured for five days of RSD. 2. Maintenance of responding without food deprivation: Rats were trained to lever press for food prior to RSD. When asymptotic responding occurred, all rats resumed free feeding. Rats where then randomly assigned to D, C, and H groups and tested on the operant task for five days of RSD. 3. Maintenance of responding with food deprivation: The protocol was identical to exp. 2 except that food deprivation (85% free-feeding weight) continued during the period of RSD.
Results: All three experiments had similar results. The most prominent findings occurred on RSD days 4 and 5, at which time D and C rats showed significantly reduced rates of responding in comparison to H rats. Furthermore, D rats always showed the lowest rates of lever pressing in all experiments. Analysis of behavior across individual sessions showed that D rats responded equivalently to H and C rats during the beginning of testing sessions, but significantly decreased their responsiveness as the session progressed in comparison to both control groups.
Conclusions: These results suggest that REM sleep deprivation produced by the "flower pot" method impairs learned instrumental behavior, or activational aspects of motivation, despite leading to increased appetite in free-feeding situations. These results are similar to those reported in rats following dopamine depletion or administration of dopamine antagonists and suggests that behavioral effects of sleep deprivation may be related to dysregulation of dopamine systems.

0429.I

The NMDA Agonist Cycloserine Does Not Affect REM Deprivation-Induced Impairment of Extinction of a Cued Conditioning Task
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Introduction: Both human and animal studies have shown that sleep deprivation affects certain types of learning, and learning can change subsequent sleep patterns. Most animal research has focused on the role of rapid eye movement (REM), or paradoxical, sleep in learning and memory consolidation. Previous research has demonstrated that 6 hours of REM sleep deprivation immediately following cued fear conditioning produces normal retention but retarded extinction of the conditioned response when tested 48 hours later (Silvestri & McMillen-Dodd, 2001). The present study was designed to elucidate the neurobiological mechanisms underlying this effect. As NMDA agonists have been shown to enhance extinction (Walker, Ressler, Lu, & Davis, 2002), this experiment was conducted to investigate their effects on REM deprivation-induced impairment of extinction.
Methods: Nineteen animals were trained in a 3-phase cued conditioning procedure. During phase 1 (habituation), each animal was exposed to the experimental chamber for approximately 30 minutes to habituate to the context. During phase 2 (conditioning), 48 hours later, each animal was presented with 5 light (5sec) + footshock (0.5sec, 0.25mA) pairings. Immediately following conditioning, animals were injected with either 15 mg/kg of the NMDA agonist D-cycloserine (DCS) or saline (SAL). After the injections, animals were subjected to REM deprivation or an appropriate control procedure for 6 hours and then returned to their home cages. During phase 3 (extinction), 48 hours later, each animal was returned to the conditioning chamber and presented with 10 light alone (i.e., extinction) trials. Trained observers recorded freezing (a reliable indicator of conditioning) during each second of the 10 light alone presentations.
Results: Analysis of freezing behavior during the 10 extinction trials revealed significant effects of group ($F[2,16]=5.74$; $p=.013$), trials ($F[9,144]=10.05$; $p<.001$), and a group x trials interaction ($F[18,144]=2.59$; $p=.001$). Post hoc tests found that non-REM deprived/DCS animals (n=6) showed significantly less freezing than both the REM-deprived/DCS animals (n=7) and the REM-deprived/SAL animals (n=6). Animals in all groups showed high levels of freezing during the first four extinction trials, indicating normal retention of conditioning. Animals in the non-REM deprived/DCS group showed a decrease in freezing throughout the remainder of the session, demonstrating normal extinction. However, animals in the REM-deprived/DCS and REM-deprived/SAL groups continued to freeze at a high level, demonstrating impaired extinction.
Conclusions: This study replicates previous research demonstrating that REM deprivation impairs extinction, but not retention, of a cued conditioning task. In addition, REM-deprived animals, regardless of whether or not the NMDA agonist DCS was administered, showed impaired extinction of freezing as compared to the non-REM deprived animals. These results indicate that REM deprivation-induced impairment of extinction may not be mediated by NMDA-dependent mechanisms.

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0430.I

Modafinil Does Not Affect Heart Rate or Heart Rate Variability from 0800-1200 hours During 88 hours of Simulated Sustained Operations
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Introduction: Modafinil has been reported to elevate heart rate (HR), however, this finding is inconsistent and the underlying mechanism(s) mediating this possible effect are not well understood. We sought to determine whether HR was altered by repeated administrations of modafinil during 88 hours of simulated sustained operations (SUSOPS), and whether these changes, if any, were coincident with alterations in vagal tone, measured indirectly by heart rate variability (HRV).
Methods: Twenty-four healthy subjects (19m, 5f; aged 21–44y) completed a 10-day in-laboratory protocol (light < 50 lx, ambient temperature = 24ºC ± 1ºC). Following 3 nights of baseline sleep, subjects remained awake for 88hrs (3.7 days) except for a 2hr nap period (TIB: 0245h–0445h) each day, followed by 3 nights of recovery sleep. Subjects were randomized to either modafinil (200mg/ 24hr) or placebo administration during the 88hr period of SUSOPS. A placebo pill was administered at 0000 hr and either a modafinil (200mg) or placebo pill was administered at 1200hr each of 3 days, starting on day 2 of extended wakefulness. Every 2 hrs during wakefulness, subjects completed a 35-min neurobehavioural battery (NAB). EEG/EOG, core body temperature, and EKG were recorded throughout the 88 hrs. Blood was sampled during the final baseline night, the 88hrs of SUSOPS and the first recovery night. Preliminary analyses of HR and HRV data were limited to 4 minute periods at 0800, 1000, and 1200 hrs when subjects were stationary in a seated position at the end of the NAB and during an assessment of drowsiness (Karolinska Drowsiness Test). To date, analyses have been completed on n=15 subjects.
Results: HR significantly increased from baseline day 3 to condition day 2 (2 Drug Condition X 2 Day X 3 Time ANOVA; $F(1,13)=5.1$, $p=.04$),

with no Drug Condition X Day interaction (p=.56). Analyses of HRV parameters indicated baseline Drug Condition differences that were maintained across days. For example, RMSSD (root mean square of successive differences of R to R intervals) were significantly different between Drug Conditions on baseline day 3 ($F(1,13)=4.0$, $p=.07$), with no Drug Condition X Day interaction (p=.26). These effects were evident in a subset of subjects (n=11) where data from condition day 3 were available for analyses.
Conclusions: Although increasing time in the SUSOPS protocol increased HR, modafinil did not appear to perturb HR or HRV estimates of vagal tone during the late morning hours among these healthy young adults. Because modafinil was ingested at noon, the effect of modafinil on HR and HRV in the morning may not have been evident. Hence, data from HR and HRV recorded in the afternoon will also be analyzed and presented.

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0431.I

Sleep Curtailment Results In Decreased Leptin Levels And Increased Hunger And Appetite

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Introduction: Chronic partial sleep deprivation is an increasingly common condition. Over the past 40 years, self-reported sleep duration in the United States has decreased by approximately 2 hours and the incidence of obesity has nearly doubled. In rodents, sleep deprivation is associated with alterations of energy homeostasis and hyperphagia.
Methods: To determine whether sleep restriction affects leptin, a hormone that signals changes in energy balance to the brain and regulates appetite, we performed two studies in healthy young adults under conditions of constant caloric intake and activity levels. In the first study, we measured the 24-hour leptin profile after 6 days of sleep restriction (4-hour bedtime) and after 6 days of sleep recovery (12-hour bedtime). In the second study, we measured daytime levels of leptin, hunger and appetite after only 2 days of sleep restriction (4-hour bedtime) or sleep extension (10-hour bedtime).
Results: Six days of sleep restriction to 4-hour bedtimes resulted in a 30% decrease in maximal leptin levels as compared to the fully rested state ($P<0.005$). The impact of sleep restriction on maximal leptin levels was similar to that of dietary restriction by ± 900 Kcal/day for 3 days. Two days of sleep restriction to 4-hour bedtimes resulted in an 19% decrease in leptin ($P=0.0413$) that was associated with a 16% increase in ratings of hunger ($P=0.0186$), and with increased appetite (+16%; $P=0.0229$), particularly for high fat, high carbohydrate foods (+24%; $P=0.0342$).
Conclusions: We conclude that sleep restriction alters leptin signaling of caloric need and stimulates hunger and appetite. Sleep restriction is therefore likely to compromise compliance to weight loss diets involving caloric restriction. Chronic sleep curtailment may promote weight gain and contribute to the current epidemic of obesity.

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0432.I

Mild Sleep Restriction Affects Cognitive Functions In Young Children: Preliminary Evidence From Brain Recordings

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Introduction: The impact of sleep on learning and attention in children is not well characterized. Furthermore, the effect of mild sleep restriction, a highly prevalent occurrence in modern society, on child neurocognitive performance is unknown.
Methods: Six normal male children, ages 7-8 years, initially underwent an overnight polysomnographic evaluation that confirmed the absence of any sleep disturbances. Actigraphic recordings were then conducted for a week of normal sleep schedules and a week of 1 hour sleep restriction (delayed bedtime). At the end of each week, auditory and visual event-related potentials (ERPs) were recorded during a series of tasks designed to elicit brain activity in different regions. The tasks included a traditional P300 paradigm (auditory; 1000 vs 1500 Hz tones), a speech sounds discrimination task (auditory; computer-generated CV syllables), and an attention task (visual). ERPs were recorded using a 128-channel high-density geodesic sensor net. The data were submitted to PCA-MANOVA analysis.
Results: Individual ERPs differed between the sleep conditions even though there were no significant differences in behavioral performance (accuracy and RT) on any task. The scalp topography of brain electrical activity elicited in the P300 paradigm changed as a function of the amount of sleep especially over the left temporal areas. Further analyses of the speech sounds and attention task indicated that sleep-related effects were present over all electrode regions for both hemispheres, beginning immediately after stimulus onset, and continuing through the entire 700 ms post-stimulus epoch.
Conclusions: The altered brain processing of task-related stimuli following sleep restriction suggests that neurocognitive functioning and development in young children is highly susceptible to sleep disruption. High-density brain mapping using specific tasks may lead to identification of children who are more cognitively vulnerable because of chronic sleep disturbances.

0433.I

The Role of Norepinephrine in the Sleep Response to Acute Stress and Sleep Deprivation Using Norepinephrine-Deficient Mice

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Introduction: Norepinephrine (NE) is thought to play a role in the regulation of sleep/wake states. In addition, NE and epinephrine are primary neurotransmitters participating in the hypothalamic-pituitary-adrenal axis during periods of stress. Both acute stress and sleep deprivation have been shown to affect sleep, usually having the effect of increasing REM, NREM, or both, depending on the methods of inducing the stress or sleep deprivation. However, there is a lack of published studies investigating how the addition of sleep deprivation, which is itself a stressor, affects sleep after a potent stressor such as physical restraint. We hypothesized that mice chronically deficient in NE would not show the same effects in their sleep as a response to stress, and/or as a response to stress preceded by sleep deprivation.
Methods: Adult NE-deficient (knockouts) and littermate controls were implanted with chronic EEG/EMG electrodes and their sleep/wake states were monitored after one hour of restraint stress, with and without 5 hours of prior sleep deprivation.
Results: Preliminary results show that the control mice did not differ from the NE-deficient mice in the distribution or amounts of their sleep/wake states for the first 6 hours after restraint stress only. However, the control mice had more bouts of NREM sleep ($p<.05$), which were

shorter in length (p<.01), when the restraint stress was preceded by 5 hours of sleep deprivation.
Conclusions: These data indicate that in normal mice, the addition of prior sleep deprivation to the stress from physical restraint causes fragmentation in NREM sleep, and that this process is mediated by NE since the NE-deficient mice did not show this sleep pattern after the two procedures.

0434.I

Individual Variability In Alpha And Its Effect On The Alpha Attenuation Test

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Introduction: In total sleep deprivation experiments, the Alpha Attenuation Test (AAT) has proven to be a sensitive measure of physiological sleepiness, except among high alpha producers. The Alpha Attenuation Coefficient (AAC), calculated as (mean absolute alpha power, eyes closed)/ (mean absolute alpha power, eyes open), is expected to fall with increasing sleepiness. The present study was aimed at investigating the previously reported individual variability in alpha and to assess the robustness of the AAT in a workplace setting.
Methods: Occipital EEG was recorded on two separate occasions from 17 trainee anaesthetists (mean age = 32 years) during a typical working week. The rested condition began at 9 am on a Tuesday and the fatigued condition began around 11 pm on a Thursday after a shift >15 hrs. For the AAT, the subject sat quietly for: 2 mins eyes open/ 2 mins eyes closed/ 2 mins eyes open/ 2 mins eyes closed. Power spectral analysis (FFT) of the EEG was performed using a custom LabVIEW™ program. For each subject and in each condition, spectral plots were visually inspected for individual variability and mean absolute power was calculated. A mixed model ANOVA (subjects as random variable) was used to test for attenuation of absolute alpha power with eyes closed, comparing the fatigued and rested conditions. Participants were ranked in terms of mean absolute alpha power (in the rested condition with eyes closed) and the top 25% were categorized as high alpha producers. Wilcoxon Signed Ranks was used to test for differences between the AAC's in the rested and fatigued conditions.
Results: For most subjects, alpha power with eyes closed was not confined to the 8-11.9 Hz range. However, there was no statistical difference between the effects found with 'individualized' alpha power and power in the more traditional 8-11.9 Hz range. Four subjects were classified as high alpha producers, but their exclusion had no significant effect on the outcome of the statistical tests. There was no significant change in outcome when relative power was used instead. A significant main effect for alpha power was seen for 'eyes open' vs. 'eyes closed' (p<0.0001), but not for the rested vs. fatigued conditions. There was no significant difference in the AAC between the rested and fatigued condition.
Conclusions: The AAT did not differentiate the rested from the fatigued condition, but individual variability in the 'alpha' frequency range or mean spectral power did not account for these findings. The AAT may not be sensitive to physiological sleepiness in this workplace setting. We are currently analysing actigraphy and sleep diaries to confirm this.

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0435.I

The Effects of Sleep Debt and Workload on Alertness during A 12-h Dayshift

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Introduction: Fatigue is known to be common with extended workdays. Our aim was to investigate the effects of partial sleep debt and workload on an operator's alertness during a single 12-h dayshift.
Methods: Twelve male process operators (aged 36-56 years) completed four experimental conditions including a night sleep and a 12-h dayshift (07:00 a.m. - 07:00 p.m.) in the laboratory. A simulated distillation process served as a work task. The conditions were a monotonous workday (stable distillation process) after normal (mean TST 442 min) and restricted sleep (mean TST 217 min) and a active workday (dynamic distillation process) after normal (mean TST 424 min) and restricted sleep (mean TST 223 min). All workdays included morning (7:30-9:00 a.m.), noon (10:50-12:20 a.m.), mid-afternoon (1:50-3:20 p.m.) and late afternoon (5:20-6:50 p.m.) work sessions. Objective sleepiness was measured with continuous EEG/EOG recordings during the work sessions and with a sleep latency test of 20 min in morning, mid-afternoon and late afternoon. In the EEG/EOG epochs of 20 sec, sleepiness was indicated by slow eye movements or theta activity (³ 5 sec). Subjective sleepiness was measured with the Karolinska Sleepiness Scale in the beginning and at the end of each work session.
Results: Fourteen percent of the EEG/EOG epochs showed the signs of sleepiness at work during the monotonous workday after sleep debt. The corresponding values were 12% for the monotonous workday after normal sleep, 11% for the active workday after sleep debt, and 5% for the active workday after normal sleep. A mixed model analysis showed that sleepiness increased with sleep debt (F(1, 11)=11.76, p=.006) and monotonous work (F(1, 11)=19.96, p=.001). Also the time of day effect was clear (F(3, 33)=4.98, p=.006). Sleepiness reached its peak in mid-afternoon. The mean KSS ratings were 5.1-5.5 in the normal sleep conditions and 6.2-6.1 in the sleep debt conditions. A mixed model analysis confirmed that subjective sleepiness increased with sleep debt (F(1, 11)=36.69, p<.001). In the sleep latency test, the mean sleep latency varied between 6.9 min (the active workday after sleep debt) and 9.9 min (the active workday after normal sleep). A mixed model analysis demonstrated a significant interaction between sleep, work pace, and time of day (F(7,77)=3.39, p=.003). The mid-afternoon sleepiness peak was only detected during the active workdays. The difference in mid-afternoon alertness between the active and monotonous workdays was intensified by sleep debt.
Conclusions: The results suggest that the amount of objective sleepiness at monitoring work is doubled by both a 50% sleep debt of one night and a monotonous task as compared to normal sleep and an active workday. The peak of sleepiness during a single 12-hr dayshift is reached in mid-afternoon, 7-8 hours since the beginning of the shift.

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0436.I

Differential Effects of Paradoxical Sleep Deprivation and Sleep Rebound on mRNA Levels of Orexin-1 and Orexin-2 Receptors in Rat Brain

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Introduction: Orexins A and B (hypocretins 1 and 2), are hypothalamic neuropeptides derived from a single precursor prepro-orexin. The orex-

ins have been associated with feeding behavior and in the regulation of the sleep-wake cycle. Two receptors for these peptides have been described, orexin-1 and -2 (OX-R1 and OX-R2). The relationship between orexins and the control of arousal prompted us to examine the effects of sleep deprivation on the expression of both OX-R1 and OX-R2, at the mRNA level.

Methods: Rats were deprived of sleep using the classical platform method. After 96 hr of sleep deprivation (SD) one group was sacrificed; a second group was returned to the home cage and allowed to sleep for 24 hr before being sacrificed (the sleep rebound group); controls remained in the home cages throughout. All brains were rapidly removed, frozen over dry ice and stored at -80 °C. Twenty micron coronal sections were pre-pared at 0.3 mm intervals covering the entire extent of the brain. In situ hybridization was performed using 35S-UTP labeled riboprobes prepared by in vitro transcription with PCR fragments primed with the following sequences: for OX-R1 1 (Genbank NM_013064.1), 918-937 and 1368-1349 and for OX-R2 (Genbank NM_013074.1), 580-599 and 1028-1005. Autoradiographic analyses were performed with the MCID AIS/C system. The OX-R1 signal was quantified in 87 brain regions and the OX-2R signal in 94 regions.

Results: Results revealed a heterogeneous effect of SD on brain mRNA levels of both receptors. Whereas little change was seen in the expression of either receptor in rats sacrificed immediately after sleep deprivation, significant changes were seen in the rebound group. OX-R1 mRNA levels increased in more than 30 different regions in this group, particularly in amygdala and hypothalamic areas, compared to controls and SD groups. The trend for OX-R2 mRNA was in the opposite direction, with decreased levels in the rebound group, particularly in cerebral cortical areas.

Conclusions: These observations suggest that SD has differential effects on orexin receptors mRNA levels and that this effect becomes significantly more pronounced following sleep rebound.

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0437.I

Effects of Paradoxical Sleep Deprivation on Serotonin Transporter (SERT) Binding

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Introduction: Sleep deprivation (SD) is known to improve the mood symptoms of depressive illness, but the mechanisms behind this effect remain unclear. Some evidence suggests that the antidepressant activity of SD is due to an enhancement of serotonergic neurotransmission. In the present study we examined the possibility that such changes may occur at the level of the serotonin transporter (SERT). To address this issue we studied the effects of SD on SERT using 3-Amino-4-(2-dimethylaminomethyl-phenylsulfanyl)-benzonitrile, labeled with carbon-11 ([11C]-DASB), a recently introduced radiotracer for imaging the serotonin transporter by positron emission tomography (PET). Previous studies indicated that [11C]-DASB is a very useful radiopharmaceutical for probing changes in SERT densities using PET imaging in the living human brain. In vitro studies have demonstrated that DASB binds with high affinity and selectivity to the SERT out of a variety of other CNS binding sites including the other monoamine transporter proteins in rat brain.

Methods: Animals were randomly assigned to sleep deprivation, sleep rebound or cage control groups. (N=8 per group). SD was induced by the modified multiple platform method. Rats were sacrificed immediately after 96 hr of sleep deprivation were completed. SERT binding was examined by autoradiography in sections incubated for 10 min in 3 nM [11C]-DASB in the presence or absence of 10 uM paroxetine. Films were exposed for 24 hr to Kodak Biomax film.

Results: Compared to controls, sleep deprived animals showed decreased binding in 36 of the 62 brain areas examined. Statistically significant reductions were seen in the anterior olfactory n. (-21%), Substantia nigra lateral part (-16%) and pars reticulata (-18%). Binding was also reduced in SERT-rich sleep-relevant areas such as the locus coeruleus (-6%) laterodorsal tegmental n.(-5%) and gigantocellular reticular n., alpha part (-12%), although these effects were not statistically significant.

Conclusions: These findings indicate that sleep deprivation affects binding to the serotonin transporter in rat brain. Our results suggest that the mechanism involved in the antidepressant action of sleep deprivation may involve SERT downregulation in important limbic structures in the rat brain. Insofar as these changes may be associated with increased levels of 5-HT in the synapse, they suggest that sleep deprivation may share some basic mechanisms of action with several current antidepressant medications. 11C-DASB may be a useful tracer for monitoring SERT status in sleep deprived humans.

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0438.I

Deficits in Avoidance Responding After Paradoxical Sleep Deprivation are Not Associated With Altered [3H] Pirenzepine Binding To M1 Muscarinic Receptors in Rat Brain

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Introduction: Previous work had indicated that animals that were sleep-deprived and then trained on a passive avoidance task show poor retention of the task 24 hr later, after being allowed to sleep freely again. Cholinergic involvement is suggested by the fact that this effect is prevented by treatment with the muscarinic agonist pilocarpine during sleep deprivation. The observation that similar deficits are observed in non-deprived rats after treatment with M1-selective antagonists compounds such as dicyclomine or pirenzepine cause similar impairments, gave rise to the hypothesis that sleep deprivation might induce significant reductions in M1 binding in brain areas involved in learning and memory processes.

Methods: Rats were deprived of sleep for 96 hr and then either immediately sacrificed, or allowed to recover sleep for 24 hr before sacrifice. [3H]pirenzepine binding to M1 sites was examined by quantitative autoradiography in 39 different brain areas in cage controls, sleep-deprived and sleep-recovered animals (N=8 per group). A separate group of animals was subjected to the sleep deprivation procedure and then trained in a simple avoidance task. Animals were then allowed to sleep and retested 24 hr later.

Results: No significant differences among groups were found in any brain region. In the other experiment the sleep-deprived group showed a significant impairment in the avoidance task compared to cage controls, in agreement with previous observations.

Conclusions: These data suggest that proactive learning/memory deficits induced by sleep deprivation cannot be attributed to altered M1 binding either immediately after deprivation (when avoidance training occurs) or after sleep has recovered (when acquisition/retention are tested). The possibility remains that alterations in M1 function occur at post-membrane second messenger systems.

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0439.I

Influence of Sleep Deprivation on Plasma Ghrelin Levels in Healthy Subjects

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Introduction: It is well established that the regulation of sleep and wakefulness and circadian rhythmicity are thightly coupled to neuroendocrine networks, the regulation of feeding and metabolism. Ghrelin is a recently discovered orexigenic peptide which promotes NREM sleep in humans. Plasma ghrelin levels increase between meals, but also in subjects fasted over night during the early morning hours. It has been unknown so far if sleep itself affects ghrelin levels.
Methods: Five healthy male volunteers (age 28 $\pm$ 1.2 years, BMI 22.8 $\pm$ 1.8) took part in the present study after written informed consent had been obtained. The study protocol had been approved by an independent ethics committee. Each subject, in randomized order, underwent twice a 24-hour protocol starting at 07:30 h. Subjects remained in a semi-recumbent position in a clinical sleep research center. Illumination was below 100 lux. Standardized breakfast, lunch and dinner were served at fixed time points (07:30, 12:00, 19:00h). Water was available ad libitum. After dinner, until the next morning, no food was available. During one of the 24-h-hour protocols subjects slept between 2300 and 0700 hours, whereas during the other protocol they were kept awake in bed by social interaction throughout the night. Polygraphic recordings of EEG, EOG and EMG were performed continously. Blood samples were collected by a through-the-wall technique and assayed for ghrelin levels hourly in duplicate using a commercially available radioimmunoassay (Phoenix Pharmaceuticals, CA. U.S.A.). Data were analyzed statistically by analysis of variance (general linear model, GLM incorporated in SPSS) with condition as between-subject factor and time as within-subject factor.
Results: In the sleep condition subjects showed a normal nocturnal sleep between 2300 and 0700 hours. Throughout the day and during the sleep deprivation schedule no major lapses into sleep (> 5 min) occurred. Ghrelin plasma levels showed the established relationship to meals, i.e. levels increased prior to every meal and sharply declined afterwards. In addition, ghrelin levels increased during night and declined during the early morning hours in both conditions. Although mean plasma ghrelin levels were higher during sleep compared to sleep deprivation, ANOVA did not reveal a statistical difference in the time course of ghrelin levels between the 2 conditions.
Conclusions: The present data suggest that plasma ghrelin levels in humans are modulated by a circadian rhythm in addition to an interaction with food intake. Our results do not provide evidence for an influence of sleep per se on plasma ghrelin levels. However, in the present small sample size statistical power is too small to detect small differences between conditions.

0440.I

Unobtrusive Detection of Drowsiness-Induced PVT Lapses Using Infrared Retinal Reflectance of Slow Eyelid Closures

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Introduction: An initial double-blind, controlled laboratory study of the scientific validity of six drowsiness-detection measures involving the head, eyes and brain waves revealed that only human-scored percent slow eyelid closures (PERCLOS) correlated highly with vigilance performance (PVT) lapses during 42-hr of wakefulness. This led to the development at Carnegie Mellon University of an infrared retinal reflectance system (The CoPilot®) for measuring PERCLOS unobtrusively in real time. An experiment was conducted to determine the degree of validity the CoPilot® had for predicting vigilance lapses. The study was performed by investigators who had no intellectual property rights or commercial connections to the CoPilot®.
Methods: Twelve healthy adults (7m, 5f; ages 21-45 years) remained awake in the laboratory for 42-hr, while working on a computerized test battery every 2-hr that included 20-min. visual PVT performance. PVT cumulative lapse duration data were recorded each minute throughout each trial. The CoPilot® measures eyelid droop using two infrared images of the eye, which are processed to a single image that is evaluated by a computer algorithm for degree of slow eyelid closure to estimate PERCLOS values. The CoPilot® was time-locked to PVT performance to evaluate coherence between PVT cumulative lapse duration and the CoPilot® PERCLOS detection algorithm output. Time series coherence was measured using correlation coefficients.
Results: PERCLOS values obtained from the Copilot® correlated highly with PVT cumulative lapse duration across the 42-hr period of wakefulness. The mean (SD) per bout (20-min) coherence between PERCLOS and PVT performance lapses was r=0.840 (0.151), and the mean (SD) per minute coherence was r=0.719 (0.162). Mean per bout and per minute coherence values for PERCLOS were found not to be statistically significantly different (p=0.152 and p=0.491) from the per bout and per minute coherence values obtained through manual scoring of PERCLOS in the first experiment we conducted, which resulted in the identification of PERCLOS as a viable measure of sleepiness in an individual attempting to perform. As in the first study, PERCLOS from the CoPilot® correlated more highly with PVT cumulative lapse duration than did subjects' own ratings of their sleepiness (t=3.57, p=0.004).
Conclusions: The findings illustrate that as an automated on-line measure of slow eyelid droop and closures (PERCLOS) in sleepy individuals attempting to perform a vigilance task, the infrared retinal reflectance system and detection algorithm contained in the CoPilot® have a robust relationship to lapses of attention, which are a hallmark of reduced behavioral alertness in sleepy individuals. The results replicate those found from an earlier study of human-scored PERCLOS, and suggest that the CoPilot® be evaluated for its durability, reliability and feasibility to detect drowsiness in actual driving scenarios. More research is needed on the subset of vigilance lapses that occur when the eyelid is open.

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0441.I

Inter-Individual Differences in Psychomotor Vigilance Performance Deficits during Repeated Exposure to Sleep Deprivation

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Introduction: Previous studies in our laboratory have shown substantial inter-individual differences in the magnitude of neurobehavioral performance deficits during extended wakefulness. This investigation assesses the extent to which these inter-individual differences reflect a trait.
Methods: Performance deficits on a 20-minute psychomotor vigilance task were assessed for n=20 subjects (age 29.4±5.4; 8 females) during 36 hours of laboratory-based sleep deprivation, which each subject underwent three times at intervals of at least 2 weeks. During the 7 days prior to each deprivation, subjects spent either 12 hours (22:00–10:00; sleep satiation) or 6 hours (04:00–10:00; sleep restriction) time in bed per day, monitored with actigraphy and, on the last day before sleep deprivation, with polysomnography. In randomized order, each subject had the sleep restriction condition once and the sleep satiation condition twice. Laboratory conditions during sleep deprivation were strictly controlled, and subjects participated in an adaptation session in the laboratory before the first sleep deprivation.
Results: Psychomotor vigilance lapses (averaged over the last 24 hours

of sleep deprivation) ranged widely (from 6.7 to 104.4) among individuals and deprivation exposures. The trait-like component of this variability was assessed using a mixed-effects analysis of variance (ANOVA) over the two sleep deprivations with prior sleep satiation, correcting for the relative order in which the prior sleep restriction condition occurred. In this mixed-effects model, the intraclass correlation (i.e., the ratio of between-subjects variance to total variance) was 0.69 (Wald Z=2.40, P=0.008), revealing the existence of significant between-subjects variance (S.D. 16.9 lapses per test bout). This trait-like variability was considerable compared to the residual within-subjects variance in the data (S.D. 11.5 lapses per test bout), which included variance due to the randomized order of conditions as well as stochastic error variance. Fixed effects representing the order of conditions were statistically significant ($F[4,23.1]=5.16$, P=0.004), indicating that there was a carry-over effect of the sleep restriction conditions affecting vulnerability to performance deficits from total sleep deprivation in subsequent sleep satiation conditions.

Conclusions: We identified a carry-over effect of exposure to total sleep deprivation preceded by sleep restriction on psychomotor vigilance performance impairment during subsequent periods of total sleep deprivation. After correcting for this order effect, substantial trait-like inter-individual variability in the vulnerability to performance impairment during 36 hours of total sleep deprivation was found. The size of the 95% prediction interval for these inter-individual differences covered a range of 67.6 lapses per 20-minute test bout. This means that some individuals were systematically much more vulnerable than others to the effects of total sleep deprivation, even though they received equal opportunities to satiate their prior need for sleep.

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0442.I

Neurobehavioural Functioning During 88 Hours of Sustained Operations: Naps and Modafinil as Countermeasures

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Introduction: Sustained military operations (SUSOPS), requiring extended periods of wakefulness over multiple circadian cycles, produce significant decrements in neurobehavioural functioning. In order to maintain optimal performance during SUSOPS, assessment of both pharmacological and non-pharmacological countermeasures is essential. This study examines the effects of a 2h nap scheduled every 24h, with and without a once-daily dose of modafinil, during 88h of simulated sustained operations in the laboratory.

Methods: Twenty-four healthy subjects (19m, 5f; aged 21–44y) completed a 10-day laboratory protocol. Following 3 nights of baseline sleep, subjects remained awake for 88h (3.7 days) except for a 2h nap period (TIB: 0245h–0445h) each day, followed by 3 nights of recovery sleep. Subjects were randomized to either modafinil (200mg; N=11) or placebo (N=13) administration during the 88h period of SUSOPS. A placebo pill was administered at 0000h and either a modafinil (200mg) or placebo pill was administered at 1200h each of 3 days, starting on day 2 of extended wakefulness. Subjects remained in the laboratory throughout the protocol, with light levels <50 lx and ambient temperature at 24ºC ± 1ºC. Every 2 hours during wakefulness, subjects completed a 35-min computerised neurobehavioural assessment battery (NAB), containing both objective tests of cognitive performance and subjective measures of fatigue and sleepiness. Polysomnographic recordings of scheduled sleep and EEG/EOG recordings of wake periods were made; and core body temperature and EKG were measured throughout the 88h period. Blood samples were taken during the final baseline night, the 88h of SUSOPS and the first recovery night and day via an indwelling cannula.

Results: Using non-linear mixed-model regression analysis, neurobehavioural functions were analyzed for the 14-hr periods following the administration of modafinil (1200h-0200h), and for the 6-hr periods following the naps (0600h-1200h). Relative to placebo, modafinil administration improved nearly all measures of neurobehavioural performance during the 1200h-0200h period (e.g., psychomotor vigilance lapses [$p<0.05$], probed recall memory [$p=0.05$], critical tracking [$p<0.01$]). Following the nap period, there was no significant difference in neurobehavioural performance between the two conditions. In contrast, none of the subjective assessments of sleepiness and alertness demonstrated any differences between the modafinil and placebo conditions for either analysis period, except for decreased physical fatigue that was observed after administration of modafinil ($p<0.01$).

Conclusions: The findings from this study illustrate that 200mg of modafinil administered at 1200h plus a daily 2h nap at 0245h-0445h during 88h of sustained operations significantly improved neurobehavioural performance on nearly all tasks measured, with only a small effect on subjective assessments of sleepiness and alertness, relative to placebo plus a daily 2h nocturnal nap. These findings suggest that strategic use of modafinil in combination with brief naps may be beneficial in situations where sustained performance and alertness are required for extended periods of time.

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0443.I

REM Sleep Deprivation Impairs Consolidation Of The Spatial Component Of Episodic Memory And Confidence In Our Own Judgment

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Introduction: Considerable evidence supports the idea that REM sleep and slow-wave sleep (SWS) act differently on memory traces, depending on the memory system they refer to. Thus, SWS facilitates consolidation of explicit (declarative) memories, whereas REM sleep facilitates consolidation of implicit memories.

Methods: We have investigated consolidation of episodic memory, defined as a system which stores events located in time and in space and characterized by autonoetic consciousness (Tulving, 2001), using an original task: the "Quoi-Où-Quand" (What-Where-When) (Guillery et al., 2000). This task consisted in memorizing two lists of 7 words ("what"), their location on a sheet ("where"), and the list they belong to ("when"). An immediate free recall, a delayed recall and a recognition task were proposed to 44 young healthy subjects (m=20.20 ± 2.06 years). The recognition task was associated with a Remember/Know/Guess paradigm in order to appreciate the degree of confidence of the subject in his response. This work investigated the consolidation of these three components (what, where, when) over intervals covering either early sleep, known to be dominated by SWS, or late sleep, in which REM sleep is dominant. Two groups of subjects were tested across 4-h periods of early and late sleep (sleep group) or corresponding intervals filled with wakefulness (wake group). Sleep was recorded polysomnographically.

Results: SWS covered on average 35% of early retention sleep but only 8% of late retention sleep ($p<0.001$). Conversely, REM sleep covered 16% of early and 25% of late retention sleep ($p<0.001$).Our preliminary results highlight the following five points: 1) Performances on immediate free recall do not differ between groups. 2) No significant differences were found concerning delayed recall or recognition of factual information. 3) Subjects with a late sleep retention interval had a significantly

more important forgetting of temporal information than subjects placed in the early sleep condition ($p<0.05$). 4) Following REM sleep deprivation, performances on delayed recall of spatial information were significantly impaired ($p<0.05$) 5) Following REM sleep deprivation, subjects gave significantly less responses associated with a "Remember" judgment (attesting the episodicity of memories) than subjects who were SWS deprived. On the other hand, subjects deprived of REM sleep gave more responses associated to the judgment "Guess" than subjects SWS deprived.

Conclusions: These results indicate that REM sleep facilitates consolidation of the spatial component, but not the temporal component, of an episodic task. They also suggest that REM sleep deprivation impairs the degree of confidence in their responses.

0444.I

Palatable Solutions Attenuate Paradoxical Sleep Deprivation-Induced HPA Axis Activation, without Interfering with Energy Expenditure

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Introduction: Paradoxical sleep deprivation (PSD) induces energy imbalance in rats, insofar as animals eat more, but loose weight throughout the deprivation period. In addition, PSD results in increased activity of the hypothalamic-pituitary-adrenal (HPA) axis that might participate in the energy imbalance. In the present study, animals were offered water, saccharin (0.13%) or sucrose (5%) to drink during the deprivation period, since it has been proposed that carbohydrates reduce the stress response.

Methods: Throughout the whole study, animals were maintained in 12:00h light/dark cycle and had free access to food and fluids. PSD was accomplished by the flower pot technique for 96h. Control animals were maintained in the same environment, except that instead of water, the containers were filled with sawdust. During PSD period, both groups received one of the solutions and animals were weighed daily and food and fluid intake was assessed twice a day (early morning and late afternoon). At the end of the PSD period, animals were sacrificed and glucose, ACTH and corticosterone (CORT) plasma levels were assayed.

Results: 1) Compared to their control counterparts, all PS-deprived animals consumed more food, but lost weight. PS-deprived animals given sucrose showed more fluid intake than their control counterparts (specially in the light phase of the day cycle). 2) PS-deprived animals showed increased food intake in all periods of the light-dark cycle. 3) Food and liquid intake were higher in the dark than in the light phase of the diurnal cycle. 4) All PS-deprived animals showed lower glucose plasma levels than control animals and increased relative adrenal weight. 5) However, when given saccharin or sucrose, PS-deprived animals showed lower ACTH and CORT plasma levels than their water-provided counterparts.

Conclusions: Intake of palatable fluids is capable of lowering HPA axis activation produced by PSD. The fact that PSD induced energy imbalance regardless of the fluid offered during the manipulation suggests that the HPA axis plays a secondary role in this phenomenon and that other mechanisms may account for this effect. We propose that PSD produce a dysregulation of the leptin-hypocretin system.

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0445.I

Physiological Sleepiness And Performance During Continuous Sleep Restriction

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Introduction: Continuous sleep restriction (CSR) is a research paradigm involving reduction of habitual sleep time over an extended period. Understanding the behavioral and physiological effects of CSR is important because many people commonly experience partial sleep deprivation. Performance deficits have been reported following this degree of sleep loss, however, the associated brain physiology has not been examined. We report herein preliminary data on EEG and performance during baseline, CSR, and recovery conditions.

Methods: Sixteen participants volunteered for a home- and lab-based study of CSR. Four participants withdrew because of difficulty with the schedule, and five were eliminated due to non-compliance. The remaining 7 participants (mean age=22) were healthy good sleepers with a regular sleep schedule (23:00-07:00). Following a screening night, participants began a 21-day protocol: Week1 (baseline, participants slept usual amount); Week2 (CSR, time in bed restricted by 33% of sleep time in week1); Week3 (recovery, participants slept desired amount). Alcohol and caffeine intake were minimal and did not vary across conditions. No daytime naps were permitted. In all conditions, sleep-and-activity diaries were completed and activity monitors were worn to verify compliance. At home, participants completed a 10-minute RT task and VAS scales of mood and sleepiness every 3hrs from 09:00 to 21:00. Lab sessions occurred on the morning of Day7 (following 7th night of baseline), Day8 (following 1st night of restricted sleep), Day11 (following 4th night of restricted sleep), Day14 (following 7th night of restricted sleep), and Day15 (following 1st night of recovery). In lab, EEG was recorded at 256Hz from 19-sites using a cap. Artifact-free epochs of EEG were submitted for spectral analysis in eyes-closed and eyes-open conditions. A computerized battery of tests was administered, including the Stanford Sleepiness Scale, Profile of Mood States, auditory event-related potential paradigms, a 10min RT task, the 2-back memory task, and the Alpha Attenuation Task. ANOVAs were run to assess differences across in-lab conditions (baseline, CSR1, CSR4, CSR7, recovery).

Results: Participants reported sleeping less during the CSR week (5.6hrs) compared to baseline (8.3) and recovery weeks (7.7). Activity monitors confirmed greater "inactivity" (i.e., sleep) during baseline ($p<.05$) and recovery ($p<.05$) compared to CSR. Significant CONDITION effects and quadratic polynomials depict changes during CSR as follows: increased subjective sleepiness (Ms=3.7, 4.0, 5.0, 5.0, 3.8); decreased mood on the Vigor-Activity subscale of the POMS (Ms=5.8, 4.7, 2.5, 2.3, 3.2); delayed speed of responding on the 2-back memory task (Ms=425.1, 436.0, 476.3, 459.7, 432.9ms); and slowed RT for the fastest 10% of trials (Ms= 236.9, 257.3, 266.8, 283.0, 254.5ms) and 1/RT[slowest 10%]. The alpha attenuation coefficient (8-10Hz) decreased linearly over the period of CSR, reflecting increasing sleepiness, at posterior (O2, T6, P4), but not anterior sites (Fp2, F8, F4).

Conclusions: These data provide support for increased physiological sleepiness coincident with behavioral changes during CSR. Preliminary analyses indicate linear changes in alpha EEG frequency during CSR are specific to posterior sites.

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0446.I

Sex Differences in Memory for a Conditioned Cue Preference Task Following Paradoxical Sleep Deprivation

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Introduction: The conditioned cue preference (CCP) task measures memory for events that have emotional significance. The preference develops while learning the association between a neutral stimulus (light) and an incentive stimulus (food). The purpose of the present study was to investigate whether paradoxical sleep deprivation (PSD) would

influence acquisition of the CCP differently in males and females.
Methods: The CCP apparatus has two arms extending opposite each other from a circular base. One of the arms has a light cue and the other remains dark. During training, food bait was placed in the light arm, but never the dark arm. Male (n=35) and female (n=33) rats received one 15 minute training trial/day. For half the subjects, only the dark arm was accessible for the first four sessions and the lighted arm for the remaining sessions. The other half of the subjects were trained in the opposite arm order. Following each training session, rats received PSD using the "platform" method. The Control group was returned to their cage immediately following training. Three groups received PSD for 4 hours either immediately (GR1-4), 4 hours (GR5-8) or 8 hours (GR9-12) after training. GR13-24 received PSD for 12 hours beginning 12 hours after training. On the ninth day subjects received a fifteen minute testing trial. Both arms were open and the light cue was present in the appropriate arm, but no food reward was available. The number of entries into each arm and the center platform and time spent in each section was recorded.
Results: Initial analyses revealed that females and all subjects from GR13-24 made a greater number of total entries into all sections of the maze. Consequently, this variable served as a covariate in subsequent analyses of the percentage of total time spent in unrewarded areas (dark arm and center platform).1) No main effect for PSD condition was found ($p>.05$).2) Females spent significantly more time in unrewarded areas than males ($p<.05$).3) Subjects that began training in the dark arm spent more time in unrewarded sections than subjects that began in the light arm ($p<.05$).4) The group by sex interaction was also significant ($p<.05$). GR1-4 females and all rats in GR5-8 spent significantly more time in unrewarded areas than GR1-4 males.
Conclusions: Surprisingly, the arm in which the subjects began their training sessions influenced acquisition of the CCP. Although females, regardless of PSD condition, spent more time in unrewarded sections of the maze than males, the GR1-4 females performed significantly worse than their male counterparts. Males and females in GR5-8 also performed worse than GR1-4 males. The considerably superior performance of the GR1-4 males may conceal another critical interval four to eight hours after training during which the CCP develops. Nonetheless, these results indicate that the effects of PSD can differentially influence acquisition of the CCP in males and females.

0447.I

Influence Of Paradoxical Sleep Deprivation And Cocaine On Development Of Spontaneous Penile Reflexes In Rats Of Different Ages
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Introduction: Recent studies have established that paradoxical sleep deprivation (PSD) and cocaine administration induce genital reflexes (penile erection and ejaculation) in adult and old rats. The aim of this study is to investigate whether PSD and/or administration of cocaine in rats of different ages (30 to 90 days old) will interfere with the frequency of spontaneous genital reflexes and to verify the effects of PSD on steroid hormones.
Methods: Rats of different ages were used: 30-day-olds (emergence of sperm in the testis), 45-day-olds (prepuberty); 60-day-olds (puberty); 75-day-olds (100% of have testicular sperm) and 90-day-olds (full sexual maturity). Cocaine (7 mg/kg) or saline was administered to the rats after a 4-day period of PSD, or at the equivalent time-point in control animals, and penile erection and ejaculation were then evaluated.
Results: In PSD rats administered with cocaine, erection was observed since 30 day-old until 90 days, when the both genital reflexes reaching a peak. Animals submitted to PSD and saline injection show erection from 60 to 90 day-old. None of the control (saline and cocaine) groups of any of the ages studied displayed these behaviors. The effects of PSD on the steroid hormones levels show that although testosterone levels increased with age, PSD caused a marked decrease in testosterone in all ages evaluated. Progesterone and corticosterone levels were higher in PSD groups when compared to respective control groups.
Conclusions: These findings suggest that the interaction of PSD and cocaine probably enhances dopaminergic transmission in the brain and may accelerate the development of genital reflexes in male rats.

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0448.I

Can Recovery From Sleep Deprivation Occur During General Anesthesia?
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Introduction: Although naturally occurring sleep and general anesthesia are similar behavioral states, whether recovery from sleep deprivation can occur during anesthesia is unknown. To answer this question, we anesthetized rats with propofol for 6 h after 24 h of total sleep deprivation, and then compared their recovery sleep with that of unanesthetized, sleep-deprived controls.
Methods: With animal care committee approval, EEG/EMG electrodes and intra-jugular cannulae were placed in 14 male Sprague-Dawley rats. After a 7-day recovery with lights on at 6:00am and off at 6:00pm, rats underwent 24 h of continuous EEG/EMG monitoring beginning at noon, followed by 24 h of sleep deprivation by the disk-over-water method. An intravenous infusion of propofol in an intralipid vehicle was then begun at 500ug/kg/min, and titrated every 15 min to reach the lowest level required to maintain loss of righting reflex and allow clip-style pulse oximetry. During anesthesia rats breathed spontaneously, temperature and oxygen saturation were monitored continuously, and a heat lamp was used to maintain normothermia. A separate group of 10 control rats underwent the same protocol, but received only the intralipid vehicle, and were allowed ad-lib activity. At 5:30pm (30 min before dark phase onset), all infusions were stopped, and anesthetized rats allowed to "wake up". EEG/EMG monitoring continued for 72 h of recovery. EEG waveforms were scored visually, and also recorded digitally to obtain delta power during nonREM sleep. Within- and between- group comparisons were made using paired and unpaired t-tests, respectively.
Results: Baseline weights, ages, 24-hour and dark phase nonREM sleep were similar for propofol and intralipid groups. Sleep deprivation increased subsequent dark phase nonREM sleep by $10.2 \pm 4.4\%$ in control rats, and $11.8 \pm 6.5\%$ in anesthetized rats, a nonsignificant difference. During the 6 hour infusion period, rats given propofol were anesthetized for 5.8 h and delta power was negligible, while control rats averaged 4.5 ± 0.4 h nonREM sleep with a doubling of delta power. When EEG data were divided into 3 h blocks, nonREM sleep in the first 18 h after infusion increased by $8.7 \pm 4.9\%$ in controls and $8.8 \pm 7.2\%$ in anesthetized rats, also a nonsignificant difference. No difference in nonREM sleep between anesthetized and control rats was observed for any block in the first 24 h after discontinuing drug infusion.
Conclusions: Prolonged lack of sleep results in an increased frequency and intensity of sleep. Although naturally occurring sleep reliably diminishes this sleep "debt", it is not known whether other non-waking states such as general anesthesia can have a similar effect. We found that anesthetizing rats for a 6 h period after 24 h of sleep deprivation resulted in electroencephalographic sleep patterns similar to those of unanesthetized control rats also exposed to sleep deprivation. These data demonstrate that a recovery process similar to that which occurs during naturally occurring sleep also takes place during general anesthesia, and suggest that sleep and anesthesia may share common neurophysiological mechanisms.

0449.I

Paradoxical Sleep Deprivation Effect On Plasma Corticosterone Levels In Three Strains Of Rats

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Introduction: Studies on paradoxical sleep (PS) deprivation show many deleterious effects, including on neurocognitive functions. The most widely used PS deprivation procedure is that of Jouvet's so-called "flower pot technique". This technique is known to induce stress, a confounding factor that is controlled for by using as a sham experimental condition where animals are placed on a platform large enough so that PS can be fully experienced. The goal of the present study was to verify whether small and large platforms are associated with comparable stress in three different strains of rats using corticosterone (CORT) as a marker.
Methods: Male rats from three strains (Wistar, n=39; Long-Evans, n=39; Sprague-Dawley, n=36) kept in standard conditions (12:12 light:dark cycle, lights on at 08h00AM) were distributed as equally as possible to one of three experimental conditions: small platform (10cm2 per 100g body weight), large platform (100cm2/100g), home cage. Treatment lasted 4 hours, starting at 08h00AM. Blood samples from tail veins were taken at baseline just before starting the experimental treatment (08h00AM) and 4 hours later, just as they were removed. Plasma CORT levels were determined by radioimmunoassay (RIA). Statistical analysis were performed using a 3 (Condition: homecage, small and large platform) X 2 (Moment: baseline and after 4 hours) X 3 (Strain) Anova.
Results: We found a significant Condition X Moment interaction. LSD post hoc tests showed that CORT levels were equal among the three conditions at baseline; after 4 h of treatment, levels were: small = large > homecage. We also found a main effect on Strains, whereas Wistar = Long Evans > Sprague Dawley.
Conclusions: These results show that the large platform is an efficient way to control for stress associated with the "flower pot technique" in three strains of rats as long as plasma CORT levels are concerned. Thus, the present study at least partially confirms the validity of earlier behavioral and electrophysiological results obtained with this PS deprivation technique.

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0450.I

Effects of Modafinil on Symptom Reports During 88 Hours of Simulated Sustained Operations

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Introduction: Previous studies have demonstrated that although classical stimulants (e.g. dexamphetamine, caffeine) help maintain performance and alertness during sustained operations (SUSOPS), these drugs can produce increased symptom complaints. Ideally, a drug that promotes neurobehavioral functioning during SUSOPS should produce few or no adverse symptoms. As part of a double-blind, placebo-controlled study on the effects of the wake-promoting drug modafinil, on performance during simulated SUSOPS, we evaluated its effect on subjective reports of somatic and neurobehavioural symptoms.
Methods: Twenty-four healthy subjects (19m, 5f; mean age 28.45y) completed a 10-day laboratory protocol. Following 3 nights of baseline sleep, subjects remained awake for 88h (3.7 days) except for a 2h nap period (TIB: 0245h-0445h) each day, followed by 3 nights of recovery sleep. Subjects were randomized to modafinil (200mg; N=11) or placebo (N=13) during the 88h period. Placebo was administered at 0000h and modafinil (200mg) or placebo at 1200h on each of 3 days, starting on day 2 of extended wakefulness. Subjects remained in the laboratory throughout the protocol, with light levels <50 lx and ambient temperature at 24ºC ± 1ºC. Every 2h during wakefulness, subjects completed a 35-min computerized neurobehavioral assessment battery (NAB), containing objective tests of performance and subjective assessments of fatigue and mood. At the end of each test bout subjects completed a 20-item symptom complaint checklist, that asked about the presence, duration and intensity of a range of somatic and neurobehavioural symptoms.
Results: Using cumulative frequency curve analysis, neurobehavioral and somatic symptoms were analyzed on each day of the SUSOPS period. Relative to placebo, subjects receiving modafinil had increased reports of headache ($x2=5.57$, $p=0.0182$), excitement ($x2=5.52$, $p=0.019$), and backaches ($x2=3.92$, $p=0.048$), with a trend for increased difficulty concentrating ($x2=3.70$, $p=0.0545$). There were no statistically significant differences in symptom reports of upset stomach, tiredness, difficulty remembering, anxious, giddiness, dizziness, ringing in the ears, irritability, confused, sadness, worried/frightened, quietness, muscular aches, joint aches, feeling too hot or too cold, and itchy skin. Despite these symptom reports, subjects receiving modafinil demonstrated higher levels of neurobehavioural performance, (e.g. significantly less performance lapses on the PVT) relative to placebo subjects ($p<0.05$) [reported elsewhere].
Conclusions: Differences were found in the reporting of somatic and neurobehavioral symptoms between the placebo and modafinil groups. Four of the 20 symptoms assessed were reported at a higher rate by subjects receiving modafinil, relative to placebo. The increased occurrence of headaches is consistent with previous studies on modafinil, and increased reports of excitement may reflect the wake-promoting effects of modafinil. The increased level of difficulty concentrating is problematic in light of the increased performance in this group, and may not be a reliable finding. It remains to be determined whether the unexpected symptom complaints associated with modafinil will replicate in future simulated SUSOPS experiments in which different dosing regimes are evaluated.

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0451.I

Role of Task Difficulty in Cerebral Compensation Following Sleep Deprivation

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Introduction: We have previously reported that total sleep deprivation (TSD) is associated with increased cerebral responses to verbal learning and this increased activation can be viewed as a compensatory response. We later proposed the Cognitive Demand Specific Hypothesis, stating that specific demands associated with a given task mediate whether and to what extent cerebral compensation is elicited during TSD. However, it is unclear exactly which demands facilitate cerebral compensation. Here, we report the role of task difficulty in the cerebral compensatory response to TSD.
Methods: Thirteen healthy young adults underwent functional magnetic resonance imaging (FMRI) while performing a verbal learning task twice: after normal sleep and following 36 hours TSD. The task alternated between blocks of memorization of nouns and blocks of case discrimination of nouns. Unknown to the subjects, half of the memorization words were easy to learn and half were hard, based on recallability norms. Two analyses are presented here: 1) the main effect of TSD on brain responses to memorization; and 2) brain regions showing an interaction between night (Normal vs. TSD) and word difficulty (Easy vs. Hard).
Results: Behaviorally, there was a significant main effect of word

(p=0.001) and a marginally significant main effect of night (p=.047), but no interaction. Long-term recall was: 4.38 ±2.6 Easy and 1.15 ±0.69 Hard words after Normal sleep, and 3.23 ±2.8 Easy and 0.69 ±0.95 Hard words following TSD.The main effect of TSD in the FMRI data was increased cerebral activation in response to verbal learning in the following areas, regardless of word type: bilateral parahippocampal gyri, temporal cortex and visual association cortex; left premotor cortex; and right superior frontal gyrus. The interaction analysis showed that TSD elicited increased activation during memorization of the Hard, but not Easy, words in: bilateral inferior parietal lobes; right inferior frontal gyrus, and temporal cortex; and left dorsolateral prefrontal cortex, premotor cortex, visual association cortex, and posterior cingulate. In contrast, no brains regions showed a compensatory response during memorization of the Easy words.

Conclusions: These data suggest the previously reported cerebral compensatory response to verbal learning following TSD is mediated by task difficulty. Specifically, verbal learning of Hard words elicited cerebral compensation after TSD in several task relevant areas, while Easy words did not elicit a compensatory response. Interestingly, this study found that Hard words elicited compensation in both similar brain regions (i.e., bilateral parietal lobes, right homologue of Broca's area) as the original study (which mixed word types) and new brain regions (right parahippocampal gyrus, left dorsolateral prefrontal cortex). These findings are consistent with our recent report that task difficulty also mediates cerebral compensation following TSD on Baddeley's logical reasoning task. Taken together, these two studies support our hypothesis that specific cognitive demands influence the brain's compensatory response to performance following TSD and strongly implicate task difficulty as one mediating factor.

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0452.I

The Walter Reed Palm-held Psychomotor Vigilance Test

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Introduction: We have developed a field-deployable Psychomotor Vigilance Test (PVT) that runs on Palm-OS © based PDAs. The software can emulate a PVT device widely used in sleep-deprivation research, but provides additional stimulus, feedback, control, and data options. The test (PalmPVT) is currently being compared with the commercial device as part of a larger study, using parameter values designed to improve subject acceptance and compliance under field conditions. The purposes of the study are to estimate time-on-task order effects, and to evaluate sensitivity while using a fixed-intensity stimulus, shortened foreperiod and test durations, and delayed vs. immediate feedback. Preliminary findings from the first 7 of 12 planned subjects are presented below.

Methods: Three men and four women in their 20's and 30's performed a series of equally-spaced physiological, behavioral and sleep latency tests for one baseline day, followed by 8 hrs in bed, 40 hrs of continuous wakefulness, 10 hrs in bed, and one recovery day. PVT sessions occurred every two hrs while awake, and consisted of a 10-min PVT-192 (Ambulatory Monitoring Inc.) task, preceded and followed by a 5-min PalmPVT task. Foreperiods varied randomly from 2-10 sec for the PVT-192 and from 1-5 sec for the PalmPVT, thus yielding about the same number of responses per test. The PVT-192 used a 'running timer' stimulus and the PalmPVTs a fixed-intensity bull's-eye target filling the LCD screen. The PVT-192 and one PalmPVT (Palm-I) displayed Immediate feedback of each RT value, while the other (Palm-D) provided only Delayed post-task feedback of the mean RT. The order of the two PalmPVTs alternated from session to session.

Results: Absolute RTs for the PVT-192 were roughly 10-40 msec faster than for the Palm-I — a difference attributable to a variety of technical and mechanical differences between the devices.. For evaluating application validity, devices were compared in terms of response speed (1/RT) relative to baseline means using a 2-point running average. All 3 devices showed the same pattern over the studies, with speed declining during sleep deprivation to a minimum around 7:30 AM on day 3, and then rising throughout the day. The PVT-192 and Palm-I declined by nearly identical amounts (max 40% and 43% respectively) while the Palm-D declined by 58%. An order effect (overall session time-on-tasks) was apparent, with speed on the "3rd PVT" typically slower than the 2nd, than the 1st. Lapse frequency and RT variance appear to be greater on the PalmPVTs but analysis is incomplete.

Conclusions: The PalmPVT is sensitive to sleep deprivation and circadian effects, and to time-on-task fatigue and order effects. Delayed feedback increases sensitivity. Shorter foreperiods and task durations on the PalmPVT produce results comparable to the longer PVT-192 in terms of relative response speed changes, in spite of different visual stimuli. Field studies are planned.

0453.I

Simulated Driving Performance During Chronic Partial Sleep Deprivation

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Introduction: Studies investigating the effects of sleep deprivation on simulated driving performance have demonstrated increased speed variability and reductions in lateral vehicle control. Such studies have typically involved performance measurement following single periods of total or partial sleep deprivation. The aim of this study was to measure the cumulative effects of chronic partial sleep deprivation, with sleep placed nocturnally and diurnally, on simulated driving performance.

Methods: Forty-six subjects (31m, 15f, 21-44y, mean=29y) participated in one of two 14-day experiments, consisting of 2 baseline days followed by a 10-day experimental period and a recovery period. In experiment 1, subjects were assigned a combination of nocturnal sleep centred around 0200h, plus a daytime nap opportunity centred around 1400h. Group 1 (n=7) was allowed 7.4-8.2h total time-in-bed (TIB) with a 6.2 or 8.2h nocturnal sleep period and group 2 (n=16) was allowed 5.4-6h TIB with a 4.2 or 5.2h nocturnal sleep period. In experiment 2, subjects were allowed an 8h (n=7) or 6h (n=16) daytime sleep opportunity terminating at 1930h. Light intensity was below 50 lux and temperature was 24±1°celsius. The STISIM Driving Simulator (Systems Technology Inc., 1997) was used to measure performance in 15-minute bouts, temporally placed such that time from termination of main sleep period was kept consistent (i.e. experiment 1: 1845-2010h, experiment 2: 0850-1045h). The STISIM, a computer-administered divided attention task designed to mimic real world driving demands, requires virtual vehicle control and response to secondary visual stimuli. Output variables include lane deviation, minimum speed, number of "off-road accidents" and mean reaction time (RT) for the secondary response task. Analyses tested performance at baseline (day 2) and during 8 bouts on consecutive experimental days.

Results: Mean RT ($p<0.001$) significantly decreased and minimum driving speed ($p<0.001$) significantly increased over the experimental period. Significant group differences ($p<0.01$) were found for the number of "off road" accidents, with subjects in diurnal sleep groups experiencing more accidents than those in groups with nocturnal sleep. Post-hoc analyses revealed significant ($p<0.05$) differences between the 7.4-8.2h group with nocturnal sleep and both the 6 and 8h diurnal sleep groups. By the last test bout, the likelihood that an individual would experience an accident was higher in the sleep debt conditions (e.g. 94% in the 6h diurnal sleep group) than in the 7.4-8.2 nocturnal sleep condition (58%).

Conclusions: Learning effects were evident in all groups as the number of experimental days increased, such that subjects drove more quickly

and responded more quickly to the secondary task. Performance deficits were observed in "off-road accidents," with results suggesting that placing at least part of the sleep period nocturnally is more beneficial for simulated driving performance than a continuous diurnal sleep period.

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0454.I

Brain Regions Underlying Differential PVT Performance

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Introduction: Psychomotor vigilance task (PVT) performance is sensitive to excessive sleepiness, sleep restriction, sleep deprivation, and circadian phase. The slowest reaction times (RT) on the PVT are typically more sensitive to sleep loss than the fastest RT's. A study was undertaken using functional magnetic resonance imaging (FMRI) to identify brain regions differentially activated during the fastest and slowest RT's on the PVT in both alert and sleep deprived subjects.
Methods: Ten young adults underwent FMRI while performing the PVT for 10 minutes in the early evening after a normal night of sleep. Eight subjects repeated the procedure after 36 hours of total sleep deprivation (TSD), although only two are reported here. Five others were in a double-blind medication study and one had excessive movement during the TSD scan. The results presented here focus on brain regions underlying the differential performance between the fastest and slowest RTs.
Results: For the 10 well-rested subjects, median overall RT = 279ms, mean RT of fastest responses = 222ms (RRT = 4.55), and mean RRT of slowest responses = 2.38.The fastest responses showed greater activation than the slowest responses in sustained attention regions in right superior parietal lobe and right middle frontal gyrus, motor response regions in left caudate and right precentral gyrus, bilateral visual association cortex, and the left multimodal inferior parietal lobe. Slowest responses were associated with increased activation in medial prefrontal cortex and posterior cingulate.Both of the subjects who were sleep deprived performed above the mean in the well-rested condition. However, they responded very differently to TSD. Subject KG showed equivalent performance following TSD vs. normal sleep, while subject BK showed decreased performance after TSD (normal vs. TSD. KG: mean fastest RT: 184ms vs. 192ms, mean slowest RRT: 3.32 vs 3.75; BK: mean fastest RT: 200ms vs. 228ms, mean slowest RRT: 2.90 vs 2.20). These two subjects also showed different brain responses to TSD, with apparent interactions between response type (fastest vs. slowest) and night (normal vs. TSD). In KG, after TSD, but not after normal sleep, fast responses were associated with greater activation in several thalamic nuclei, caudate, and left middle frontal gyrus compared to slow responses. For BK, the thalamus and caudate showed greater activation for the fast vs. slow contrast in the well-rested condition than during TSD.
Conclusions: After normal sleep, the fastest responses on the PVT are associated with increased activation mainly in sustained attention and visual processing regions. The power of this methodology, though, is in measuring changes with sleep loss. The results from our first two sleep deprived subjects suggest that thalamic regions involved in cortical arousal, and possibly sustained attention regions, mediate PVT performance after TSD. FMRI may also help discriminate neurophysiologically between those with differential vulnerabilities to sleep loss, thus providing new insights into individual differences in response to sleep loss.

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0455.I

Effects of Displaced Sleep on Circulating Leukocytes

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Introduction: Numerous studies have shown that total sleep deprivation disrupts human immune function. One of the most important conclusions is that nocturnal sleep is necessary for normal rhythmicity in several immune parameters. However, there is, today, no knowledge of whether sleep at other times has the same regulatory effects. Therefore, the present study sought to evaluate whether diurnal sleep has the same regulatory effects on circulating leukocytes as nocturnal sleep.
Methods: Seven healthy males completed the study protocol (mean age 25±1SE years), which, besides an adaptation night, included a night sleep (N=23-07) and a day sleep condition (D=07-15), in a balanced order. Subjects, who stayed in a supine position throughout the protocol, had a venous catheter inserted at 18:00 and blood was drawn every hour for 24 hours starting at 21:00. Blood was analysed for subsets of leukocytes and hormones (total leukocytes, neutrophils, lymphocytes and monocytes are presented). Repeated measure ANOVA:s were used to compare the entire 24-hour periods, with contrasts between corresponding time points. A separate ANOVA compared the sleep periods. Units are presented as cells/m L, condition=S, time=T, interaction=I.
Results: Even though no leukocyte type differed significantly for condition across the 24-hour period, all parameters changed across time and all, but monocytes, showed a significant interaction, leukocytes (N=5.8±.1, D=6.2±.1, S=.07, T<.001, I<.05), neutrophils (N=3.3±.1, D=3.6±.1, S=.07, T<.001, I<.05), lymphocytes (N=1.98±.04, D=1.86±.03, S=.15, T<.001, I=.05) and monocytes (N=.34±.01, D=.39±.01, S=.07, T<.05, I=.32). The contrasts at different times of day showed significantly increased levels during the day sleep condition, but the times differed slightly between parameters, total leukocytes (03-11), neutrophils (04, 06-10) and lymphocytes (02-07). The comparison between the two sleep periods showed that the circulating levels of neutrophils ($p<.01$) and monocytes ($p<.05$) were higher during day sleep compared to night sleep, while total leukocytes ($p=.29$) or lymphocytes ($p=.25$) were not. On the other hand, levels of total leukocytes ($p<.05$) and lymphocytes ($p<.05$) declined during both diurnal and nocturnal sleep.
Conclusions: The acute sleep shift disrupted the normal "down regulation" of circulating leukocytes that occurs during nocturnal sleep. For neutrophils and monocytes, the displaced sleep suppressed the amplitude and circulating levels were higher during day sleep than night sleep. Staying awake at night, compared to sleeping, increased the lymphocyte levels during the early morning. In addition, the decline of circulating lymphocytes and total leukocytes during both sleep conditions suggests that sleep, per se, has redistributing properties. It seems as if the acute sleep shift disturbed the normal redistribution of leukocytes. The reasons may, at least partly, depend on circadian aspects, e.g. increased cortisol levels during day sleep, or the fact that staying awake at night is a stressor with indirect effects on immune regulation. Nevertheless, acute sleep shifts disrupts the normal rhythmicity of circulating leukocytes, which, in turn, may have consequences for an adaptive host response.

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0456.I

A Prospective Study Of Sleep Duration And Mortality Risk In Women

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Introduction: It is commonly believed that 8 hours of sleep nightly is needed for optimum health. Recently, Kripke et al demonstrated in a large prospective study that mortality risk had a U-shaped distribution relative to self-reported sleep time with the least risk in those reporting sleeping 7 hours. This study, however, was unable to control for the effects of several potential confounders (e.g. depression, alcohol use, shiftworking, and sleep disordered breathing). We sought to address this limitation by using the Nurses' Health Study (NHS) cohort. Specifically, we wanted to assess whether the mortality risk attributed to sleep time could be explained by one of these confounders.

Methods: We studied a cohort of 82,975 U.S. female nurses (aged 45 to 65 years old) who responded to the 1986 NHS questionnaire. This survey contained the following question: "Indicate total hours of actual sleep in a 24-hour period". Subjects were then followed until 1998 for all cause mortality. Cox proportional hazards models were used to assess the relative mortality risk associated with responses to the 1986 question. Appropriate adjustment for a variety of potential confounders was performed. In order to avoid confounding by illness, we also analyzed a subset of individuals (n=38,859) who were free of chronic disease in 1986 and performed analyses excluding deaths within 2 and 4 years of the questionnaire response. Finally, analyses were conducted for 5 specific mortality causes (cancer, coronary artery disease, stroke, obstructive lung disease, and suicide).

Results: A total of 4042 deaths were documented during 12 years of follow up. The age-adjusted relative risk (RR) of death for sleeping 5 hours or less relative to 7 hours was elevated at 1.44. After adjusting for age, smoking, body mass index, exercise level, diabetes, hypertension, and history of cancer and cardiovascular disease, the RR remained significant at 1.20. After additional adjustment for alcohol use, depression, shiftworking, and snoring, however, this increased risk was no longer apparent. Accounting for shiftworking history was responsible for the majority of the drop in risk. Among long sleepers, the age-adjusted mortality risk was elevated (RR=1.20, 1.66, and 2.57 for sleeping 8, 9, or 10 or more hours respectively). Adjustment for age, smoking, body mass index, exercise, diabetes, hypertension, and history of cancer and cardiovascular disease resulted in lower but still significant mortality risk (RR=1.13, 1.41, and 1.78 for 8, 9, and 10 or more hours respectively). Additional adjustment for alcohol use, depression, shifworking, and snoring did not substantially change the mortality risk of sleeping more than 7 hours (RR=1.13, 1.40, 1.70 for 8, 9, and 10 or more hours respectively). Analyses restricted to those with no chronic disease and 2- and 4-year lagged analyses revealed similar patterns. This mortality risk was not confined to one particular mechanism as long sleep times predicted mortality for all 5 specific mortality causes.

Conclusions: Our results confirm that mortality risk in women has a U-shaped distribution relative to self-reported sleep time with a minimum risk for those reporting 7 hours of sleep. After controlling for depression, alcohol use, shiftworking, and snoring, short sleep times were no longer associated with increased mortality risk with shiftworking playing the largest role. However, sleep durations greater than 7 hours per day remained an independent risk factor for mortality.

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0457.I

Effects Of REM Sleep Deprivation On Behavioral And Hormonal Responses In Rats

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Introduction: Sleep deprivation is known to have significant effects on cognitive function and mood. Early studies in rats demonstrated that REM sleep deprivation (RSD) increased exploratory behaviors, suggesting increased sensitivity to environmental stimuli and/or diminished fear. We sought to confirm whether RSD causes consistent changes in a group of tests measuring anxiety-like behaviors and behavioral responses to stressors in rats.

Methods: Male Long Evans rats approximately 3 months of age were used. Animals were divided into home cage controls (H), apparatus controls (C), and REM sleep deprived (D), 6 to 9 animals per group. The flowerpot method was used to produce 5d RSD. D and C animals were housed on pots protruding approximately 3 cm from a water bath. Pots were 6.5 (D) and 13cm (C) in diameter. Each animal had multiple platforms to minimize restraint effects. Rats were tested by individuals blind to condition in: elevated plus maze; open field; shock-induced freezing; and locomotor activity. To ensure that RSD had not diminished sensitivity, a heat test was performed on day 5. This consisted of timing a 'lick' response to placement on a hot plate (52 degrees C). Animals were sacrificed after 3, 4 or 5 days of RSD to measure serum corticosterone levels.

Results: REM sleep deprivation produced significant effects in all behaviors tested. In the plus maze, D rats showed increased exploration of the open arms of the maze, suggesting decreased fearfulness (D 46.5 $\pm$ 2.2, C 35.2 $\pm$ 5.5, H 23.9 $\pm$ 6.0 entries into open arms; $p < 0.05$ for D vs. H and C). Similarly, in the open field test, D rats showed increased exploratory behavior (D 44 $\pm$ 4.8, C 37 $\pm$ 4.3, H 21 $\pm$ 3.3 center crossings; $p < 0.05$ for D vs. H and C). D rats also exhibited the shortest freezing time in response to shock (D 3 $\pm$ 0.0007, C 8 $\pm$ 0.0009, H 14 $\pm$ 0.0004 min; $p < 0.05$ for D vs. H and C). In contrast, D rats were more sensitive to heat (D 4.9 $\pm$ 0.7, C 6.5 $\pm$ 0.6, H 17.3 $\pm$ 1.8 sec; $p < 0.05$ for D vs. H), suggesting that reduced freezing was not secondary to an elevated pain threshold. D rats also showed increased locomotor activity (D 267 $\pm$ 41, C 199 $\pm$ 13, H 193 $\pm$ 14 photocell crossings; $p < 0.05$ for D vs. H and C). Corticosterone levels were similar among groups.

Conclusions: These results confirm earlier studies suggesting that RSD increases exploratory behaviors in standard tests such as open field and plus maze. Furthermore, D rats showed significantly shortened freezing responses following electric shock. RSD may lead to decreased anxiety-type responses, but the results may also be explained by a primary effect on increasing motor activity.

0458.I

Tumor Clearance is Decreased in F344 Rats Subjected to REM Sleep Deprivation Procedures and Reversed by Recovery

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Introduction: Previous studies in sleep-deprived rats have shown evidence for immune suppression, immune enhancement, or no change depending upon the immune indicator and the duration of sleep loss. We previously showed no effect of 72 h REM sleep deprivation (REMSD) by the small platform method in F344 rats on natural killer (NK) cell activity as measured *ex vivo* in the standard chromium release assay in peripheral mononuclear cells (PBMCs). To study the effects of REMSD procedures on NK cell activity *in vivo* we used a NK cell specific tumor cell clearance assay and also measured NK cell activity in PBMCs in vitro. After tumor cell innoculation, we compared NK cell activity

among rats maintained under REMSD conditions, permitted recovery, and dry cage controls.
Methods: Male F344 rats, 160-day old upon arrival to the laboratory, were individually housed in 25-liter buckets containing an inverted flower pot with a round top (8 cm) and randomly assigned to experimental or control groups. Food and water were available within easy reach of the rat on the platform. After 18 days of adaptation, REMSD was accomplished by replacing wood shavings with 2.5 cm of water in the bucket. A syngeneic mammary adenocarcinoma cell line, MADB106, was used for the in vivo assessment. After I.V. injection, MADB106 cells metastasize only to the lungs and are lysed by NK cells during the first 24 h. After 72 h of REMSD, rats were anesthetized with isoflourane and 4 x 105 125-Iododeoxyuridine radiolabeled MADB106 cells/kg were injected I.V. Following tumor inoculation, REMSD rats were either maintained in deprivation conditions surrounded by water, or permitted recovery by replacing the water with wood shavings. Lungs and a sample of trunk blood were removed from experimental and control rats 20 h later. Aliquots of PBMCs were incubated with NK cell sensitive YAC-1 target cells in a standard NK cell 4-h chromium release assay for the *ex vivo* assessment. Analysis of variance with post-hoc group comparisons was used to test group differences.
Results: There was a greater mean percent retention of tumor cells in the lungs of REMSD rats (0.7 $\pm$ 0.6, n = 13,) compared to REMSD + recovery (0.3 $\pm$ 0.2, n=13) and controls (0.2 $\pm$ 0.1, n=14, P<.003), indicative of reduced NK cell activity *in vivo*. Post-hoc group comparisons revealed significant differences between REMSD and REMSD + recovery (P< .01) and REMSD and control (P<.001). There were no differences among groups in percent killing of NK cell activity in the *in vitro* assessment.
Conclusions: *Ex vivo* assessments of NK cell activity may not be reflective of immune system challenge in sleep deprived subjects. Findings from this study provide evidence for REMSD-associated suppression of NK cell activity that is rapidly, and almost completely, reversed by recovery sleep

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0459.I

Sleep Deprivation Does Not Increase Seizure Occurrence During Inpatient Monitoring In Epilepsy Patients
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Introduction: For several decades, sleep deprivation has been believed to precipitate epileptic seizures. Acute sleep deprivation is used in some epilepsy monitoring units to facilitate seizure recordings as part of the evaluation for epilepsy. The efficacy of acute sleep deprivation in provoking seizures during inpatient continuous video-EEG monitoring, however, has not been assessed in a controlled fashion. Our objective was to determine whether acute sleep deprivation facilitates seizures during inpatient monitoring in epilepsy patients.
Methods: Eighty-four patients with intractable partial epilepsy undergoing inpatient monitoring were assigned in consecutive blocks to either sleep deprivation (SD) every other night or to normal sleep (NS). In both groups, subjects were requested to stay awake during the day, from 6 AM to 10 PM. In the SD group, patients also stayed awake between 10 PM and 6 AM every other night beginning with day 2. Patients were removed from SD if they had two or more secondarily generalized (SG) seizures within 24 hours. Patients were removed from NS and were sleep deprived if they did not have a complex partial (CP) or SG seizure by day 6 of monitoring. In these patients removed from SD or from NS, data were analyzed up to and including the day of removal from the protocol. Prior to initiation of the study, we calculated a sample size of 42 subjects in each group, using data collected from our laboratory prior to June 1998, when all patients were sleep-deprived. This sample size was based upon detecting a clinically meaningful difference of 1.0 seizures/day (four seizures in four days) in the SD group and 0.6 seizures/day (four seizures in seven days) in the NS group, assuming a significance level of 0.05, a two-sided test, a standard deviation of approximately 0.80, and 90% power. Characteristics in the SD and NS groups were compared using independent sample two-tailed t-tests and chi-square tests. For all statistical tests, the level of significance was set at a = 0.05.
Results: The SD and NS subjects did not differ in age, gender, seizure localization, or percent dosage reduction in antiepileptic drugs from baseline at day 1-3 of monitoring. Protocol duration was 6.5 ± 2.4 days (mean ± standard deviation) for SD group and 5.8 ± 2.0 days for NS group. Seizures per day for CP, SG, and combined CP and SG, calculated from admission until end of protocol, did not differ significantly between the two groups. CP seizures per day for the SD group were 0.75 ± 0.71 and in the NS group were 0.73 ± 0.80. The SD group had a higher seizure rate at baseline (prior to admission) than the NS group (12.6 ± 14.8 vs. 7.3 ± 7.2; p = 0.04).
Conclusions: Acute sleep deprivation did not affect seizure frequency during inpatient monitoring in our patients with intractable complex partial seizures with secondary generalization.

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0460.I

Dependence Of REM Sleep Latency On The Level Of Prior Wakefulness
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Introduction: Introduction: REM sleep (REMS) latency variation is one of the basic indices for determining any degree of REMS need. Moreover, REMS latency is taken into account while making diagnosis of various psychoneurologic disorders. There is quite a number of works on the relation of wakefulness (W) duration with the latency of subsequent REMS. However, less attention has been devoted to clarifying the dependence of the time of REMS onsets and its need on various levels of W. The present work was aimed at studying the effect of artificially induced episodes of passive, active and emotional W on the subsequent REMS latency.
Methods: Methods: Experiments were carried out in mature cats (n=8) with the electrodes chronically implanted in different brain structures, oculomotor and cervical muscles for polygraphic recording of sleep-wakefulness cycle in baseline and during REMS deprivation with two methods: 1. Classic one of short-term awakening and 2. Replacement of REMS by W. In the latter case, after behavioral awakening of the animal from REMS, in the first series of experiments, passive W, in the second, active W and in the third, emotional W were maintained for 10 min. With a view to manipulating the W levels, parameters of direct electrical stimulation of MRF / posterior hypothalamus varied within wide ranges. Before the onset of each REMS duration of W and non-REM sleep was measured. Data obtained with the second method of REMS deprivation under the three experimental conditions were compared with baseline and classic method of REMS deprivation. Significance of the difference was verified by Student's t-criterion.
Results: Results: During 72-h deprivation of REMS via its replacement by the three W levels REMS latency considerably increases, as compared with classic method. Highly significant increase was noted when REMS had been replaced with active and emotional W. As expected, time of REMS onsets, when the classic method was used, gradually decreases more and more, compared with baseline, suggesting the enhancement of the pressure of unsatisfied need for REMS. Comparison of data obtained during replacement of REMS with W of various levels

with baseline has shown: a) in the case of passive W maintenance REMS latency is decreased insignificantly; b) in the case of maintenance of active W it is increased; c) REMS onsets are very much delayed after emotional W evoking and correspondingly, there is a highly significant increase in REMS latency.
Conclusions: Conclusion: Different level of W has a varying effect on the velocity of formation of REMS need and respectively alters its latency. It is supposed that by creating conditions for activity in daytime in the individuals suffering from endogenous depressions it is possible to lengthen the latency of REMS preventing thereby enhanced need for it.

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0461.I

Selective and Amphetamine-like Effects of Modafinil on the Homeostatic and Circadian Regulation of the Human Waking EEG

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Introduction: Modafinil, a new wake-promoting agent, reduces the need for prolonged recovery sleep and decreases the rebound in EEG slow wave activity following sleep deprivation. These diachronic effects suggest an action of modafinil on the homeostatic sleep regulatory process. The aim of this study was to determine how modafinil, in comparison to d-amphetamine and placebo, would affect the circadian and homeostatic processes that also influence EEG activity during waking.
Methods: Thirty-three healthy subjects were investigated during 60 hours of prolonged wakefulness in a randomized double-blind placebo-controlled mixed-design study during which the effects of 300-mg of modafinil and 20-mg of d-amphetamine administered at three different times were evaluated. A 4-min eye-closed maintenance-of-wakefulness test combined with continuous polygraphic (EEG, EOG and EMG) recordings was administrated hourly allowing the concomitant measurement of sleep latency and waking EEG activity. Visual sleep-wake stage scoring and quantitative EEG analysis of the iterative MWT recording sequences were undertaken using the PRANA© software (PhiTools Software, Strasbourg, FRANCE). According to the distribution of the data, parametric or non-parametric statistical models were used to assess both "time" and "drug" effects. Multiple comparisons were performed using the Bonferroni's correction.
Results: Both stimulants increased sleep latency during 10-12 hours following ingestion, independently of the time of administration. At the level of the waking EEG spectrum, d-amphetamine strongly attenuated natural circadian rhythms and dramatically suppressed the sleep deprivation-related increases in EEG low frequency activity (0.5-7 Hz). Modafinil showed a transient amphetamine-like effect marked by a decrease in low frequency activity during 3-6 hours after administrations. Contrasting with d-amphetamine, modafinil had virtually no effect on circadian rhythms but allowed for a maintenance of EEG slow alpha (8.5-11.5 Hz) activity, which exhibited a homeostatic decrease proportional to time awake under placebo.
Conclusions: These findings demonstrate that the wake-promoting action of modafinil and d-amphetamine involves different EEG frequency bands and resides on distinct physiological regulatory processes. From a functional point of view, d-amphetamine may inhibit the expression of a sleep-related process, probably through a direct cortical activation masking EEG circadian rhythms, while modafinil seems to disrupt preferentially the homeostatic down-regulation of an arousal process.

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0462.I

The Effect of Self-Imposed Sleep Loss on Effort, Sleepiness and Exam Performance

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Introduction: The purpose of the current study was to compare self-reported sleep before exams and lectures and to determine whether self-imposed sleep loss impacts effort, sleepiness and exam performance.
Methods: Participants were 82 undergraduate students (53 females and 29 males) who completed a questionnaire twice following lectures and exams. The questionnaire included a sleep and activities diary, concentration and effort questions, the Stanford Sleepiness Scale, and a non-academic task-choice question. For the task-choice question, an objective measure of effort, participants selected one task, from a list of five, they would willingly perform for the next 20 minutes. Normative values on the difficulty of the five tasks had been obtained previously. Participants' exam grades were collected for the two exam days on which questionnaire data was obtained.
Results: Data from the first lecture was eliminated due to procedural difficulties. Students decreased their total sleep time on nights prior to exams as compared to nights prior to the lecture (Exam 1 vs. Lecture, $t(81) = 1.948$, $p = .055$, and Exam 2 vs. Lecture, $t(81) = 2.055$, $p < .05$). They also increased the amount of time spent studying after 9pm on exam days (Exam 1 vs. Lecture, $t(81) = 11.071$, $p < .001$, and Exam 2 vs. Lecture, $t(81) = 12.238$, $p < .001$). On exam days, students reported more sleepiness, concentration, and effort when compared to the lecture day (resulting in significance findings of $p < .05$).Total sleep time was positively correlated with feeling refreshed on Exam 1 ($r = .521$, $p < .001$) and Exam 2 ($r = .314$, $p < .01$). Total sleep time, sleepiness, and feeling refreshed were not correlated with exam grades. However, sleepiness was negatively correlated with task-choice on Exam 1 ($r = -.314$, $p < .01$) and feeling refreshed was positively correlated with task choice on Exam 2 ($r = .315$, $p < .01$). In addition, task-choice was positively correlated with perceived effort ($r = .354$, $p = .001$) on the lecture day.
Conclusions: Increased feelings of sleepiness on exam days followed reductions in total sleep time and increased study time at night. Total sleep time, sleepiness, and feeling refreshed were not related to exam performance and students reported increases in concentration and effort on exam days. Increased feelings of sleepiness and decreases in feeling refreshed predicted the choice of tasks of lower difficulty. Two hypotheses may explain the results. Under self-imposed sleep loss, differential energy is applied to the primary task (the exam), while effort is reduced for those tasks not considered primary. Alternatively, under sleep loss conditions, when no choice is given (i.e. performance on the exam) participants will direct energy to that task, however, when choices are offered (i.e. task choice measure), participants will conserve energy by choosing tasks of lower difficulty.

0463.I

The Impact of Naturally Occurring Sleep Loss on Effort, Mood and Sleepiness

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Introduction: Recent studies show that sleep loss results in decreases in objectively measured effort with no change in subjective reports of effort. This study examined the relationship between the range of naturally occurring sleep loss on objective and subjective measures of effort, mood and performance.
Methods: Participants were 188 undergraduate students (119 females

and 69 males) with ages ranging from 18 to 61 years(mean age 22.55 years). Participants self-selected a morning (10:00 AM), midday (1:00 PM) or an evening (6:00 PM) computer-based assessment session. The assessment included a sleep diary. A task choice question, measuring objective effort, asked participants to select one task from a list of five, that they were willing to perform in the next twenty minutes. Normative values of perceived difficulty had been previously obtained for these tasks. A second effort task, the Math Effort Task, presented a series of 40 addition problems with five levels of difficulty. The choice of difficulty level indicated effort. Participants rated the effort they applied to the entire assessment. Simple reaction time, sleepiness and mood were assessed as well.

Results: The percentage of optimal sleep obtained (POS; total sleep divided by perceived optimal sleep) was negatively correlated with sleepiness ($r = -.344$, $p < .001$) and positively correlated with feeling refreshed ($r = .434$, $p < .001$). The greater the POS, the more difficult the task chosen on the task choice question ($r = .199$, $p = .006$). Participants were more likely to select the difficult tasks when they were refreshed after sleep ($r = .163$, $p = .025$) and felt more vigorous, as measured by the POMS ($r = .249$, $p < .001$). POS did not show a significant correlation with math difficulty level chosen. However, task choice and math difficulty level selected were positively correlated ($r = .150$, $p = .039$).Participants' subjective report of effort was greatest when they felt the most vigorous ($r = .186$, $p = .010$). Likewise, they reported the least subjective effort when they were sleepy ($r = -.148$, $p = .042$), fatigued ($r = -.157$, $p = .032$), and tense ($r = -.148$, $p = .043$). No time of day effects were found on effort-related variables.

Conclusions: Effortful behavior is negatively affected by sleep loss. The fewer the hours of sleep obtained relative to optimal amounts, the lower the difficulty of the task selected. Similarly, decreased levels of vigor predicted the selection of simpler tasks. In addition, increased sleepiness, fatigue, and tension were related to lower subjective effort. The lack of significant time of day effects on objectively measured effort is likely due to the participants' self-selection of their assessment times. Within-subjects analyses of effortful behavior at varying times of day may prove valuable.

0464.I

Changes in Brain NF-kappa-Driven Gene Transcription Associated With Sleep Deprivation and Fragmentation in Mice

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Introduction: NF-kappaB is an ubiquitous transcription factor that regulates the expression of multiple genes. Sleep deprivation is associated with activation of NF-kappaB, and conversely, multiple sleep-inducing substances, such as adenosine and cytokines, are potent activators of NF-kappaB. However, the effect of sleep fragmentation, as occurs in multiple sleep disorders, on NF-kappaB-mediated gene transcription is currently unknown.

Methods: Male transgenic mice carrying a LacZ reporter gene under the control of a NF-kappa B-responsive promoter were used for all studies (n=9). Mice were subjected to total sleep deprivation for 24 hours (Sdep; n=3), sleep fragmentation for 6 hours (Sfrag; sleep interruption every 120 sec; n=3), or undisturbed sleep schedules for 24 hours (Co; n=3). After pentobarbital anesthesia, animals were perfused, the brain removed, and 40 micron serial sections of the whole brain were stained for beta-galactosidase (Bgal) activity. Sections were then visualized under light microscopy by 2 blinded investigators.

Results: In Co mice, Bgal was present in occasional cells except for the abundant expression within the dentate gyrus of the hippocampus. In Sdep mice, increases in Bgal activity occurred throughout the brain with preferential localization in frontal cortex, basal forebrain, entorrhinal cortex, hypothalamus, and ventral hippocampus, as well as within multiple nuclei within pontomesencephalic regions. Sfrag mice demonstrated a markedly enhanced expression of Bgal in the same regions as those induced by Sdep. However, the extent and magnitude of Bgal expression were clearly greater in SFrag compared to Sdep.

Conclusions: Sleep fragmentation and deprivation induce activation of NF-kappaB driven gene transcription in multiple brain regions that have been previously recognized as susceptible to sleep disruption. However, despite the shorter duration of sleep fragmentation compared to that of sleep deprivation, the induction of NF-kappaB was markedly greater following Sfrag. Thus, assuming that NF-kappaB gene induction parallels the magnitude of underlying sleep pressure, Sfrag may be associated with increased sleep propensity compared to Sdep.

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0465.I

Effects Of Modafinil On Working Memory Load Responses After Overnight Sleep Deprivation: A Functional Magnetic Resonance Imaging Study

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Introduction: Executive functions such as planning, reasoning, problem solving, response selection / inhibition, short term/working memory, task organization, creativity are dependent on a interactions within a distributed neural network that includes the dorsolateral prefrontal cortex, the anterior cingulate in the medial wall, and the posterior parietal cortex. States of excessive daytime sleepiness such as obstructive sleep apnea and sleep deprivation are associated with executive dysfunction. Working memory is a system used for temporary storage, active monitoring of and manipulation of information, and is a critical executive function. We have previously demonstrated that Modafinil preserves working memory performance on a verbal 2-back task and associated neural activation following overnight sleep deprivation. This report explores the effect of Modafinil on parametric load responses and quantitative signal change following sleep deprivation.

Methods: Randomized, placebo controlled, double blind evaluation of performance and functional activation following overnight (24-hours) sleep deprivation in 8 healthy males, aged 21-35 years. Each subject was scanned in a 3-Tesla MRI scanner, using gradient echoplanar imaging, 4 times: after a night of sleep deprivation or sleep, and following treatment with 200 mg Modafinil or placebo 2 hours before scanning. To minimize circadian effects, all imaging was done between 8 and 10 A.M. The task paradigm was a block design, verbal 1, 2 and 3-back, with 6 blocks of alternating baseline (a simple discrimination of the * and + symbols) and task. As measures of vigilance, 10-minute PVT reaction times were obtained before and after scanning, and a modified PVT-type task was performed in the scanner. Activation patterns and % blood oxygen level dependent signal were assessed from regions of interest in the medial and lateral prefrontal cortex and posterior parietal cortex. Statistical analysis utilized a randomized block ANOVA with subject as a blocking factor.

Results: Data analysis is currently ongoing. The preliminary analysis shows that sleep deprivation reduces ("flattens") the normal rising slope of prefrontal activation in response to parametric working memory load increases. A single 200 mg dose of Modafinil restores the response slope and maintains performance. Correlations between regional % blood oxygen level dependent signal change and performance inside and outside the scanner are being computed.

Conclusions: Sleep deprivation appears to impair working memory load responses, and this is associated with disproportionate prefrontal hypoactivation. A single 200 mg dose of Modafinil is sufficient to preserve

performance and activation in the executive network. These results have implications for complex decision-making in the sleep deprived state, such as physicians on call, shift-workers, armed forces personnel, and emergency services.

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0466.I

Sleep EEG Measure of Slow Wave Activity During the First Five Recovery Nights

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Introduction: Previous investigations of recovery sleep following total sleep deprivation have reported that EEG slow wave activity (SWA) is increased for two nights. However, it is unknown whether sleep EEG recovery responses extend beyond two recovery nights. We therefore examined the recovery pattern of sleep staging and SWA for five consecutive nights following 40-h of total sleep deprivation.
Methods: Healthy young adults (5M, 1F, aged 30 „b 6.9 yr) maintained consistent 8:16 sleep:wakefulness schedules for three weeks at home, verified by wrist actigraphy, sleep logs and call in time to a time stamped voice recorder. Upon admission to the laboratory, the 8:16 schedule was continued for six baseline days. Next, participants were sleep deprived for 40hr and subsequently resumed an 8:16 recovery schedule. Sleep recordings for baseline and post sleep deprivation nights were visually scored from C3 or C4 in 30-second epochs according to standard Rechtschaffen and Kales criteria. EEG signals were digitized using a 12 bit AD converter, stored at a sampling rate of 128 Hz and filtered at 0.3 to 35 Hz. Slow wave power spectra (0.75-3.75 Hz) were examined during the first 4 h of sleep. Repeated measures ANOVAs were performed to compare pre-deprivation (Day 6) with each recovery nights (Days 7-11).
Results: Significant increases in visually scored SWS and significant reductions in sleep onset latency were observed on the first night following sleep deprivation (both $p < 0.05$). In addition, the amount of wakefulness after sleep onset was reduced for four nights following sleep deprivation ($p < 0.01$). Significant increases in SWA were observed on the first and second recovery nights following sleep deprivation (both $p < 0.01$). During the first recovery night SWA was enhanced in the first two NREM episodes, whereas during the second recovery night SWA was higher in the second but not the first NREM episode.
Conclusions: The current findings for increased visually scored SWS on the first recovery night and for increased quantitative EEG SWA on the first and second recovery nights following total sleep deprivation are consistent with previously reported findings. The finding that wakefulness after sleep onset was reduced for four nights following one night of total sleep deprivation suggests that EEG recovery responses may extend beyond two nights of recovery sleep. Additional analyses are necessary to expand upon these preliminary results and examine other quantitative EEG spectra to determine their recovery response to sleep deprivation.

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0467.I

Validity And Reproducibility Of Self-Reported Sleep Duration

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Introduction: Several studies have shown that self-reported sleep durations are an independent risk factor for cardiovascular disease, diabetes, and all cause mortality. These studies have relied on self-reported questionnaire data to assess sleep duration. However, the validity and reproducibility of these measures are unclear. Therefore, we sought to determine how reproducible self-reported questionnaire data on sleep duration are over time and how they compare with rigorously documented sleep schedules over the course of seven days.
Methods: We recruited women participating in the Nurses Health Study (NHS), a large ongoing prospective cohort of female nurses. The 2000 NHS questionnaire included the following question: "On average, how many hours of actual sleep do you get in a 24-hour period?" Two years later, a subgroup of 480 women who had responded to this question were mailed a supplemental questionnaire about sleep habits. This included the original question about sleep duration as well as a sleep diary for one week. Each morning, subjects recorded their recalled sleep duration from the preceding night as well as any time spent in daytime naps. Daily sleep durations were averaged over the week of data collection. Equal numbers of women were randomly chosen from each category of reported sleep duration on the 2000 questionnaire. Validity was assessed by comparing the responses from the sleep diary to the 2002 response using Spearman correlation coefficients. Reproducibility of the response to the sleep question in 2000 and 2002 was assessed with the kappa statistic.
Results: A total of 253 women (52%) responded to the supplemental questionnaire and 165 (34%) completed at least 6 days of the sleep diary. The mean (SD) age was 65.7 (7.1) years. The average time spent asleep over 24 hours on the sleep diaries was 6.2 hours for the group reporting 5 hours or less on the 2002 questionnaire; 6.4 for those reporting 6 hours; 7.1 for those reporting 7 hours; 7.4 for those reporting 8 hours; and 8.0 for those reporting 9 or more hours. The Spearman correlation coefficient for questionnaire response with diary-reported sleep was 0.41 ($p=0.0001$). Although sleep durations from sleep diaries were positively correlated with questionnaire response, the slope of this relationship was only 0.41. In other words, the deviation from a sleep time of 7 hours on sleep diaries was less than half as great on average as would be expected by questionnaire response. The kappa statistic for response to the sleep duration question on the 2000 questionnaire and 2002 supplement was 0.39 ($p<<0.0001$). The weighted kappa when a deviation of one hour was allowed was 0.82 ($p<<0.0001$).
Conclusions: Good correlation was observed between subjective sleep duration measured by response to a questionnaire and one week of rigorous sleep diaries. Questionnaire response also demonstrated excellent reproducibility after two years. Because the slope of the relationship between sleep time by diaries and reported sleep time was less than 1, health risks assessed by sleep questionnaire may underestimate the magnitude of effect of sleep time on health.

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0468.I

MSLT Across 36 Hours of Sleep Loss in Adolescents

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Introduction: Sleep/wake regulation can be described by a homeostatic process (S), where sleep drive rises as wake accumulates and decreases as sleep accumulates, and a circadian process (C), where sleep drive oscillates over 24-hours. We examined these processes with multiple sleep latency test (MSLT) data obtained from adolescents during a 36-h constant routine. We also examined the effects of pubertal status on MSLT across this interval.
Methods: Our sample included 25 male and 25 female adolescents ages 9 to 15 years (M=12.7, SD=1.4). Pubertal status was obtained using Tanner staging (pubic hair growth) determined by consensus among three physician examiners. Participants slept at home on a fixed schedule (lights off = 2200 h, lights on = 0800 h) for at least 10 nights, with compliance checked by telephone calls, sleep logs, and wrist actigraphy. After one in-lab night on this schedule, participants began a 36-h constant routine, with semi-recumbent posture (45 degrees) in a dimly lit room (15-20 lux), while eating small meals, completing performance tests, and undergoing the SLT at 2-h intervals. A series of 17 SLTs began at 1030 h. The first 6 tests lasted 20 minutes; thereafter tests ended at unequivocal sleep or 20 minutes if no sleep occurred.
Results: A regression analysis of all subjects' SLTs examined process S and process C. A significant linear component ($R2(1, 848) = 0.66$, $p < .0001$) was found across the MSLT series, reflecting reduced sleep latencies from beginning to end of the 36-h protocol. Residuals from the linear analysis showed a pattern indicating circadian rhythmicity, with a peak at 2230 h and a trough spanning 0230 to 0630 h. Effects of pubertal status were examined using data from the Tanner 1 (N=9) and Tanner 5 (N=12) groups. Repeated measures ANOVA showed significant group by time differences ($F(16, 304)= 2.96$, $p < .001$), with post hoc tests revealing significant differences at 2230 h (Tanner 1 mean MSLT= 9.2, Tanner 5 mean MSLT=15.0; $F(1, 19)= 4.72$, $p < .05$) and 0030 h (Tanner 1 mean MSLT= 3.6, Tanner 5 mean MSLT=8.6; $F(1, 19)= 5.59$, $p < .05$), and trends (p's<.10>.05) at 1430 (lower in Tanner 5), 0230 (lower in Tanner 1), and 1430 the next day (lower in Tanner 1).
Conclusions: Overall, MSLT data showed a significant increase in homeostatic sleep drive in adolescents across a 36-h constant routine. A clear circadian pattern was also apparent in spite of ceiling and floor effects in SLTs. Of greatest interest was the significant difference in sleep latencies on tests occurring at 2230 and 0030. The pattern of longer sleep latencies in the more mature adolescents may reflect a change that contributes to the reorganization of sleep patterns during adolescent development. In other words, older adolescents may be able to delay bedtime because it is easier for them to stay awake.

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0469.I

Spectral Analysis Of The Sleep EEG During Adolescence: Effects Of Pubertal Stage And 36-h Sleep Deprivation

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Introduction: Slow wave sleep declines by almost 40% across puberty. Yet, developmental changes of sleep physiology from late childhood through adolescence have rarely been examined using spectral analysis of the sleep EEG. Moreover, effects of sleep deprivation on the adolescent sleep EEG have not been investigated using quantitative EEG analysis.
Methods: After at least 10 nights on a fixed 10-h sleep schedule, sleep was recorded in 12 children under baseline conditions and during recovery from a 36-h constant routine procedure involving total sleep deprivation. Six children were classified as Tanner stages 1 or 2 (pre- or early pubertal; mean age 11.8±0.9 years, one boy) and six children as Tanner 5 (mature; 14.3±1.4 years, three boys). Sleep stages were scored according to conventional criteria. EEG power spectra (of derivation C3/A2) were calculated and then matched with corresponding sleep states.
Results: Effects of pubertal stage: EEG power density during NREMS was significantly reduced in the low delta range (EEG power < 2 Hz) and in the theta range (4-6 Hz) for mature adolescents compared to pre-pubertal children; whereas REMS reductions in power were limited to the high delta (2.6-4.6 Hz) and the alpha band (8-10 Hz). Total EEG power in the low delta band was 64% lower in mature versus pre-pubertal children. Effects of 36-h sleep deprivation: A significant enhancement of power density in NREMS during recovery was present in the delta band of both pre-pubertal and mature children. In pre-pubertal children, however, the average increase of NREMS power density comparing recovery to baseline was less pronounced (approximately 30%) compared to mature adolescents (70%) and was limited to the frequency range between 1.6 and 4.2 Hz. In mature adolescents, frequencies from 0.6 Hz up to 6 Hz were significantly enhanced in recovery. No consistent changes in the sigma range (12-15 Hz) were present in either group. In REMS, recovery sleep power density was significantly increased below 4 Hz in both ages and decreased in the alpha band of pre-pubertal children.
Conclusions: Mature adolescents exhibit effects of sleep deprivation on the sleep EEG similar to young adults. In contrast to mature adolescents or adults, the EEG response to sleep loss in pre-pubertal children was less pronounced and limited to a narrow frequency range. This pattern may indicate that the pre-pubertal child's brain quickly reaches the capacity to generate low frequency activity during sleep.

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0470.I

Prevalence of Objective Daytime Sleepiness in the General Population

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Introduction: Daytime sleepiness is a widespread problem that often results from an inadequate amount of nocturnal sleep. Excessive daytime sleepiness due to sleep deprivation is reaching epidemic proportions and represents a major public health issue. Although survey data from the Sleep in America poll indicate that up to 7% of adults report symptoms of daytime sleepiness every day or almost every day, the prevalence of objective daytime sleepiness based on the multiple sleep latency test (MSLT) is not known. The aim of this study was to determine the prevalence of MSLT-defined sleepiness in the general adult population.
Methods: A probability sample of men and women ages 30 to 60 years was recruited as part of an ongoing population-based longitudinal study of sleep-disordered breathing. Participants were followed at four-year intervals with overnight polysomnography. During the second visit, a subset of 662 participants underwent a MSLT, which consisted of four daytime nap trials performed according to published guidelines. The mean and median latency from the four naps were used to grade the level of objective daytime sleepiness. Given that the MSLT represents time-to-event data with censoring at 20-minutes, techniques of survival analysis were used to estimate the prevalence of MSLT-defined sleepiness.

Prevalence estimates were standardized to the mean age of the cohort (50.8 years) and the average body mass index (BMI: 26.3 kg/m2) of the general population derived from the third National Health and Nutrition Examination Survey. Analyses were weighted to account for the probability sampling of the cohort.
Results: The cohort consisted of 388 men and 274 women. Using a threshold of 5 and 10-minutes in the mean MSLT to indicate objective daytime sleepiness, the age and BMI-standardized prevalence of daytime sleepiness was 17.1% and 50.7%, respectively. At each of the above MSLT cut-points, the prevalence of daytime sleepiness was higher if the median was used instead of the mean to summarize the MSLT results (20.9% and 54.6%, respectively). Age was not associated with the prevalence of objective daytime sleepiness. However, daytime sleepiness was more common in men than women. The prevalence estimates for a mean MSLT less than 5 and 10 minutes in women were 15.4% and 45.6% respectively. In contrast, the prevalence estimates for a mean MSLT less than 5 and 10 minutes in men were 19.1% and 56.8%.
Conclusions: Objective daytime sleepiness, as defined by the MSLT, is highly prevalent in the general population. Compared to prevalence estimates of subjective daytime sleepiness, the current data suggest that excessive sleepiness is more prevalent in the general population than is currently recognized. The public health implications of excessive sleepiness are far reaching and include deficits in cognitive performance, reduced work-related productivity, increased risk of automobile accidents, and decrements in quality of life. Educational programs about the health-related risks of daytime sleepiness and methods to identify at risk individuals are needed for physicians and the general public.

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0471.I

Are EEG/EOG Measures of Alertness Sensitive to Prior Sleep in an Operational Setting?

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Introduction: Sleep loss is a recognized feature of night work, due to short, poor quality daytime sleep. Scheduled naps are a potentially useful countermeasure, but we still know little about their ability to counter prior the effects of sleep loss in a work setting. With recent technological developments the measurement of neurophysiological changes in alertness via the electroencephalogram (EEG) and electro-oculogram (EOG) are possible in field settings, thus allowing the recording of alertness while work tasks are performed. The present study investigated changes in neurophysiological alertness in relation to prior sleep for operational air traffic controllers (ATCs).
Methods: ATCs (N = 28, mean age = 35.5 years, 19 males and 9 females) completed 4 roster cycles (afternoon, day, morning, and night shift starting at 2230 or 2330). On two of the four night shifts individuals were provided with a 40-minute nap opportunity. Neurophysiological data were recorded to determine the amount of nap sleep obtained and alertness during the last hour of the night shift. Data from O2-Oz were subject to Fast Fourier Transform (FFT) in 5.12 second epochs. Spectral power was binned in the traditional frequency bands (delta, theta, alpha and beta) and EOG data were visually screened for the presence of slow rolling eye movements (SEMs). Acute sleep debt in the prior 24-hours was determined from actigraphy data. Mixed model ANOVAs were utilized to determine how the amount of nap sleep, acute sleep loss in the preceding 24-hours, and the shift type worked (early or late starting) influenced neurophysiological parameters.
Results: By the end of a night shift controllers experienced a median acute sleep loss of 4.6 hours when working the early starting night shift (N= 47, Range = 2.3-7.6 hours) and 5.4 hours on the late starting night shift (N= 48, Range = 2.8-7.9 hours). During the workplace nap individuals slept for a mean of 17.7 minutes (SD = 12.2, Range 0 - 47, N = 54), with the majority of sleep being S2 (X = 12.8, SD = 8.5, Range = 0 - 30.5, N = 49) and the remainder S1 (X = 5, SD = 2.9, Range = 0.3-12.3, N = 49). During the last hour of shift, acute sleep loss and nap sleep duration both reached significance for delta power ($F(1, 474) = 8.48$, $p = .004$ and $F(1, 438) = 3.97$, $p = .047$), theta power ($F(1, 440) = 11.85$, $p < .001$ and $F(1, 408) = 4.30$, $p = .039$), alpha power ($F(1, 487) = 12.61$, $p < .001$ and $F(1, 450) = 10.39$, $p = .001$), and beta power ($F(1, 366) = 5.63$, $p = .018$ and $F(1, 337) = 16.87$, $p < .001$). The occurrence of SEMs were significantly affected only by the amount of sleep obtained during the 40-minute nap opportunity ($F(1, 68) = 4.80$, $p = .032$).
Conclusions: Findings indicate that the short workplace nap significantly reduced the occurrence of neurophysiological indicators of lowered alertness. In addition, EEG spectral power may be more sensitive to homeostatic influences than the EOG. Despite the relative sensitivity of both measures the cost/benefit analysis of such recordings in a field setting needs to be carefully considered.

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0472.I

Perception Of Drowsiness While Driving: Preliminary Analysis

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Introduction: Alcohol consumption and sleepiness both contribute to motor vehicle accidents. The ability of a driver to recognise a state of sleepiness and altered performance ability is of critical importance in preventing accidents. We hypothesized that the alcohol (within legal Australian blood alcohol limits; <0.05 mg/dL), in the presence of sleep restriction would decrease the perception of drowsiness and driving performance and would influence an individual's decision to continue driving in the face of severe driving impairment.
Methods: 18 normal healthy volunteers (8 males; mean age 22.8, SD 3.6) participated in the study. Subjects underwent two nights of testing separated by one week. Both test nights were proceeded by a night of sleep restriction (5 hours sleep; monitored by actigraphy/sleep diaries). Randomized to one night of the study was alcohol consumption. It was administered as two drinks separated by 1 hour (beginning at 10:30pm), to a total of 1.5mL of 50% alcohol per kg body weight. Subjects then completed the psychomotor vigilance task (PVT) followed by a 70 minute AusEd-driving simulation program beginning at 1:00am. During the driving task subjects were monitored continuously with EEG and were probed with an auditory tone every 4.5 minutes on their perceived driving performance, level of drowsiness, and crash risk using three questionnaires. For driving performance (steering deviation), drowsiness (alpha content of EEG) and crashes (off road) we derived performance/perception indexes (PPI) as follows. The median value of a particular parameter for all subjects was computed and each subject's data normalised by dividing by the group median. The normalised objective measure (eg steering deviation) was then divided by the normalised subjective measure (eg self-rating of driving performance). A PPI of 1 indicates approximate concordance between objective and subjective measures of performance. A PPI > 1 would indicate subjective underestimation of driving performance, drowsiness or crash propensity.
Results: Mean BAC was 0.039 (mg/dL). The combination of sleep restriction/alcohol increased median PVT reaction time (p=.04), EEG alpha (p=.05) and crashes (p=.006) compared with sleep restriction alone. PPI crash was higher on the sleep restriction/alcohol night (0.87 vs 2.75, p=.03) compared with sleep restriction alone. PPI drowsiness

and PPI driving performance were not different between study nights.
Conclusions: Ingestion of alcohol while sleep restricted slows reaction time and increases drowsiness but does not affect perception of drowsiness. Alcohol at legal blood levels while sleep restricted caused more driving simulator crashes and significantly reduced the ability to self-assess crash risk.

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0473.I

The Subjective Alertness Benefits of Brief Naps Following Nocturnal Sleep Restriction

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Introduction: The negative effects on objective alertness and performance following sleep restriction have been shown to be ameliorated by brief naps. The present study addressed the issue of whether brief naps also improve subjective experiences of alertness, fatigue and vigour following mildly restricted nocturnal sleep.
Methods: The sample comprised 24 self-reported good sleepers (Mean Age =23.67 yrs, SD=5.74). Subjects participated in a repeated-measures experiment incorporating five experimental napping conditions: no-nap and 5, 10, 20 and 30 mins of polysomnographically determined sleep (all scheduled to terminate at approximately 15:00 hrs). On the evening preceding laboratory sessions, nocturnal sleep was restricted to between 02:00 and 07:00 hrs (M=4.77 hrs, SD=0.19). Assessment of subjective alertness (Stanford Sleepiness Scale), fatigue and vigour (Profile of Mood States) occurred prior to napping and at times beginning 5, 35, 95 and 155 mins after napping.
Results: The 5-min nap did not differ significantly from no nap on any of the dependent variables examined. In contrast, the 10-min nap demonstrated significantly improved subjective alertness, vigour and reduced fatigue, relative to the no-nap condition, at all post-nap testing times. The 20-min nap showed significantly reduced fatigue 95 mins after napping but no other significant benefits. The 30-min nap impaired subjective alertness and increased fatigue immediately after napping (indicative of sleep inertia) then showed significant improvements in subjective alertness and fatigue 95 mins after napping, with improvements in subjective alertness maintained at 155 mins post-nap.
Conclusions: On balance, the findings of the current investigation indicated that, following mild nocturnal sleep restriction, there was no significant improvement of subjective alertness obtained from a 5-minute nap and limited benefit from a 20-minute nap. A 30-min nap, after an initial period of sleep inertia, provided some benefit. On the other hand, immediate and consistent subjective improvements of alertness, vigour, and fatigue followed a 10-min afternoon nap for at least 155 minutes.

0474.I

Effects of Modafinil on Nap Polysomnography During 88 Hours of Simulated Sustained Operations

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Introduction: Previous studies have demonstrated that although the stimulants caffeine and dextroamphetamine help maintain performance and alertness in healthy people undergoing multiple days of sleep deprivation associated with sustained operations (SUSOPS), these stimulants have detrimental effects on nap sleep quality and physiology. Ideally, a drug that promotes neurobehavioral function during SUSOPS should not interfere with the benefits of prophylactic naps during SUSOPS. The wake-promoting drug modafinil may be such a compound. As part of a study on its effects on performance and alertness, modafinil was experimentally evaluated in a double-blind, placebo-controlled trial of simulated SUSOPS to determine its effects on daily prophylactic naps.
Methods: Seventeen healthy subjects (15m; 2f; aged 21-40y, mean=28y sd=6.5y) completed a 10-day laboratory protocol. Following three nights of baseline sleep, they remained awake for 88 hours (3.67d), followed by 3 recovery sleep periods. During each 24-hr period of the 88 hours, subjects were allowed a 2h TIB period for a nap (0245h-0445h). Subjects were randomized to receive either 200mg modafinil (N=8) or placebo (N=9) at 1200h on each day, starting on the second day of wakefulness, in a double-blind fashion. Subjects remained in the laboratory throughout the protocol, with light levels < 50lx and ambient temperature at 24°C ± 1°C. PSG recordings of EEG (FZ, C3, O2), EOG and EMG were measured during all sleep periods. All nap sleep periods were scored using the standard criteria (R&K). Every 2 h during wakefulness, subjects completed a 35-min neurobehavioral assessment battery. Blood samples (via indwelling canula), core body temperature, and EKG were measured.
Results: Preliminary analysis showed no significant differences in nap total sleep time (TST), sleep latency, wake after sleep onset (WASO), minutes of REM or slow wave sleep (SWS) between modafinil and placebo groups. However, during the final nap on the last day of the 88h period, modafinil administration was associated with increased nap sleep latency (mean [sd] 14.18 [13.64] vs. 4.09 [3.45], p=0.045) and reduced nap sleep efficiency (mean [sd] 83.49 [10.23] vs. 91.30 [4.19], p=0.049). There were trends for decreased TST (mean [sd] 105.24 [11.18] vs. 111.70 [5.86], p=0.096) and increased SWS ((mean [sd] 38.13 [21.29] vs. 18.78 [15.91], p=0.076) in this final nap, in the modafinil group relative to placebo.
Conclusions: This study illustrates that throughout a 4-day period of simulated SUSOPS, a daily 200mg dose of modafinil at 1200h had very little adverse effect on a daily prophylactic nap at 0245h. Only the nap taken on the third and final night of the 88h trial showed effects, and these were confined to modestly reduced nap sleep latency and mean 8% reduced sleep efficiency associated with modafinil. Elsewhere we report the effects of modafinil plus a daily nap on alertness and neurobehavioral performance functions during sustained operations.

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0475.I

Brain Lactate Response to Cognitive Stimulation Vanishes During Prolonged Wakefulness and With Age

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Introduction: The physiological response to sensory stimulation in young subjects is a transient increase in brain lactate concentration. Lactate can be used as an energy source for neurons under normoxic conditions, and it may even be preferred to glucose during neuronal activity. Disturbances of brain energy metabolism have been observed during sleep deprivation in animals. In humans, sleep deprivation leads to impairment of the frontal lobe functions, but the metabolic events related to it are incompletely understood. Interestingly, normal aging has detrimental effects on cognitive functions similar to sleep deprivation. Recently, it has become possible to measure the metabolic events of neuronal activity in humans with 1H MR spectroscopy (1H MRS). With 1H MRS, we studied the effects of age and sleep deprivation on the brain lactate response induced by a frontal lobe-oriented cognitive stimulus.
Methods: 12 young (20-30 years old) and 12 old (60-69 years old) healthy female volunteers were sleep-deprived for 40 hours. They went through a three-week period of actigraph registration and a one-week period of adaptation to regular sleep and nutrition schedule before the

sleep deprivation. During the sleep deprivation period, the brain lactate response to cognitive stimulation was measured four times (at 12-hour intervals) in the young, and 2 times (36-hour interval) in the old subjects. The first measurement was performed in the morning after a normal night's sleep. Functional MRI (fMRI) was performed to determine the brain areas activated during performance of the cognitive task, a silent word generation test. A 6.6cm3 (+0.1, SEM) 1H MRS (1.5 T, PRESS-sequence) voxel for lactate measurements was placed according to the results of fMRI (left frontal lobe, inferior frontal gyrus). Each lactate 1H MRS study consisted of a baseline measurement (duration 10.5 min, with orderly listing of numbers) followed by the silent word generation task.

Results: Lactate levels (measured as lactate/NAA-ratio) increased significantly during silent word generation compared to the baseline in the young alert subjects (paired t-test, $p>0.05$). The cognitive task did not induce elevation of lactate in the old subjects (alert or sleep deprived) nor in the sleep-deprived young subjects.

Conclusions: The physiological lactate response to cognitive stimulation could not be detected in old subjects, and in the young subjects the lactate response disappeared gradually in the course of prolonged wakefulness. The absence of the lactate response suggests that the brain cells were not able to respond normally to the stimulus-induced increase in energy demand. The functional impairment of the prefrontal cortex with aging and prolonged wakefulness may arise from dysfunction of this mechanism.

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0476.I

Sleepiness And Car Accidents: Whath Are The Risk Factors?

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Introduction: The prevalence of sleepiness related vehicle accidents (SRVA) varies between 3% - 23% depending on surveys. Risk factors for SRVA are still not defined.

Methods: We evaluated all crashes monitored by the Police Departments on non-urban roads of Emilia -Romagna and Lombardia (northern Italy) during 12 consecutive months. At the crash site the policeman administered a two-part questionnaire. Part I consisted of detailed information on crash aspects and was always completed. Part II investigated driver's sleep habits and was completed only when the driver was present and agreed to cooperate. The driver possibly responsible for the accident was indicated. We considered Sleepiness Related Vehicle Accidents (SRVA) either those attributed to falling asleep at the wheel by policemen or those fitting Horne's criteria on the basis of crash characteristics (BMJ 1995; 310: 565-567).

Results: We collected 21.469 questionnaires and evaluated 17.268 in which the driver responsible for the crash was identified. ; 4656 (27%) drivers responsible answered part II of the questionnaire. SRVA were 8.5% of total accidents.Pearson's analysis showed the following objective variables as significantly correlated with SRVA: time of accident, type of road, type of vehicle, site of accident ($p<0.000$), gender ($p<0.004$), day of the week ($p<0.005$); age and driving alone were not correlated.Among the subjective variables the following were significantly correlated: sleep quality and hours of sleep the night before the accident, time spent awake before the accident, being a shift worker, complaint of sleepiness in boring or relaxing situation ($p<0.000$), insomnia ($p<0.003$), snoring ($p<0.012$). Stepwise regression analysis demonstrated that the risk for SRVA increased: when drivers slept <6 hours the night before the accident (OR=1.9 respect >6 hours); driver had been awake >17 hours (OR=2.6 respect <17 hours); driving a truck (OR=1.8 respect a car); complaint of sleepiness (OR=1.5 respect no sleepiness); driving during the week-end (OR=1.3 respect the other days).Driving on trunk road is a protective factor for SRVA with respect to driving on freeway (OR=0.6). In summary, sleeping less than 6 hours, being awake longer than 17 hours, driving a truck on the freeway at the week-end and complaining of sleepiness in boring and relaxing situation increases the likelihood of having SRVA from 0.07 to 0.95, i.e. an increase of 88%.

Conclusions: We confirm that driving on freeway favours SRVA; other risk factors are the weekend and driving a truck. Age is not significantly correlated to SRVA:the relative percentage of SRVA with respect to total accidents did not vary among different age groups.Our results demonstrated that insufficient sleep the night before the accident, being awake for a long period and complaining of sleepiness in boring and relaxed situation are strong risk factors for SRVA.

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0477.I

Sleep Deprivation And Shiftwork: The Importance of The Morning Shift

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Introduction: Work organization has a significant influence upon adaptation to shift work. Working in shifts may reduce the worker performance, increase the risk of accidents and expose them to harmful agents, which may cause premature functional disability. In most interventions, however, only the night shift is taken into consideration, and the sleep deficit caused by reduction in the night sleep preceding the morning journey when it begins too early is ignored. In addition, not always is the damage suffered by those working under a fixed morning schedule evaluated. Within this context, the present study aims at comparing three fixed shifts, that is, morning, evening and night shifts with regard to workers sleepiness, sleep duration and quality.

Methods: The study was carried out with male individuals working at the Maintenance Department of a transportation company in São Paulo, Brazil. Such workers used to work in fixed shifts which might go from 07:00am to 03:30pm (morning shift); from 03:30pm to 11:15pm (evening shift); or from 11:00pm to 07:30am (night shift). The company's allocates around 65 workers to the morning shift, 62 to the evening shift and 62 to the night shift – all male individuals. Thirty two workers out of this total agreed on participating in the study: 8 from the morning shift, 12 from the evening shift, and 12 from the night shift. Sleep duration was assessed during a period of 10 consecutive days with the use of actigraphs and sleep questionnaires. Also data on sleepiness and sleep quality were collected by means of questionnaires filled out by the workers themselves.

Results: The average of total sleep duration from morning workers was shorter than the one registered for night workers (343 minutes and 380 minutes, respectively). The result of Kruskal-Walis analysis as to sleep quality was statistically significant (p£0,01); the quality of sleep experienced by the morning shift workers was considered the best, followed by that of the evening shiftworkers and, in third place, that of the night shiftworkers. The averages concerning sleepiness self-evaluation were higher among the morning shiftworkers, and the lowest ones were found among the evening shiftworkers. The Tukey test confirmed the differences among the shifts with regard to sleepiness obtained through ANOVA (p£0,05). Sleepiness levels were lower at 12 noon, 03:00pm and 06:00pm and, according to the Tukey test, in statistic terms they are different from the other ones (p£0,0002).

Conclusions: The results obtained point to the need of evaluating the morning shifts, particularly with regard to sleepiness deriving from par-

tial sleep deprivation. Social pressures to keep awake associated with biological rhythms make it difficult to fall asleep earlier, thus generating sleep deprivation. The earlier the work journey starts, the greater the deprivation, and this causes damage to workers, sometimes similar, sometimes worse than those suffered by night shift workers.

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0478.I

Intervening Variables Influence The Impact Of Extended Wakefulness On Air Refueling Performance

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Introduction: In this acute sleep deprivation study of performance in pilots during a simulated overnight flight, individual differences began to discriminate smaller groups within the study sample. In earlier analysis, Air Refueling Instructor Pilots (IPs) were found to perform better in a divided visual attention task than non-instructor pilots. Additional differences were noted between the simulator Instructor Pilots (SIM-IPs) and an actual aircraft Instructor Pilot (AC-IP) in performance on the visual divided attention task. The SIM-IPs and the AC-IP responded differently on simulated air refueling performance when sleep deprived, possibly due to the introduction of an uncontrolled variable. This abstract addresses the possibility.
Methods: Eight, right-handed male pilots certified on an Air Refueling Part Task Trainer (flight simulator) participated, two were SIM-IPs and one AC-IP. Boom time, azimuth deviations, and simulator shut downs during refueling were used to measure flight performance. Pilots were trained on day 1 of the study, released to sleep from midnight to 6, and returned at 8 am to begin testing. Four 15-minute refueling test periods occurred at 14.17, 18, 22 and 25.5 hours awake. One instructor pilot's supervisor made an unscheduled visit to the simulator during the test period at 22 hours awake inserting a possible uncontrolled variable.
Results: For the IPs, azimuth deviations and boom time were significantly negatively correlated (r=-.982, p=. 014), that is, as azimuth deviations increased boom time decreased. SIM-IP1 was not significantly different on azimuth deviations from SIM-IP2 (p=.11) or AC-IP (p=.057) but SIM-IP2 was from AC-IP (p=.026). SIM-IP1's azimuth deviations were consistent across all four refueling periods whereas SIM-IP2 and AC-IP doubled their azimuth deviations between the trial at 22 and 25.5 hours awake. However for boom time, the SIM-IPs did not differ significantly (p=.46) and they both differed from the AC-IP (p=.009). The SIM-IPs' boom time was relatively consistent though decreasing across all refueling periods however the AC-IP's boom time increased at 22 hours awake then declined at 25.5 hours. No simulator shutdowns occurred while refueling within the first 24 hours however the AC-IP had a simulator shutdown during the last refueling period at 25.5 hours awake.
Conclusions: The IPs appeared to have similar performance patterns on boom time and azimuth deviations except the AC-IP's increased boom time at 22 hours awake. During this time period the AC-IP's supervisor visited the simulator to observe the study. It may be that this visit motivated the AC-IP resulting in better performance for this time period, with associated increased expenditure of cognitive resources. The motivation-induced expenditure of cognitive resources may have depleted available resources, possibly explaining the AC-IP's rapid performance decline noted at 25.5 hours awake.

0479.I

Lifetime Accumulated Exposure To Night-Work Increases Sleep Disturbances And Reduces Subjective Health In Monozygotic Twins

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Introduction: The effect of night-work on sleep and health is a debated issue. Almost no lifetime follow-up has been carried out and when attempted, selection may have biased the results because of insufficient control over individual factors. The most powerful design available to control for individual factors is the comparison of monozygotic twins. The present study sought to investigate the effect of exposure to night work over the life span in monozygotic twins discordant on the exposure to night-work.
Methods: The Swedish twin registry collects questionnaire data from all twins that are born in Sweden. Because the focus of this study was exposure over the working life span, only twins 65 years or older (the normal age of retirement in Sweden) was analyzed. A total of 720 monozygotic twin pairs were available and 200 were discordant on night work exposure - one twin had no exposure and the other at least one year (mean exposure to night work = 13 years). The latter 200 pairs (101 men, 99 women, mean age 69 years) were used to analyze differences within pairs on subjective questionnaire data. Variables describe habitual bedtime, rise time and time in bed, as well as items (1-5 with 5 as the most positive outcome - less frequent complaints) describing disturbed sleep, early awakening, well rested and self rated health. Diurnal type was scored 1-5 with 5 as extreme eveningness. One control variable was available describing the number of years of formal education. The effect of exposure to night work was analyzed using ANOVA for dependent measures between paired twins.
Results: There were no differences between paired twins on habitual bedtime, rise time, time in bed, early awakening, well rested, diurnal type or the number of years of formal education. There was however, a significant difference for disturbed sleep (p=.002) and self rated health (p=.021). Twins exposed to night-work reported more frequent complaints of disturbed sleep (4.2/pm.08 vs 4.5/pm.07 mean /pm sem) and poorer self rated health (3.6/pm.08 vs 3.8/pm.07). In a second analysis, twins were matched according to their formal education in four groups corresponding to elementary school, high school, college and university degree. A total of 109 twin-pairs were left with equal level of formal education and the effect of night-work was tested with ANOVA. The results confirm the prior analyses. Disturbed sleep was more pronounced (p=.002) and self rated health poorer (p=.016) in twins exposed to night-work.The effect of gender was also investigated by introducing gender as a between groups factor. No significant interaction was found between gender and exposure to night-work on any of the studied variables.
Conclusions: The results suggests that lifetime accumulated exposure to night-work has negative effects on subjective sleep and health in monozygotic twins. The effect seems to be independent of gender and the level of formal education.

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0480.I

Effects of Sleep Restriction on Performance of a Combined Driving Simulation/Cognitive Task

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Introduction: Pilot data from a combined driving simulation/cognitive task following modest sleep restriction in young adolescents did not show predicted performance deterioration. Adjustments were made to improve the task. In general, we hypothesize that a greater demand for attentional resources will produce greater sensitivity to moderate sleep

loss for a combined task than either a driving or cognitive task alone.
Methods: Normal healthy young adult males (n=12) and females (n=10) ages 18-26 years kept an assigned sleep schedule (confirmed by actigraphy) attempting to sleep 8.5 hours at home for three consecutive nights. Training (1.5 hours) occurred after the first night; baseline data were collected after the third night. The next two nights participants were randomized to control (8.5 hours for both nights, n=11) or restricted (5 hours one night, 3 hours next night, n=11) sleep schedules. The experimental performance test session occurred the next day. The 30-minute task included a 5-minute block of subtraction, driving, and combined driving/subtraction each 15 minutes. When driving, participants were asked to keep a computer-generated simulated car in the center of the right lane, obeying the speed limit. Test sessions occurred between 1500 and 1800 hours, each followed by a 10-minute version of the Dinges psychomotor vigilance test (PVT).
Results: Driving variables (lane deviation, lane variability, speed deviation, speed variability, lane incidents, wind reaction time [RT]) were analyzed using repeated-measures ANOVAs with group (control or restricted) as between-subject and session (baseline or experimental) and task type (drive or drive/subtract combined) as within-subject variables. Cognitive variables (RT, percentage no-responses, percentage correct, speed/accuracy difference) and PVT variables (mean RT, lapses, mean fastest 10% RT) were analyzed with similar repeated-measures ANOVAs for the subtract and drive/subtract combined. Significant interactions of group and session (worse performance in restricted group at experimental session) occurred for lane variability [$F(1,21) = 4.87$, $p = .039$] and lane incidents [$F(1,21) = 5.96$, $p = .024$], and a trend for wind RT [$F(1,21) = 4.05$, $p = .058$]. Groups differed significantly on speed/accuracy (restricted group fewer correct and/or responded slower [$F(1,21) = 7.66$, $p = .012$]). Lane variability showed an interaction of group and task (restricted group worse during combined task [$F(1,21) = 5.29$, $p = .032$]). The only significant interaction of group, session, and task occurred for lane variability (combined performance worse in restricted group at experimental session) during the last half of the task [$F(1,21) = 4.36$, $p = .05$]. No significant effects occurred for RT, lapses, and fastest 10% RT on the PVT.
Conclusions: The driving simulator identified performance decrements following sleep restriction, although only one variable (lane variability) supported our hypothesis that the combined task would show greater impairment. On the other hand, the driving tasks identified performance impairment not observed with PVT, which may speak to the sensitivity of a dual task.

0481.I

Population-Based, Normative Data for the Epworth Sleepiness Scale
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Introduction: In clinical and research settings, the Epworth Sleepiness Scale (ESS) is a widely used measure of daytime sleepiness. Since 1991, publications presenting ESS data have grown in number steadily from 3 during 1992 to over 50 during 2002. However, US studies describing, population-based data for the ESS in persons aged 18-65 don't exist. Without normative data one must use on clinic-based samples with the inherent selection bias related to individuals seeking care or volunteers with similar limitations. To provide unbiased normative data, the present study assessed daytime sleepiness in a population-based sample.
Methods: A sample of 2,513 individuals 18-65 years was randomly selected from the tri-county Detroit area. Random-digit dialing techniques were used and daytime sleepiness was evaluated using the ESS. Demographic, sleep, and health variables were also assessed during the interview. Demographic and sleep habit categories were compared using Analysis of covariance (ANCOVA) and student t-tests. Sleep habits and demographic associations with the ESS were investigated using multiple regression analyses.
Results: The demographic characteristics were: mean age = 41.7 $\pm$ 12.7; 50.7 % female; 65.2% greater than high school education; 69% Caucasian; 25% African American. The characteristics of the sample were similar to the 2000 census data for the area. The mean ESS score for the total sample was 7.9 $\pm$ 4.5 with 20.3% scoring in the "sleepy" range (i.e., >10). The oldest cohort (56-65) had the least sleepiness (mean ESS for ages [18-25] = 8.3; [26-35] = 8.2; [36-45] = 7.9; [46-55] = 8.2; [56-65] = 6.9). There were significant age effects, omnibus $F(4,2491) = 6.05$, $p < .001$. Post-hoc tests showed that the oldest cohort was significantly different from each of the younger cohorts (all $p < .01$), but there were no significant differences between other age groups. Age remained significant after controlling for BMI, depression, habitual sleep time, health status, and insomnia. African Americans had significantly higher ESS scores compared with Caucasians (9.1 vs. 7.4; $p < .001$). This remained significant after controlling for age, gender, health status, BMI, habitual sleep time, and insomnia. The relative risk for having excessive daytime sleepiness (ESS > 10) in African Americans was 1.62, 95% C.I. = 1.42 to 1.86. ESS scores did not differ by gender. Multiple regression analyses indicated that age, depression, snoring, body mass index, habitual sleep time, and race were independent predictors of daytime sleepiness ($p < .01$ for all).
Conclusions: In addition to providing population-based norms for the ESS, the results demonstrate greater daytime sleepiness in African Americans compared to Caucasians. Reasons for this finding are not known, but results remained significant after controlling for other important variables. Consistent with previous data, individuals aged 56-65 reported less daytime sleepiness than younger individuals. Future studies should determine if cultural differences regarding specific items account for the associations identified and whether differences can be confirmed with objective testing.

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0482.I

Central Arousal Response to an Experimental Model of Sleep Disruption in Healthy Adults
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Introduction: A number of research groups have over the years used various noise models of sleep disruption. We modified the psychobiological stimulus used by Cluydts et al to allow the presentation of traffic noise to 12 beds simultaneously. In order to the efficacy of our model of sleep disruption in a ward setting, a randomised, investigator blinded study of central EEG arousals was performed on 36 healthy volunteers with and without noise.
Methods: 36 healthy subjects without known sleep disorders participated in the study which study comprised of two overnight visits on consecutive nights proceeded by an adaptation night to familiarise subjects with the sleeping environment. Traffic noise was then presented on the second of two experimental nights. EEG data was scored blind according to R&K and central arousals the scored according to the ASDA criteria.The stimulus consisted of pre-recorded traffic noise continuously presented to the subjects during the experimental nights (2300-0700hrs) in a 12-bed hospital style ward. The mean overall noise level was 52dB(A), with a dynamic range of 34 to 77dB(A). Sleep EEG and sound levels were recorded using a Vitaport 3 recorder. Analysis of EEG arousal parameters were performed as a function of time, by the arousal index (arousal #/hr of total sleep time) and the expression of arousals within the first 4 hours of recording (LNA – 2300-0300hrs) against the 2nd 4 hours of recording (EMA – 0300-0700hrs).Tests for treatment differences were obtained using a paired 2-tailed t test with significance set at p=0.05.

Results: The presentation of EEG arousals revealed a significant increase in the arousal index when subjects were exposed to the experimental model compared to the non-noise condition. Similarly, observations made of the number of central arousals presenting during the 5th, 6th and 7th hour of sleep were significantly higher than the non-noise condition. Analysis of the number of arousals defined by the time of presentation (LNA or EMA) was performed between the two conditions with only EMA reaching statistical significance.
Conclusions: The aim of this study was to demonstrate the efficacy of our experimental model of sleep disruption with regard to central EEG arousals. We also set out to demonstrate that the model of Cluydts et al could be used on a larger scale than previously attempted. We found statistically significant effects on EEG arousal parameters. The noise exhibited a greater effect on arousal presentation during the early morning hours where stage 2 and REM predominate. Such a model may be useful in the measurement of duration of hypnotic action.

0483.I

Sleep Deprivation Impacts Air Refueling Instructor Pilots Differently Based On Simulator Experience

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Introduction: Aerial refueling is challenging and requires many hours of practice to maintain proficiency. Practicing on actual aircraft is not always practical so pilots retain some proficiency using an aircraft simulator. In an earlier analysis, Instructor Pilots (IPs) were found to perform better in a divided visual attention task then non-instructor pilots, utilizing flight performance on an Air Refueling Part Task Trainer (ARPTT) as the primary task across 27 hours of wakefulness. Differences may be related to the decreased cognitive workload associated with increased training and familiarity conferring resistance to performance decrements on these simulator tasks. Interestingly, differences emerged between IPs who taught using the simulator (SIM-IPs) and an IP who taught primary during actual flight situations (AC-IP). Preliminary analyses examine these possible differences.
Methods: Eight, right-handed male pilots certified on the ARPTT participated, two were refueling simulator Instructor Pilots, or SIM-IPs (SIM-IP1 and SIM-IP2), while the other one was an actual aircraft refueling instructor, or AC-IP. Divided visual attention was measured using the Lateral Vision Field Tester (LVFT) as the secondary task. Flying the simulator in the pre-contact position (50 feet aft and below the tanker) was the primary task. The LVFT is horseshoe shaped with 11 light sources placed at 15-degree intervals along a horizontal plane from 0 to 75 degrees on the left and right hand side. One or two lights were presented in a random fashion at random intervals. Pilots responded verbally to visual stimuli. LVFT was scored by failure to respond to the visual stimuli. Pilots' flight performance was measured by azimuth deviations that occurred during LVFT trials. 15 LVFT trials were administered across 27 hours of continuous wakefulness.
Results: All IPs maintained 4 or fewer response omissions throughout the first 13 LVFT trials (3.5 to 23 hours awake), however on LVFT trials 14 and 15 (25 to 26 hours awake) the AC-IP's response omissions increased sharply whereas the SIM-IPs remained consistent. SIM-IP1 was not different from SIM-IP2 (t=1.6, p=. 1) or AC-IP (t=-1.9, p=.08) however SIM-IP2 is significantly different from AC-IP (t=-2.96, p=.01). Including all LVFT trials, the AC-IP averaged twice as many response omissions than the SIM-IPs (3.36 to 1.57& 0.87). Azimuth deviations for IPs remained constant through LVFT trial 10 (3.5 to 19 hours awake). SIM-IP1 had fewer deviations than SIM-IP2 and AC-IP (t=-4.276, t=-4.371; p<. 001 respectively), and SIM IP2 had fewer deviations than AC-IP (t=-2.655, p<. 02). AC-IP markedly increased azimuth deviations at 21.5, 23 and 25 hours awake. The SIM-IPs increased at a slower rate.
Conclusions: It appears that compared to the actual flight refueling instructor, the simulator instructor pilots' familiarity with the ARPTT may enable them to partially compensate for the effects of sleep deprivation, possibly by lowering overall cognitive workload.

0484.I

Sleep Deprivation In The Pigeon (Columba livia) By The Disk-over-water Method

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Introduction: Sleep deprivation in the rat by the disk-over-water (DOW) method results in a distinct syndrome characterized by increased food intake, weight loss, thermoregulatory changes, debilitated appearance, skin lesions and ultimately death. Despite extensive research, the mechanisms mediating the syndrome and its implications for understanding the function of sleep remain unclear. Our interpretation of the syndrome may be limited in part by the fact that other species have not been studied using the DOW (Rechtschaffen and Bergmann, 2002); it is unclear whether the syndrome reflects fundamental aspects of sleep loss or species-specific effects. Although studies using other mammalian species would be informative, perhaps the most evolutionarily independent and therefore powerful comparison would be to study birds, the only non-mammalian taxonomic group to display unequivocal slow-wave sleep and REM sleep. We herein present the first description of sleep deprivation in a bird, the pigeon, using the DOW.
Methods: Only one modification was required to adapt the DOW apparatus for use with pigeons. Since the relatively shallow water used for rats was not noxious to pigeons, we increased the water depth to 9.0 cm. At this depth pigeons standing in the water were wet up to the lower edge of their wings, a situation that they actively avoided. Four adult male pigeons (two experimental and two controls) were instrumented for recording the EEG from the left and right hemispheres, EOG and EMG. After post-operative recovery and adaptation to the DOW apparatus, a baseline recording was obtained for one week followed by total sleep deprivation for up to one week. As in rats, disk rotation was triggered by a computer when EEG and EMG amplitude reached values indicative of slow-wave sleep. Since birds do not exhibit a REM-related theta rhythm, a combination of high amplitude EOG and low amplitude EEG and EMG were used to detect REM sleep. The birds were recorded for an additional week following deprivation.
Results: The pigeons readily adapted to the DOW apparatus. Once the appropriate values were determined the computer reliably detected sleep onset. Initially, the birds responded to the disk rotation by awakening immediately and walking. As deprivation progressed, the birds began to sleep as the disk turned, only awakening when they were pushed against the enclosure wall. However, none of the birds ever fell in to the water. The pigeons' food intake and weight remained constant throughout deprivation periods of up to one week, and no changes in plumage were detected. Preliminary analyses of the EEG suggest that sleep intensity increased above baseline levels during recovery.
Conclusions: Our preliminary results indicate that the DOW method can be effectively used to deprive pigeons of sleep. We are currently extending the deprivation period beyond one week to determine whether pigeons will develop signs of the syndrome observed in rats. In addition, we are exploring the feasibility of performing unihemispheric sleep deprivation in pigeons.

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0485.I

Pain Threshold and Sleep Loss

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Introduction: Nathaniel Kleitman reported in his 1939 book that during sleep deprivation he found "cutaneous sensitivity to touch remained unchanged", whereas "that to pain showed a progressive increase during the period of wakefulness". This observation often is made anecdotally in studies of sleep loss, but over the years it has received limited systematic evaluation. This study evaluated pain threshold in healthy normals after a single night of no sleep and a night of restricted sleep.
Methods: Six healthy, normal adults, 21-35 yrs old, participated. All were in good medical and psychiatric health with no history of alcoholism or drug abuse. All had sleep efficiencies >85% on a screening 8 hr NPSG with no evidence of primary sleep disorders and an average sleep latency of >8 min on a standard MSLT conducted on the following day. Each underwent four conditions presented in a Latin Square design: 8 hrs time in bed (TIB) + placebo, 8 hrs TIB + codeine 60 mg bid, 4 hrs TIB + placebo, and 0 hrs TIB + placebo. In the 8 hrs TIB conditions bedtime was set to 2300-0700 hrs, in the 4 hrs TIB 0300-0700 hrs, and in the 0 hrs TIB no sleep was allowed. The following day after arising at 0700 hrs and a breakfast (0800-0830 hrs) each participant received codeine 60 mg or placebo at 0900 and 1300 hrs (the codeine data are presented in a companion abstract). Pain threshold assessments were done at 1030 and 1430 hrs using a novel radiant heat stimulation method. At each assessment finger withdrawal latency (sec) was measured for 5 randomly presented intensities of radiant heat directed to the index finger pad.
Results: On the am testing finger withdrawal latency was reduced significantly as a function of stimulus intensity (main effect of intensity: $F4, 20 = 29.5$, $p<.001$). A significant main effect of TIB ($F2,10 = 10.2$, $p<.001$) and an interaction of intensity by TIB were also found ($F8,40 = 4.31$, $p<.001$). At the lowest stimulus intensity withdrawal latency was significantly reduced in the 0 hrs condition relative to 4 and 8 hrs ($p<.01$), while at the intermediate intensities the 4 hrs and 0 hrs were similarly reduced and differed from the 8 hrs TIB ($p<.01$). Finally at the highest intensity no TIB effects were found. On the pm testing a significant main effect of TIB ($F2,10 = 7.67$, $p<.01$), intensity ($F4, 20 = 8.29$, $p<.001$), and no interaction was found. The 4 hrs and 0 hrs TIB differed from the 8 hrs TIB and each other.
Conclusions: The results of this study indicate that sleep loss (4-8 hrs) causes hyperalagesia (i.e. reduces pain threshold) for a radiant heat stimulus. Further the sleep related changes in pain sensitivity increase as a function of thermal stimulus intensity.

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0486.I

Efficacy Of Multiple Caffeine Doses For Maintenance of Vigilance During Early Morning Operations

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Introduction: Caffeine is one of the most widely used drugs in the world and is commonly used to counteract the sleepiness associated with irregular work/rest schedules or sleep deprivation. This study examined the ability of a novel caffeine chewing gum delivery system to maintain vigilance for an extended period of time using a multiple dose paradigm during a night without sleep.
Methods: Forty-eight healthy, non-smoking males (N=28) and females (N=20) who habitually consumed less then 300 mg of caffeine per day volunteered for this study. Subjects were divided into groups of four with each of the four subjects randomly assigned to one of the four dose groups (placebo, 50, 100, or 200 mg caffeine gum). Subjects reported to the lab at 1900, had EEG electrodes attached, and completed an eight hr sleep period (2300-0700). They were awakened at 0700 (Day 2) and were kept awake for the next 29 hr. Control data was collected until 0300 (Day 3) at which time subjects began the first of three two hr test blocks (0300-0500, 0500-0700, 0700-0900). At the beginning of each two hr test block subjects' chewed two sticks of gum (Stay Alert® chewing gum, Amurol Confectioners, Yorkville, IL) containing the appropriate caffeine dose for five min. Subjects completed seven ten-min sessions on a simple vigilance task in each two hr test block. The Stanford Sleepiness Scale (SSS) followed each test. Additional tests were completed between 0900-1200 followed by an eight hr recovery sleep period (1200-2000).
Results: Lapses on the PVT were identified as, and divided into response times with durations greater than 1 sec, 3 sec, or 5 sec. ANOVA found overall significant differences ($p<0.05$) for Group, Session, and the Group by Session interaction for each of the lapse durations. Further examination of simple effects showed significant differences between Sessions in the Placebo Group for all three lapse durations ($p<0.000$) and also in the 100 mg ($p<0.05$) and 50 mg ($p<0.003$) groups for Lapses > 1 second, but no significant differences in any condition for the 200 mg group. Post-hoc comparisons found significant differences between each group and every other group for each of the three conditions. During the six hr test period the placebo group had significantly more peak (mean) 1 sec (18), 3 sec (9) and 5 sec (3.5 vs <0.5) lapses as compared to the 200 mg group (2-1 sec, 1-3 sec, and <0.5-5 sec lapses). Performance for the 50 and 100 mg groups was between that of placebo and 200 mg in a dose dependent fashion. Speed was not significantly affected by treatment. There was a significant main effect in the SSS for Session ($p = 0.000$), however there were no significant differences between groups.
Conclusions: A single night without sleep had a significant negative affect on vigilance during the early morning hours. Any dose of caffeine significantly improved performance as compared to the placebo. The 200 mg group was able to maintain vigilance for the entire six-hour period.

0487.I

Gender Differences in Time in Bed in Sleep Disorders Patients

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Introduction: There are few studies on gender differences in patients with sleep disorders as compared to studies comparing gender differences in the general population. In a preliminary study Shaffer et al reported that female sleep disorders patients spent slightly more time in bed than male patients (8.5 hours versus 8.08 hours). In the present study the sample size was increased from 113 patients (47 females, 66 males) to 311 patients (124 females, 187 males).
Methods: In the present study we examined the two week sleep diaries of of 311 consecutive patients. Each patient filled in a two week sleep diary prior to their polysomnographic laboratory evaluation. "Time in Bed" was calculated from the time the patients reported their intent to fall asleep until their reported final awakening and leaving their bed.
Results: The average age ranges for females and males were comparable (females = 51.1 years, SD = 13.43, and males = 50.45 years, SD= 14.96). The gender differences in average time in bed were statistically non significicant with females spending slightly more time in bed (females= 8.25 hours SD = 2.21, males = 7.96 hours, SD= 1.80, $t=1.22$, $p>.20$). However, when sleep deprivation was defined as spending seven or less hours in bed there were significant gender differences. Of the 124 females in the study, 7 reported spending seven or less hours (10.5 %) in bed compared to 31 out of 187 males (16.6%) who reported spending seven or less hours in bed.

Conclusions: The present study verifies the clinical importance of obtaining sleep diaries for sleep disorders patients. The extensive prior survey research that females are more sleep deprived than males may not apply to patients studied in sleep disorders laboratories. Further data is needed to relate time in bed to such variables as age and diagnostic category to obtain a more definitive assessment of gender differences in sleep disorders patients.

0488.I

Relationships Among Neurobehavioral Performance Measures During Two Nights of Sleep Deprivation

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Introduction: It is well established that sleep deprivation impairs human performance. However, whether sleep deprivation produces similar performance decrements in all types of brain function for an individual or whether inter-individuals differences in performance impairment are dependent upon the type of brain function examined is unknown. The current study addressed the latter.
Methods: Females and males (N=28) between the ages of 18-28 years were scheduled to sleep for 10 hours in the laboratory prior to two nights of sleep deprivation. Participants were sleep deprived using a modified constant routine procedure that controlled for physical activity, light exposure (< 100 lux) and nutrition intake. Alertness and performance measures were assessed from 2000-0800 h each night including: a 15 minute version of the Maintenance of Wakefulness Test (MWT), a modified version of the Psychomotor Vigilance Test (PVT; false starts, lapses and reciprocal reaction time), the Switching Task (Math accuracy and mean correct reaction time [MCRT] and Manikin accuracy and MCRT), and the Wilkinson Four Choice Reaction Time Task (accuracy and speed). Participants had sufficient exposure to tasks to minimize practice effects. Changes in performance from 2000 h on Night 1 to the average performance between 0200 and 0800 hr on Night 2 were examined with t-tests. Person correlations were computed to test for significant relationships among neurobehavioral performance measures on Night 2.
Results: Neurobehavioral performance measures were impaired by sleep deprivation (all $p < 0.01$) with the exception of Math and Manikin MCRT. Performance on Night 2 of sleep deprivation was significantly correlated between the following measures (r ranged from 0.38 to 0.90; all $p<0.05$): All PVT measures correlated with each other; PVT false starts correlated with the Manikin accuracy; Wilkinson speed correlated with PVT lapses, Math and Manikin MCRT; Math MCRT correlated with Manikin MCRT; Math accuracy correlated with Manikin accuracy; MWT correlated with Math accuracy. Wilkinson accuracy did not correlate with any measure.
Conclusions: Sleep deprivation impaired most measures of neurobehavioral alertness and performance. However, performance impairments on one neurobehavioral measure were not necessarily correlated with performance impairments on other measures. For example, not all measures of accuracy were related, whereas, most measures of speed were related. These preliminary analyses suggest that inter-individual differences in performance impairment during sleep deprivation are dependent upon the type of brain function examined.

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0489.I

Sleep Restriction Causes A Desensitization Of The Serotonin 1A Receptor System In Rats

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Introduction: Sleep loss has adverse effects on mood and cognition. Generally most effects of short sleep deprivation are reversible by subsequent recovery sleep. However, frequent and repeated sleep loss may gradually result in more serious changes. It has been hypothesized that chronic sleep disturbance may sensitize individuals for psychopathologies like depression. The neurobiological abnormalities in depression are not fully understood but alterations in the serotonergic and cholinergic system are among the prime candidates. Not only is depression associated with alterations in serotonergic and cholinergic receptor sensitivity but, also, antidepressant treatment reverses some of these changes. The present study in rats aimed to establish the effects of chronically restricted sleep on the functional sensitivity of serotonergic and cholinergic receptors in the brain, particularly serotonergic 1A receptors and cholinergic muscarinic receptors.
Methods: The study was performed with adult male Wistar rats (n=12). Half of the animals served as control. The other half was subjected to a chronic sleep restriction schedule allowing them to sleep 4h per day at the beginning of the light phase. The remainder of the time, the animals were kept awake by placing them in slowly rotating wheels. The sleep restriction schedule lasted for one week. To determine the effects of sleep loss on serotonergic 1A receptor sensitivity, the rats received an IP injection with the 1A agonist 8-OH-DPAT. To determine the cholinergic muscarinic receptor sensitivity, rats were injected with the muscarinic agonist oxotremorine. The sensitivity to the drugs was determined by measuring the acute hypothermic response by means of radio telemetry.
Results: Both drugs induced an acute and short-lasting drop in body temperature. Sleep restriction significantly reduced the hypothermic response to the serotonergic 1A receptor agonist 8OH-DPAT but did not affect the response to the muscarinic agonist oxotremorine.
Conclusions: The present study shows that sleep restriction causes a desensitization of the serotonin 1A receptor system but does not affect the sensitivity of the cholinergic muscarinic receptor system. Given the wealth of data indicating a role of the serotonin 1A receptor system in the regulation of behavior, emotionality and mood, it seems likely that sleep restriction along this way may affect the functional output of the brain. Further studies are needed to establish the importance of these changes for the development of depression-like behavior.

0490.I

Personality as a Predictor of Objective and Subjective Impact of Sleep Deprivation

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Introduction: In normal populations, sleep deprivation (SD) produces declines in mood, behavioral and cognitive performance, and increased subjective sleepiness. Individual variation in response to sleep deprivation is well known. The construct of personality as a possible predictor of the impact of sleep deprivation has been examined and has shown high neuroticism to be associated with a decline in logical reasoning (cognitive measure) and an increase in total mood disturbance (TMDs). No single investigation to date has examined the extent that personality variables can predict changes in behavioral performance, subjective sleepiness, mood disturbance, and cognitive deficits.
Methods: 28 healthy college students (14 males, 14 females, mean age 20.5) were deprived of one night of sleep (awake from normal wake time through 1730 hr. the following evening). Subjective sleepiness was

assessed every hour using the Stanford Sleepiness Scale (SSS). Every other hour, TMDs was assessed using the Profile of Mood States and behavioral performance using a 10-minute auditory oddball reaction time task (RTT). At 1700 hr. on the pre and post deprivation day, subjects completed a 30-minute multi-task cognitive performance battery (including a memory task, visual and auditory monitoring, and self-paced arithmetic task: SynWin). Effects of SD were examined using change scores (postdeprivation minus baseline). All subjects were administered a personality measure (NEO-PI-R) and ESS the first evening. For some analyses, subjects were tri- or dichotomized within the five NEO-PI personality domains (Neuroticism, Extraversion, Openness, Agreeableness, and Conscientiousness).

Results: Overall, a significant increase in TMDs followed SD (15.04 pre vs. 23.32 postdeprivation, $t(24)=1.88$, $p<.05$). Analyses conducted on categorized subjects revealed significant increases in TMDs following SD only for intermediate scorers on Agreeableness (11.00 pre vs. 27.11 postdeprivation, $t(8)=2.36$, $p<.05$) and Neuroticism (-.78 pre vs. 12.44 postdeprivation, $t(8)=2.00$, $p<.05$) not for high or low scorers. Low scorers on Neuroticism, Conscientiousness, and Agreeableness showed significant improvement on the pre vs. postdeprivation SynWin administration, whereas learning for high scorers on these domains was significantly impaired. For the behavioral RTT, high scorers on Neuroticism and low scorers on Extroversion, Agreeableness, and Conscientiousness showed significantly impaired performance following SD. Neuroticism was positively correlated with ESS ($r(26)=.332$, $p<.05$) and SSS change scores ($r(26)=.421$, $p<.05$).

Conclusions: Personality factors were significantly related to changes in mood, cognitive and behavioral performance, and subjective sleepiness following SD. Differences were found through categorization of personality domains. In some cases (i.e. TMDs), scoring especially high or low within a personality domain (A or N) may have helped to buffer against the effects of SD. Individuals with these polarized domain scores may have exhibited behavioral/affective rigidity whereas moderate scorers may have been more influenced by situational variables, such as SD. Other maladaptively polarized domain scores (N, i.e. for SynWin, RTT and SSS) may have reflected a limited behavioral repertoire or decreased ability to cope in stressful situations that intensified the detrimental effects of SD.

0491.I

Epworth Sleepiness Scale and Sleepiness Complaints in a Group of 13,869 Workers of One Transportation Company

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Introduction: Sleepiness is a severe problem at work especially in transportation companies. However the impact of working conditions on the feeling of sleepiness in workers has not been yet evaluated in big groups. The goal was to describe sleepiness in a large group of workers of a same transportation company.

Methods: We sent a questionnaire based on the Epworth Sleepiness Scale and exploring several aspects of sleepiness to the 41 229 employees of a big city transportation in the Paris area, France. We got 13869 complete questionnaires and we made statistical analyses between subgroups using the SAS epidemiological software.We also secondly interviewed a group of 145 non respondents to the questionnaire to compare the results to those of the first group.

Results: 78.3% of the respondents were males and the average age was 39.9 years old. The respondent group included 4205 bus drivers, 1088 train drivers and 1690 metro drivers. 5% of the total group complained of sleepiness each day and 22.6% each week. 63.1% said they sometimes had nap. 16.7% had nap more than 5 a week. Shift workers and irregular scheduled workers had more naps than regular. 20% took more than 5 cups of coffee a day. 24.7% had an Epworth Sleepiness Scale (ESS) score between 9 and 12, 13.7% between 12 and 18 and 0.13% more than 18. 9.3% of all train drivers had an ESS scale >12 and 15% of bus drivers.45.5% were snoring and 11.9% witnessed that their bedpartner had sometimes observe apnea.

Conclusions: Sleepiness appear to be very prevalent in this working group. More analyses have to be made to separate the effect of working conditions and the consequences of pathologies such as sleep apnea. Education and information programs would be implemented in this company.

0492.I

The Effect of 24-hour Sleep Deprivation on Reaction to Emotion-provoking Pictures

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Introduction: It has long been recognized that sleep deprivation may lead to mood changes. However, the effect of sleep deprivation on the process of emotional stimulus has not been well studied. The reaction to emotional stimulus comprises of at least two dimensions: valence and arousal. These two dimensions were reported to be associated with different physiological responses, and were suggested to relate to different neural circuits. This study aimed to investigate the effect of sleep deprivation on these two dimensions of emotional process.

Methods: Twenty-four subjects (12 males; 12 females), aged 19 to 23, participated in the study. Their reaction to emotion-provoking pictures was assessed on three consecutive mornings: baseline session, after 24 hours of sleep deprivation, and after recovery sleep. One hundred and twenty pictures were selected from the International Affective Picture System and were assigned to 4 categories: neutral-low arousal (NL), neutral-high arousal (NH), pleasant-high arousal (PH), and unpleasant-high arousal (UH). Before the beginning of the baseline session, another set of 16 pictures was presented for adaptation purpose. During each session, subjects were presented with 10 pictures from each category. Each picture was presented for 5 seconds, with an ISI of 5 seconds. Subjects' reactions to the pictures were assessed with 9-point scales along valence (unpleasant to pleasant) and arousal (low to high) dimensions.

Results: On valence ratings, ANOVA showed a significant category main effect ($p<.001$) and a session x picture interaction ($p<.05$). The subjects rated pleasant pictures most positive (6.16¡Ó0.21), followed by neutral pictures (NL=5.34¡Ó0.08; NH=4.82¡Ó0.13), and followed by unpleasant pictures (2.62¡Ó0.20). Post-hoc comparisons showed that subjects¡¦ ratings on unpleasant pictures became less negative after sleep deprivation (from 2.37¡Ó0.98 to 2.78¡Ó1.02) and remained no change following recovery night (2.71¡Ó1.15). The rest of the categories did not showed significant changes over the days. On arousal ratings, ANOVA showed both significant session ($p<.05$) and picture ($p<.001$) main effects. Overall, subjects rated UH pictures most arousing (5.72¡Ó0.39), followed by NH pictures (3.87¡Ó0.30) and PH pictures (3.78¡Ó0.28), and followed by NL pictures (2.39¡Ó0.22). The arousal ratings declined after sleep deprivation (from 4.22¡Ó0.24 to 3.81¡Ó0.26) and remained lower after recovery night (3.79¡Ó0.30).

Conclusions: The results indicated that subjects perceived unpleasant pictures less negatively after 24 hours of sleep deprivation. However, sleep deprivation showed no effects on valence ratings of positive and neutral pictures. Previous studies with EEG and fMRI showed that brain reactivity was lateralized towards the left hemisphere for positive stimuli and towards the right hemisphere for negative stimuli. Sleep deprivation may also has an asymmetrical effect on brain activation. In addition, the subjects perceived the pictures less arousing after sleep deprivation for all types of pictures, reflecting a general effect of sleep deprivation on the arousal dimension. However, the effects were maintained following a night of recovery sleep, indicating that these effects may be

partially due to adaptation to the stimuli.

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0493.I

Chronic Sleep Loss and Circadian Phase Misalignment Impairs Learning

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Introduction: One night of total sleep deprivation has been recently reported to impair verbal learning in humans. The current study examined whether cognitive learning is impaired by chronic sleep loss associated with circadian phase misalignment.
Methods: Healthy, drug free females and males (N=17) aged 20-41 participated. After three weeks of maintaining a consistent sleep-wake schedule at home, six laboratory baseline days and nights, a 40-hr constant routine to estimate circadian melatonin phase and an 8-hr recovery sleep episode, participants were scheduled to a 25-day work-rest wakefulness-sleep schedule that resulted in sleep and circadian disruption for eight of the seventeen subjects. A second constant routine was conducted to assess circadian phase on day 33. Sleep was recorded and scored from central EEG leads. Performance on a mathematical addition test was measured seven times per day, every two hours from two though 14 hr of scheduled wakefulness. Changes in melatonin phase, sleep staging and average daily performance was examined with repeated measure Anova.
Results: The phase angle relationship between the dim light melatonin onset (DLMO25%) and scheduled sleep was maintained in 9 participants whereas phase angle was abnormally advanced in the remaining 8 participants (i.e., circadian misalignment; Condition x Day of Study interaction; $p < 0.05$). Wakefulness after sleep onset was higher (Condition x Day of Study interaction, $p < 0.01$) and performance on the mathematical addition test was lower (Condition x Day of Study interaction, $p < 0.0001$) in participants who exhibited circadian phase misalignment. Participants who exhibited normal sleep and normal circadian phase showed improved performance across the study (i.e., learning) whereas participants who exhibited disturbed sleep and circadian phase misalignment showed attenuated learning.
Conclusions: Chronic sleep loss and/or circadian phase misalignment was associated with impaired cognitive learning. This finding is consistent with previously reported findings that acute total sleep deprivation impaired verbal learning. The current results suggest that sleep and wakefulness need to occur at the correct internal biological time for improved performance.

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0494.I

Differential Expression of the Heat Shock Chaperone Protein BiP in Drosophila Following Sleep Deprivation

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Introduction: From previous studies it is known that sleep deprivation (SD) influences the overall level of transcription and translation of many genes in the brain. The expression of the heat shock/stress response gene, immunoglobulin binding protein (BiP)/glucose regulated protein 78 (GRP78) has been shown, both in mice and Drosophila, to be increased in the brain following SD. It has further been shown in Drosophila that the expression of heat shock or stress response genes protects against the lethal effects of sleep deprivation (SD) in the Cyco clock mutant. The Cyco mutant succumbs to death following 10 hours of SD. Induction of heat shock genes in the Cyco flies, reduced mortality following SD compared to untreated flies. As the upregulation of BiP occurs during SD we hypothesize that a differential expression of the protein also occurs during SD as part of a general stress response. We have used the clock mutant Cyco, which displays an acute response to sleep deprivation, and a wild type Canton-S (CS) strain as tools to examine BiP expression. BiP expression was examined following SD for 6 hours in both strains.
Methods: The wild-type strain, CS was used as the control. CS and Cyco flies were maintained at 25oC and 40% humidity in a 12:12 light:dark cycle. Flies were sleep deprived between ZT 18 - ZT 24, using random stimuli mechanically applied throughout the observation period. The control group received no stimulation throughout the entire rest/observation period. Flies were sacrificed at the end of the deprivation or rest period. A third group was allowed to recover for 2 hours following SD before sacrifice. Protein expression was assayed by SDS-PAGE and Western analysis of fly-head homogenates.
Results: BiP expression in Cyco is approximately 60 to 70% that of wild type flies at ZT 8 and ZT 14. Both Cyco and CS flies exhibit an increase in BiP expression following SD. Recovery rest in both genotypes results in the reduced expression of BiP.
Conclusions: Sleep deprivation elicits a stress response in Drosophila resulting in the increased expression of the heat shock protein BiP. Rest recovery restores BiP expression to normal levels. Cyco flies appear to be able to mount the same response as control flies, but the reduced level of BiP expression does not appear sufficient to offset the stress induced by sleep deprivation. The data suggest that the acute response of Cyco flies to SD may in part be due to reduced expression of heat shock proteins.

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0495.I

Sleep Deprivation Reduces Proliferation of New Cells in the Dentate Gyrus of the Dorsal Hippocampus

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Introduction: The dentate gyrus (DG) of the adult hippocampus gives rise to progenitor cells, which have potential to differentiate into neurons. Neurogenesis, the process whereby cells proliferate, migrate and differentiate into neurons, has been shown to occur in different species including humans. Several factors are known to affect the proliferation of these new cells, i.e. hippocampal-dependent learning tasks, antidepressant drugs, exercise and stress. Many of those factors are known to have effects on the sleep-wake cycle. We reported previously that SD reduced proliferation of new cells in the DG. We now report additional control procedure that suggests that effects of SD do not result from stress or exercise.
Methods: Male rats were implanted for polysomnographic recording, and divided into treadmill sleep deprived (SD), treadmill control (TC) and cage control (CC) groups. SD and TC rats were kept for 96 h on a treadmill that moved either for 3 sec on/12 sec off (SD group), or 15 min on/60 min off (TC group) to equate total movement but permit sustained rest periods in TC animals. To label proliferating cells the thymidine analog 5-bromo-2'-deoxyuridine (BrdU) was injected after the first 48 h

of the experimental procedure in all groups (50 mg kg-1, i.p.). In another group of rats (divided in the above mentioned groups) blood samples were collected for analysis of corticosterone.
Results: The percentage of time awake per day was 93.2% in the SD group vs 59.6% in the TC group and 49.9% in the CC group ($P < 0.001$). Stereological analysis showed that the number of BrdU-positive cells in the DG of the dorsal hippocampus was reduced by 54% in the SD group in comparison with the TC and by 68% in comparison with CC group. No significant differences were observed in serum corticosterone levels between SD, TC and CC groups ($P = 0.227$, One Way ANOVA).
Conclusions: These results suggest that SD reduces proliferation of cells in the DG of the dorsal hippocampus; and that this effect is not due to nonspecific stress, or to the forced locomotion used to produce SD.

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0496.I

Gender and Sleep Deprivation Effects on the Relationship Between Subjective Task Demands and Performance

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Introduction: Past research has investigated sleep loss-related impairment of self-monitoring of performance, but gender differences are rarely addressed. We report gender differences in the relationship between subjective task demands and task performance in well-rested and sleep deprived subjects.
Methods: 22 healthy adults (11M, age=29 $\pm$5 years; 11F, age=33 $\pm$12 years) performed an arithmetic working memory task (serial subtraction) twice: after a normal night of sleep and following 36 hours total sleep deprivation (TSD). Immediately following the task, subjects verbally rated task demands on the following 10-point Lickert scales: task difficulty, effort required, motivation, concentration levels, and effort invested in the task. Results presented focus on whether subjective assessment of task demands is related to task accuracy and response speed, if this relationship changes with TSD, and whether gender mediates these relationships. All tests were protected at an alpha = 0.05.
Results: The only main effect of gender or TSD on arithmetic performance or subjective assessment of task demands was males showed greater accuracy than females (normal vs. TSD. males: 91.5 $\pm$7.0% vs. 92.5 $\pm$5.8%; females: 80.5 $\pm$8.5% vs. 79.3 $\pm$11.0%).The relationship between subjective task demands and performance differed both between genders and across nights. After normal sleep, males levels of motivation to perform the task well positively predicted both response speed (r=0.70) and accuracy (r=0.71). Additionally, effort invested in the task correlated positively with response speed (r=0.64), and concentration levels correlated positively with accuracy (r=0.75). However, after TSD, only motivation levels predicted performance (again, both response speed, r=0.64, and accuracy, r=0.61). For females, after normal sleep, increased subjective task difficulty (r=-0.65), effort required by (r=-0.56), and effort invested in (r=-0.61) the task all correlated with slower response speeds. Difficulty (r=-0.57) and effort invested (r=-0.56) correlated negatively with accuracy. However, after TSD there were no significant correlations between performance and subjective responses.
Conclusions: Subjective task demands are correlated with task performance for both males and females. However, different aspects of task demands correlate with performance for males and females and TSD affects the relationship between task demands and performance differently for each gender. When both well-rested and during TSD, males subjective levels of motivation to perform the task predicted performance accuracy and response speed. For females, on the other hand, subjective task difficulty and effort-related demands predicted performance, but only when well-rested. No subjective task demands predicted performance during TSD for females. These differences occurred despite the fact the mean subjective assessment scores were not different between genders or across nights. These preliminary findings are consistent with the reported notion that sleep deprivation inhibits the accuracy of self-assessment of performance and suggests the effect is different for males and females. An increased sample size and the inclusion of a question related to perceived performance would enhance our ability to understand these apparently gender-mediated relationships.

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0497.I

Changes of IL-1beta Levels Induced by Total Sleep Deprivation in Different Brain Regions

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Introduction: Interleukin-1 (IL-1) is one of the best characterized sleep regulatory substances. Exogenous IL-1 enhances non-rapid eye move ment sleep in different species. Inhibition of endogenous IL-1 inhibits spontaneous sleep and sleep responses to sleep promoting stimuli. Further, IL-1beta mRNA levels in the brain vary with sleep waking cycles and increases after total sleep deprivation (TSD) or other sleep-promoting stimuli. However,it is not clear whether IL-1beta responds to TSD similarly at protein levels. In the present study, we determined the effects of TSD on IL-1beta protein levels in different brain regions.
Methods: Adult male Sprague-Dawley rats were used in the experiment. Animals were maintained on 12:12h light-dark cycles. TSD was started at light onset. Sleep-deprived rats were sacrificed after 3h, 6h TSD or 6h TSD plus 2h recovery sleep, and control rats sacrificed at the same time points (10 rats in each group at each time point). IL-1beta levels in different brain regions were determined by enzyme-linked immunosorbent assay.
Results: TDS induced differential alterations of IL-1beta in different brain regions. 1. Cortex. Compared to the control animals, IL-1beta levels were slightly decreased after 3h TSD (21.816 ± 1.372 vs. 25.853 ± 1.020 pg/mg protein, $t(18)=2.3618$; $p<0.03$), but not after 6h TSD or after recovery sleep following TSD. 2. Hippocampus. IL-1beta levels were significantly decreased after 3h TSD (19.233 ± 1.155 vs. 25.537 ± 0.973, $t(18)=4.1756$; $p<0.0006$), but significantly increased after 6h TSD (13.707 ± 1.155 vs. 18.307 ± 0.949, $t(18)=-2.3357$; $p<0.04$). After recovery sleep, IL-1beta levels were still slightly above, but not significantly different from, the control levels. 3. Hypothalamus. IL-1beta levels were not altered after 3h TSD, but significantly reduced after 6h TSD compared to the controls. After recovery sleep following TSD, IL-1beta levels were significantly increased in TSD rats compared to the controls. 4. Brainstem. IL-1beta levels were not significantly altered by TSD.
Conclusions: The IL-1beta levels reflect a dynamic balance between production and release/clearance. Since IL-1beta mRNA is increased by TSD, the reduction of IL-1beta protein levels may reflect increased release and clearance during sleep deprivation. The delayed increase of IL-1beta levels in the hippocampus and hypothalamus may reflect increased rate of production. The hypothalamus and hippocampus express high levels of IL-1 receptors compared to other brain regions. The alterations of IL-1beta levels in the hypothalamus is consistent with its role in sleep regulation and may contribute to sleep rebound. Since IL-1beta selectively impairs hippocampus-dependent memory, the alterations of IL-1beta in the hippocampus may also be involved in the deficits of learning and memory related to sleep loss.

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0498.I

Sleep Behaviors And Attitudes Among Internal Medicine Housestaff

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Introduction: Long work hours are a time-honored tradition in most residency programs. Recently, such demanding schedules have been called into question and suggested as a contributing factor to medical errors. However, the medical community continues to debate the evidence regarding the impact of sleep deprivation and fatigue on resident trainees. Furthermore, the relationship of imposed schedules to actual sleep quantity is unknown. This study examined 1) the state of and attitudes about sleepiness and 2) how rotation and call cycle are related to acute and chronic sleep deprivation.

Methods: A survey was administered in June 2001 to 53 incoming interns and 79 current housestaff at a university-based internal medicine residency program. The instrument contained items about respondent demographics, current rotation, call cycle frequency, and call status. Sleep deprivation was assessed with items asking for hours of sleep the prior night (acute sleep deprivation) and prior seven days (chronic sleep deprivation). Subjective sleepiness was measured using the Stanford and Karolinska Sleepiness Scales. Other questions related to attitudes about and perceptions of the effects of sleepiness on work and non-work performance.

Results: Chronic sleep deprivation (defined as less than 42 hours of sleep in the previous week) was a significant problem for current housestaff compared to incoming interns (65% vs. 6%; $p < 0.0001$). More than 40% of the current housestaff admitted to the possibility of dozing while performing various work-related tasks such as writing notes in charts (69%), reviewing medication lists (61%), interpreting labs (51%), and taking a medical history (39%). Current housestaff were more likely than incoming interns to feel they had learned to tolerate sleep deprivation (70% vs. 42%, $p = .0013$). Regardless of the degree of sleep restriction, both groups felt their patients received good care (54% vs. 54%, $p = .89$) and that they were able to react effectively in critical situations (46% vs. 66%, $p = .06$). Furthermore, half of all respondents felt that sleep deprivation was a necessary part of residency training ($p = .36$). Chronic sleep deprivation was more likely to be reported by residents rotating in the ICUs (83%) and on wards (74%) than on other rotations (36%, $p = 0.01$). Housestaff currently on call every 3rd night had a higher prevalence of chronic sleep deprivation compared to those on a less frequent call schedule (89% vs. 58%, $p = 0.04$). Despite these significant differences in self-reported chronic sleep deprivation, Stanford and Karolinska sleepiness scores did not differ based on rotation or call cycle frequency.

Conclusions: Chronic sleep deprivation is an important contributor to resident fatigue. Investigation of factors contributing to chronic sleep deprivation in this population, including moonlighting and family responsibilities, is warranted. The widespread beliefs of physicians-in-training that sleep deprivation is an expected part of residency and that their patients get good care suggest the need for a large scale educational effort by both the sleep and medical education communities.

0499.I

Sleep Loss and Fatigue in Graduate Medical Education: A Model

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Introduction: Sleep loss and fatigue (SL/F) are commonplace for interns and residents and affect patient care and resident performance (as reviewed in Veasey S. JAMA. 2002; 288:1116-24). The purpose of this study was to develop a psychosocial model on the effects of SL/F in graduate education using residents' perceptions and language that can inform future research in this area.

Methods: This qualitative study is based on 22 focus groups with an average of 7 residents (range=3-14) per group involving a total of 149 residents. Eight groups were interns and 14 groups were primarily senior residents. Groups included residents from programs affiliated with 5 US Medical Schools. Focus group discussions lasted about an hour. Using standard focus group methodology, discussions were audio taped, transcribed, coded, and analyzed using NVivo Software. Specialties were: Family Medicine, Internal Medicine, Emergency Medicine, Surgery, Obstetrics and Gynecology, and Pediatrics.

Results: Coding revealed three dominant themes in which SL/F affected resident physicians: patient care tasks and professionalism, learning and cognition, and personal life. Dominant themes are defined as those that emerged in > 75% of the focus groups. Adversely affected by SL/F are: Patient care tasks: increased likelihood of making errors or mistakes (n=18); Professionalism: interactions with and attitudes towards patients (n=21), objectification of patients (n=18), and impatience with staff (n=17); Learning and Cognition: ability to think and learn (n=22), impairment of cognitive abilities and complex thinking skills (n=20); Personal life: Physical and psychological health (n=21), constricted life space (n=19), driving impairment (n=19), Relationships: with spouse or significant other (n=17).

Conclusions: Residents' perceptions of SL/F are predominantly negative across many training programs. In particular, the fact that SL/F adversely affects professionalism receives inadequate emphasis in the current literature. Resident physician well being, in its broadest sense, needs to be considered in educational interventions and policy research.

0500.I

Daytime Melatonin-Zolpidem Cocktail: I. Effects on Daytime Sleep

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Introduction: When administered prior to a daytime nap, the benzodiazepine (BZ) receptor agonist zolpidem dose-dependently decreases sleep latency and increases total sleep time (TST). However, zolpidem also dose-dependently impairs cognitive performance at estimated peak plasma concentrations. Exogenously administered synthetic versions of the pineal hormone melatonin decrease sleep latency, but it is unclear whether melatonin also substantially improves TST. The present study was designed to determine whether combining a low dose of zolpidem with melatonin would improve daytime sleep without impairing learning/memory. Daytime sleep results are reported here. Effects on cognitive performance and salivary melatonin levels are reported in companion abstracts (Killgore et al., Wesensten et al., this issue).

Methods: Following undisturbed nocturnal sleep (2300-0700), 80 healthy men and women underwent cognitive performance testing at 0900 hours. At 1000 hours, they ingested double-blind zolpidem (ZOL) 0, 5, 10, or 20 mg (n=20 per group), then slept under non-conducive conditions (seated upright in a noisy, bright room). At 1030 hours, subjects were awakened (if asleep) to ingest synthetic melatonin (MEL) 0 or 5 mg (n=10 per group – half of the 20 subjects from each zolpidem dose) then continued napping until 1130 hours. Following post-drug cognitive performance testing (1130 to 1230 hours), subjects again napped under non-conducive conditions from 1245 to 1600 hours. They were awakened and tested a final time. Polysomnography was recorded continuously and scored off-line using conventional procedures. Results are for the second nap.

Results: Latency to stage 2. Relative to placebo (latency = 56.9 min) ZOL 10 and 20 mg (latencies = 26.2 and 23.3 min, respectively) and all ZOL-MEL cocktails (latencies = 20.9, 18.5, and 15.2 min for ZOL 5, 10, and 20 mg plus MEL) decreased sleep latency ($p=0.001$). MEL alone (latency = 29.1 min) marginally decreased sleep latency ($p = 0.06$). Total

sleep time (TST). ZOL 20 mg + MEL 5 mg increased TST (137.3 min) relative to placebo (82.2 min, $p < .05$) and ZOL 5 mg alone (82.6 min, $p = 0.06$). MEL alone also marginally increased TST (128.9 min; $p = 0.09$) relative to placebo. Due to equipment failure 8 subjects' data were lost. Final N = 72.

Conclusions: Melatonin augmented the sleep-inducing properties of low-dose zolpidem via decreased sleep latency. Melatonin alone also appeared to improve daytime sleep by increasing TST. Since performance for the low-dose zolpidem/melatonin and melatonin alone groups was unaffected (Wesensten et al., this volume), the results suggest that combining melatonin with low-dose zolpidem to induce daytime sleep is preferable to using higher doses of zolpidem alone.

0501.I

Variation in Sensitivity to Sleep Restriction as a Function of Age Revealed by Growth Modeling Analysis

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Introduction: Recent advances in statistical methodology have yielded exciting new ways to analyze longitudinal data. We applied linear growth curve modeling to longitudinal sleep restriction data.

Methods: We conducted a 14-day residential sleep dose-response study involving 66 subjects, with 3 days of training and baseline (8 hours time in bed each night), followed by 7 days of sleep restriction or augmentation (3, 5, 7 or 9 hours time in bed each night), followed by 3 days of recovery (8 hours time in bed each night). Performance was measured at frequent intervals while the subjects were awake using the psychomotor vigilance task (PVT).

Results: ANOVA revealed clear sleep-dose group dependent effects on psychomotor vigilance task (PVT) performance. Linear growth curve modeling of these data revealed that the relationship between sleep restriction and performance on the PVT was variable across individuals. Performance for some individuals was degraded by sleep restriction whereas performance for other individuals was unaffected. The growth modeling analysis revealed that in comparison to younger individuals, older individuals did not perform as well in the baseline condition but were more likely to maintain baseline performance during sleep restriction.

Conclusions: Linear growth curve modeling revealed that age accounts for a significant portion of the variance in performance between individuals during sleep restriction. This relationship was not apparent using conventional (ANOVA or ANCOVA) statistical techniques. Linear growth curve modeling may be a valuable tool for exploring relationships in complex, longitudinal data sets such as the sleep dose-response data reported here.

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0502.I

Visual Task Performance As A Measure of Drowsiness

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Introduction: A visual task, the Lateral Visual Field Test (LVFT), was administered to allow the assessment of alertness levels by evaluating changes in the EEG during transitions between wake and sleep. Previously used as a secondary task, the results of which were presented at the Army Science Conference, (Russo, 2002), the LVFT in this experiment was used to facilitate induction of drowsiness. Measures of reaction time, lapses, and incorrect responses, as indicators of sleepiness, are presented here.

Methods: Eleven healthy subjects (6 m, 5 f; mean age = 30) participated in the study. On Day 1, following a briefing and electrode application, subjects were trained on a series of tests, including the LVFT, which continued until midnight. After 8 hours in bed, subjects continued the same sequence of tests until midnight of Day 3, concluding 40 hours of sleep deprivation. They were then allowed 10 hours in bed. On Day 4, subjects began testing immediately again until 1800 at which time the electrodes were removed and the subjects were debriefed and released.

The LVFT consists of a tubular arc in which 11 lamps (LEDs) are embedded at 15-degree intervals from 75 degrees left to 75 degrees right. It is positioned at eye level for the subject with the center lamp as focus and fixation point. During this test, 150 sequential single or double light stimuli are presented at random intervals, each for a duration of 0.25 seconds. Subjects responded to the stimuli by pressing a button that corresponded to the left-light-only presentation, left + center light, center, right + center, or right only. Three seconds were allowed for each response before the trial was terminated.

Results: In this preliminary analysis, daily means of comparable time points were computed for reaction time, number of lapses, and number of incorrect responses. Pairwise comparisons between Baseline Day (Day 2) and Day 3 revealed significant differences for reaction time (M = 1291.656, SD = 330.058; M = 1807.764, SD = 394.350, respectively) and lapses (M = 10.636, SD = 18.209, M = 45.891, SD = 24.641), all ps <.05, with Dunnett's corrections. Differences between Baseline and Recovery (Day 4) were not significant for any measure.

Conclusions: These results suggest that reaction time and lapses during performance of the LVFT are negatively affected by sleep deprivation and therefore are suitable indicators of sleepiness. Because EEG acquisition is time-synchronized with the performance of this task, all stimuli presentations and responses can be correlated with EEG. This will allow for the determination of waveform patterns as the subjects transition from wake to drowsiness to sleep. Further analyses will be performed to determine subject variability and specific aspects of peripheral visual neglect.

0503.I

Daytime Melatonin-Zolpidem Cocktail: II. Effects on Memory and Vigilance

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Introduction: At estimated peak plasma concentrations, the benzodiazepine (BZ) receptor agonist zolpidem dose-dependently improves daytime sleep but impairs cognitive performance. Because melatonin decreases sleep latency, we investigated whether combining melatonin with low-dose zolpidem would improve daytime sleep without impairing cognitive performance. Effects on daytime sleep and salivary melatonin levels are reported in companion abstracts (Killgore et al., Reichardt et al., this issue).

Methods: Following undisturbed nocturnal sleep (2300-0700), 80 healthy men and women performed Restricted Reminding (RRT), Paired-Associates (PA), and Psychomotor Vigilance (PVT) Testing at 0900 hours. At 1000 hours, they ingested double-blind zolpidem 0, 5, 10, or 20 mg (n=20 per group), then slept under nonconducive conditions (seated upright in a noisy, bright room). At 1030 hours, subjects were awakened (if asleep) to ingest synthetic melatonin 0 or 5 mg (n=10 per group – half of the 20 subjects from each zolpidem dose) then continued napping until 1130 hours. Following post-drug cognitive performance testing (1130 to 1230 hours), subjects again napped under nonconducive conditions from 1245 to 1600 hours. They were awakened and tested a final time. RRT. Subjects heard 20 words from the same semantic category, then attempted to recall the entire list. On subsequent trials, subjects were "reminded" only of words they missed on the preceding trial, then attempted to recall all 20 words. This continued until

subjects recalled the entire list on two consecutive trials or 8 trials had been administered. A different list was presented at 0900, 1130, and 1600. P-A. Subjects heard 10 pairs of words. They then heard the first word of a pair and supplied its associate. Subjects received the first P-A list for immediate recall prior to drug administration. After the first nap, they performed one trial of delayed recall for the first list. Next, they received a second list for immediate recall. After the second nap, they performed one trial of delayed recall for each of the first and second lists. PVT. Subjects responded as quickly as possible via keypress to an incrementing timer. Task duration was 10 min.
Results: At estimated peak effect, zolpidem dose-dependently impaired performance (RRT number of missed items Drug x Session, p = 0.0000; P-A number correct, immediate recall Drug x Session, p = 0.0002; delayed recall Drug, p = 0.0000; PVT mean speed Drug x Session, p = 0.0000). Combining melatonin with zolpidem did not further impair performance; melatonin alone did not impair performance.
Conclusions: Despite its sleep-promoting properties (Reichardt et al., this volume), melatonin (unlike zolpidem) did not impair performance. These findings suggest that unlike BZ agonists, melatonin's sleep-promoting effects are not functionally coupled to performance impairment, thus combining melatonin with low-dose zolpidem may be preferable to a sleep-inducing dose of zolpidem alone for daytime naps. The locus of melatonin's sleep-promoting effects may reside in its effects on body temperature.

0504.I

Daytime Melatonin-Zolpidem Cocktail: III. Effects on Salivary Melatonin and Performance

Killgore W, Reichardt R, Kautz M, Belenky G, Balkin T, Wesensten N
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Introduction: The benzodiazepine (BZ) receptor agonist zolpidem dose-dependently improves daytime sleep but impairs cognitive performance at estimated peak plasma concentrations. Because melatonin decreases sleep latency, we investigated whether combining melatonin with low-dose zolpidem would improve daytime sleep without impairing cognitive performance. Effects on salivary melatonin (SM) levels and correlations with cognitive performance are reported here. Effects on daytime sleep and cognitive performance are reported in Reichardt et al. and Wesensten et al. (this issue).
Methods: Following undisturbed nocturnal sleep (2300-0700), 80 healthy men and women underwent cognitive testing, and saliva sampling at 0900 hours. At 1000 hours, they ingested double-blind zolpidem (ZOL) 0, 5, 10, or 20 mg (n=20 per group), then tried to sleep under nonconducive conditions (seated upright in a noisy, bright room). At 1030 hours, subjects were awakened (if asleep) to ingest melatonin (MEL) 0 or 5 mg (n=10 per group – half of the 20 subjects from each zolpidem dose). The nap continued until 1130 hours. Following post-drug cognitive testing (1130-1230 hours), TT and saliva were taken. Subjects were then asked to sleep under the same nonconducive conditions from 1245 to 1600 hours. They were then awakened and tested, followed by TT measurement and saliva collection.
Results: Salivary Melatonin. At 1130, MEL (with or without ZOL) increased SM ($p < .05$) compared to placebo and ZOL alone—MEL + ZOL 5mg yielded highest SM levels (120.6 pg/ml). At 1600, SM was still elevated in MEL alone and MEL + ZOL 20 (76.2 and 66.6 pg/ml, respectively) compared to ZOL alone and placebo (both less than 1.0 pg/ml; $p < .05$) and for MEL + ZOL5 (37.0 pg/ml) compared to placebo ($p < .05$). MEL+ZOL in any combination did not yield significantly different SM levels than MEL alone (ps > .05). Salivary Melatonin Performance Correlations: Regardless of level of ZOL, higher SM levels were associated with slower reaction times (RT) at 1600 hours (partial r=.41, p=.003). SM and performance on learning and memory tasks were unrelated (ps > .05) regardless of MEL or ZOL condition.
Conclusions: The combined effects of ZOL+MEL on SM were comparable to those of MEL alone. Furthermore, in subjects receiving MEL the relationship between SM and RT remained significant regardless of ZOL levels. The present results support our other findings that combining low-dose ZOL with MEL to promote daytime sleep induction may be preferable to administering high-dose ZOL alone.

0505.I

Sleep Rebound Response In Mice Devoid Of Prion Gene After Total Sleep Deprivation

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Introduction: Prion (PrP) diseases are neurodegenerative disorders of infectious, inherited, or sporadic origin in humans and animals. Fatal familial insomnia (FFI) is one of many genetic PrP diseases in humans. In FFI there is a significant reduction of sleep, loss of neurons and astrogliosis. It is still unclear whether these changes are consequence of loss of normal PrP protein function or the accumulation of abnormal prion protein. Because of the potential involvement of prion in sleep processes, we investigated the physiological role of PrP gene in sleep.
Methods: We characterized the sleep patterns in transgenic mice whose PrP gene was knocked out (KO) and not replaced, and C57BL/10 mice (wild type) as a control group. Animals were implanted with a set of electrodes for sleep recording. Two weeks after surgery they were habituated to the recording conditions and recorded for 24 h (baseline), followed by total sleep deprivation during 24 h and recorded for 24 h. The dark-light cycle was controlled (12:12). The electroencephalogram (EEG) was scored and wakefulness (W), slow-wave sleep (SWS) and rapid eye movement (REM) sleep were determined. For statistical analysis we used ANOVA and the post-hoc Sheffé test.
Results: PrPKO and wild type mice showed no significant differences in the frequency and total amount of W, SWS, or REM sleep during baseline. However, in contrast to wild type, PrPKO mice showed increase in W and decrease in SWS prior to the onset of dark cycle and a decrease in W and an increase in SWS prior to the onset of light cycle. Also, REM sleep showed changes in distribution during the second half of the dark period. These changes were characterized by a decrease and then by an important increase prior to the onset of the light period. After total sleep deprivation, mice devoid of prion gene showed a significant decrease in the amount of SWS during the following 15 h accompanied by a high fragmentation of the EEG architecture. Also, PrPKO mice showed a significant increase in W and reduction in REM sleep only after 12 h of sleep deprivation. Latency to SWS and REM sleep was not different in both lines.
Conclusions: These data suggest that the absence of PrP gene induces changes in the distribution of different sleep stages but their total amount remains the same. Total sleep deprivation has the greater effect in SWS in mice devoid of prion gene.

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0506.I

Morningness-Eveningness Differences in Sleepiness During 72 Hours of Sleep Deprivation

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Introduction: Individual differences exist in the timing of 24-hr diurnal activities. Such "chronotypes" on each end of this continuum are early-rising "morning types" (M-types) and late-rising "evening types" (E-types). Results from partial sleep deprivation and phase shift studies suggest that M-types are more sensitive to sleep disruption than E-types.

However, chronotype differences in sensitivity to total sleep deprivation are not well described. In the present study, we determined sleep deprivation sensitivity by evaluating sleepiness itself (objective and subjective) during extended wakefulness.
Methods: Fourteen healthy subjects (age 18-30 yrs, 12 male/2 female) participated in a laboratory-based sleep deprivation study. Subjects slept from 2300-0700 h, then remained awake for 72 hours during which time they completed alternating hourly test batteries. From the 8 E-types and 6 M-types who completed the study, in this paper we compared 4 M-types and 7 E-types) with complete data on both subjective and objective sleepiness measures. Subjective sleepiness was defined as a rating on the 6-point Stanford Sleepiness Scale (SSS). Objective sleepiness was latency to polysomnographically-defined stage 1 (ST1) and stage 2 (ST2) sleep during a modified Maintenance of Wakefulness Tests (MWT) in which subjects were asked to remain awake while lying in a darkened bedroom for 15 min. Dependent measures were analyzed with ANOVA for day (first, second third), time of day (12 sessions per day), and chronotype (M-type or E-type).
Results: A significant Day x Time interaction for both objective (ST1 and ST2 latency, $p<.001$) and subjective sleepiness (SSS, $p<.001$) confirmed previous findings that sleep deprivation exacerbates the early morning increase in sleepiness. A Chronotype x Day interaction for ST2 latency ($p<.05$) indicated that as sleep deprivation progressed, E-types appeared to be more resistant to sleepiness than M-types (Day 3 latencies: E-types = 7.02 min, M-types = 5.06 min). ST1 latency showed a similar trend ($p=.07$), while SSS did not ($p>.10$).
Conclusions: These results confirm previous suggestions that M-types are more vulnerable to sleep deprivation than are E-types, but indicate that vulnerability to sleep loss in M-types manifests only in objective sleepiness. That subjective sleepiness did not increase concurrent with objective sleepiness in M-types suggests that for M-types, subjective measures may not be appropriate substitutes for determining physiological sleepiness.

Research was conducted at WRAIR performed while the first author held a National Research Council Research Associateship Award at WRAIR.

0507.I

Response Of Unrestrained Rhesus Monkeys To 24-Hour Total Sleep Deprivation

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Introduction: Homeostatic sleep regulation in rhesus monkeys is poorly understood. Studies in squirrel monkeys showed that sleep duration and delta activity are only weakly influenced by prior wake duration (Klerman et al, 1999), suggesting that sleep regulation differs between humans and squirrel monkeys. Little information is available on sleep in rhesus monkeys, a widely used biomedical model, and no sleep study has been published for unrestrained rhesus monkeys.
Methods: The effects of 24-hours of sleep deprivation in 6 adult male rhesus monkeys were monitored at two circadian phases using implanted biotelemetry transmitters (Konigsberg Instruments Inc, Pasadena, CA), allowing us to record EEG, EOG, EMG and brain temperature long-term in freely-moving animals sleeping in their natural postures. Animals were individually housed in isolation chambers to eliminate social cues. In separate studies, animals were acclimated to two days of constant dim light (LL) then sleep-deprived at either the normal lights-off time (2200 PST) or lights-on time (0600 PST). Twenty-four hours of total sleep deprivation was achieved by gentle disturbance, consisting of tapping or shaking the cages and periodically giving small pieces of fruit. During this period the animals were awake on average 96.3% of the time as determined by polysomnographic criteria. Following sleep deprivation, animals were allowed to sleep *ad lib*. in LL for 4 days. An automatic scoring routine using neural network algorithms checked against visual scoring was used to categorize the behavioral states into 4 stages: wake/artifact, REM, SWS1-2, and SWS3-4. EEG delta activity (0.1-4Hz) was evaluated after discarding epochs of waking and artifacts.
Results: A strong rebound of SWS3-4 was seen on the first recovery day in both studies, but the rebound starting at the habitual lights-off time (2.3 fold of baseline) was significantly higher ($p=0.006$) than the rebound starting on habitual lights-on time (1.6 fold of baseline). Delta activity was 1.7 and 1.5 fold of baseline level respectively on the first recovery day, and increased delta activity, equivalent to that lost during sleep deprivation, was seen during the first three recovery days. The total increase in delta activity was 100±5% and 97±3% (Mean ± S.E.) of baseline level, suggesting homeostatic regulation of delta activity. The maxima of delta activity and SWS3-4 occurred during the fourth hour of recovery sleep in both studies, rather than at the beginning of recovery sleep, similar to findings in squirrel monkeys. REM sleep was suppressed only during the first few hours of recovery sleep and showed only a small rebound on the second (127±7% of baseline) and third (119±8% of baseline) recovery days.
Conclusions: These results show a strong homeostatic drive for sleep regulation in the rhesus monkey, and that rhesus monkeys respond to sleep deprivation much like humans, supporting the use of the rhesus monkey as a diurnal biomedical model for the study of human sleep disturbances.

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0508.I

COX Activity Is Different In Sleep And Sleep Deprivation In Mouse Cortex

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Introduction: Cytochrome c oxidase (COX) plays a crucial role in ATP synthesis. It consists of 13 subunits derived from both mitochondrial and nuclear genomes. Increased mRNA expression of COX catalytic subunit I after 3hrs of sleep deprivation suggests that transcriptional control of this enzyme can be temporally regulated. Overall regulation of COX activity is complex. The allosteric modifications, direct phosphorylation as well as the increase in turnover number have been well described. This study was carried out to fully understand how COX is regulated in relationship to sleep/wakefulness and sleep deprivation not only at the mRNA level, but also at the level of protein expression and enzyme activity.
Methods: All experiments were performed on dissected mouse cortex. Rest/activity recordings in C57/B6 mice were assessed by electronic beam break during the first 3hrs after lights on/off. Sleep deprivation (SD) was carried out by gentle handling. The following groups were generated: 3hrs Sleep (3S), 3hrs Wakefulness (3W), 0, 3, 6, 9, and 12 hrs Sleep Deprivation (0SD, 3SD, 6SD, 9SD and 12SD, respectively). Gene expression patterns for energy-related genes were profiled as part of a cDNA microarray analysis. COX activity was measured spectrophotometrically at 550nm by detecting decrease of absorbance of reduced cytochrome c within 1min. Protein expression of COX subunit I was determined by Western analysis.
Results: (1) mRNA expression of COX subunit I, cytochrome c, ATP synthase subunit beta was increased after 3hrs of sleep deprivation and returned to the baseline with longer durations of sleep deprivation. (2) Preliminary Western analysis indicates that COX subunit I expression shows the same temporal pattern. (3) There is no decline in COX activity up to 12hrs of sleep deprivation. However, COX activity is increased in both wakefulness and sleep deprivation when compared to sleep.
Conclusions: At the transcriptional and protein levels there is an increase in COX subunit I reflecting changes in regulation of ATP

machinery in early sleep deprivation. However, with longer durations of sleep deprivation these changes are not seen. The actual COX activity follows the same pattern for early sleep deprivation, but the decline at longer durations is not observed. Further studies of all components of ATP machinery at longer duration of sleep deprivation are needed.

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0509.I

Reduced Frequency of Sleep Spindles After Sleep Loss

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Introduction: Sleep spindles are a prominent feature of non-rapid eye movement (nonREM) sleep. Most evident in sleep stage 2, they are present in all nonREM sleep stages. Together with slow-waves, spindles are hallmarks of nonREM sleep homeostasis and their precise regulation is an indication of their fundamental role in the sleep process. Enhancing 'sleep pressure' by sleep deprivation has been shown to reduce power in the spindle range in nonREM sleep. Although it has been demonstrated that the extent of these changes is determined by the duration of prior wakefulness, the physiological significance and the underlying mechanisms are poorly understood. The effect of sleep deprivation on the spectral signature of spindles was investigated in the electroencephalogram (EEG) of eight healthy young men recorded at night during baseline sleep and during recovery sleep after 40 h of wakefulness.
Methods: The EEG was recorded form 27 scalp electrodes. As spindles are most prominent over central locations, the derivation Cz (average reference) was analyzed. For both nights, average power spectra were calculated for sleep stage 2, slow-wave sleep (SWS; stages 3 and 4) and nonREM sleep (stages 2 to 4). Spectral densities were analyzed across the maximum common length of the sleep episodes of both nights (first 7 h 32 min after sleep onset), and for each of the first four nonREM sleep cycles. The frequency corresponding to the spindle peak in the average power spectra was calculated in each subject and night by determining the bin with maximum power in the 11-16 Hz range.
Results: Comparison of the spectra averaged for all nonREM states, SWS, and stage 2 revealed, in each case, a significant reduction of the frequency of the spectral peak in the spindle range after sleep deprivation. A closer analysis across the first four nonREM sleep cycles of both nights showed that the frequency shift could be detected significantly in three of the four cycles. Simulation of the effects of a small (0.25 °C) brain temperature reduction from baseline to recovery remarkably reproduced the (spindle) peak shift observed in the spectra.
Conclusions: This data demonstrate, for the first time, a significant shift of the sleep spindle activity peak toward slower frequencies in the recovery night after prolonged wakefulness. Since power density in the range of spindles is known to be closely associated with sleep spindles, these data suggest that extended wakefulness may decrease the oscillation frequency of sleep spindles in the subsequent sleep episode. The frequency was reduced at the beginning of the night, when sleep pressure is high, yet the effect persisted across the first four sleep cycles. These finding may have important implications for understanding the functional significance of sleep spindles, of brain dynamics during sleep, and the susceptibility of these mechanisms to sleep deprivation.

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0510.I

Early Morning Awakening is Stressful

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Introduction: Many people suffer from inadequate amounts of sleep. Shift work frequently involves curtailed sleep as well as awakening at an altered circadian phase. We present preliminary data on the effects of chronic partial sleep restriction on morning awakening cortisol levels.
Methods: As part of an ongoing study 10 healthy volunteers (ages 21-40) stayed at the Clinical Research Center for 16 days. Following two baseline nights (8h sleep/night), subjects were randomized to one of two sleep conditions: 8h sleep condition (8HSC;N=5) or 4h sleep condition (4HSC;N=5). In the 4HSC, subjects were permitted to sleep between 2300 and 0300h, and remained awake in a reclined position (in<50 Lux) between 0300 and 0700h. Subjects performed a battery of computerized performance tests, which were administered every 2 hours beginning immediately after waking. Subjects also underwent two 25-hour days of physiological testing (baseline day and 10th day of sleep restriction) consisting of frequent blood draws, urine, and saliva samples. Cortisol levels were analyzed in serum with a radio-immuno-assay.
Results: The 24h diurnal rhythm of cortisol was seen in the baseline condition in all subjects, showing a 1am nadir, and an early morning peak after rising. After 12 days of sleep restriction, similar cortisol levels were seen during the day in both conditions. In the second half of the night, when subjects in the 4HSC awoke, cortisol levels were significantly higher than levels in the 8HSC ($p<0.01$) and continued to be significant for 50 minutes after waking. The diurnal period was divided into 2 phases split at 7am and 7pm. While daytime levels showed no significant difference in cortisol levels (4h:8.00 ± 1.49 vs. 8h:9.39 ± 1.16ug/dl), the nocturnal period in the 4HSC showed a strong trend towards elevated values (4h:7.26 ± 1.43 vs. 8h:5.63 ± 0.99ug/dl; $p=0.07$).After 11 nights of sleep restriction, during the immediate post-awakening performance testing, subjects answered the questions, "How adequate was the amount of sleep?" and "How refreshed do you feel now?" with significantly lower responses in the 4HSC. ($p<.05$). Subjects in the 4HSC answered that they felt that the adequacy of their sleep was ~20%, while subjects in the 8HSC averaged ~80%. When asked how refreshed they felt, subjects in the 4HSC responded that they felt ~22% refreshed, in comparison with ~63% for the 8HSC. In response to the question, "How sleepy do you feel now?", subjects in the 4HSC indicated that they felt ~60% sleepy while subjects in the 8HSC indicated they were only ~15% sleepy ($p<.05$).
Conclusions: Early morning awakening is associated with a large increase in cortisol levels compared to pre-waking levels, and causes the overall cortisol level to increase in the nocturnal phase. Early morning arousal as may frequently occur in rotating shift workers may be physiologically stressful and contribute to known increased vulnerability to cardiovascular disease and other illnesses.

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0511.I

Transcranial Magnetic Stimulation in Non-Sleep-Deprived and Sleep-Deprived Patients

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Introduction: Sleep deprivation affects cognitive performance. Functional MRI (fMRI) has identified cortical areas, most notably the dorsolateral prefontal cortex (DLPFC) and parietal lobes, which are affected by sleep-deprivation. These areas are also implicated in verbal working memory (VWM) tasks. Transcranial Magnetic Stimulation (TMS) has been shown to modulate cortical excitability in a complex fashion, depending on pulse intensity, pulse timing, and train duration. This study was designed with multiple aims: to characterize neural networks which are affected by total sleep deprivation using fMRI, to investigate the

impact of TMS on reaction time by stimulating specific cortical areas during VWM tasks, and, ultimately, to investigate the impact of TMS applied to these key cortical areas during VWM and divided-attention tasks following total sleep deprivation (> 48h). We are presently reporting the results to date of TMS in non-sleep-deprived subjects.

Methods: TMS was applied to normal healthy volunteers during performance of the Sternberg Task at the DLPFC and parietal lobes. Time-locked TMS trains were administered either during the retention (rehearsal) or probe (retrieval) phases of the task at frequencies of 1, 5, or 20 Hz, at 100% Motor Threshold (MT), with different memory loads (set sizes of 1 or 6). Single-blinded sham TMS was performed as a control. Response times greater than 2 SD from the mean response time (MRT) for each condition were excluded as outliers. The percent change in MRT for correct responses during the active TMS as compared to the sham TMS conditions (deltaRT) was calculated and tested for significance with the t-test.

Results: Fifteen non-sleep-deprived subjects have been evaluated to date. TMS had a negative impact on MRT under the following conditions: DLPFC 5 Hz during retention, Set Size 1 (N = 18, deltaRT = +8.3%, t = 1.9206, $p < 0.05$), parietal 5 Hz during retention, Set Size 1 (N = 13, deltaRT = +8.9%, t = 2.3186, $p < 0.05$), and parietal 5 Hz during retention, Set Size = 6 (N = 12, deltaRT = +7.8%, t = 1.9812, $p < 0.05$). Parietal stimulation during probe suggests improved reaction times, but sample sizes are still small. Other conditions either show no significant effect or are as yet incompletely evaluated.

Conclusions: TMS to the DLPFC or parietal lobe during the retention phase of the Sternberg task can significantly impair reaction time in non-sleep-deprived normal volunteers. Similar stimulation during the probe phase may improve reaction time. We have begun to apply TMS to sleep-deprived subjects at those sites and frequencies which have demonstrable or promising effect on MRT. As the fMRI arm of this experiment informs us of additional networks which are affected by sleep-deprivation, we will begin TMS during VWM and other tasks at those sites as well.

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0512.I

Correlation Between PERCLOS (Percentage Of Eyelid Closure) and Auditory Vigilance Lapses During 42 Hours of Sustained Wakefulness

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Introduction: Slow eyelid closures have been demonstrated to correlate highly with lapses in visual vigilance. If slow eyelid closures are measuring a fundamental biobehavioural marker of drowsiness, then slow eyelid closures should also correlate with lapses in auditory vigilance. The present study investigated this question using an objective assessment of PERCLOS (percentage of eyelid closure) – the CoPilot® and an auditory psychomotor vigilance task (A-PVT).

Methods: Twelve healthy adults (7m, 5f; ages 21-45 years) maintained wakefulness for 42 hours while completing a computerized neurobehavioural test battery every 2 hours that included a 10-min A-PVT. A-PVT cumulative lapse duration data were recorded each minute throughout each trial. In addition, a 20-min visual PVT (V-PVT) was performed during each trial, (reported elsewhere). The CoPilot® measures eyelid droop using two infrared images of the eye, which are processed to a single image that is evaluated by a computer algorithm for degree of slow eyelid closure to estimate PERCLOS values. The CoPilot® was time-locked to A-PVT performance to evaluate coherence between A-PVT cumulative lapse duration and the CoPilot® PERCLOS detection algorithm output. Time series coherence was measured using correlation coefficients.

Results: PERCLOS values from the Copilot® had the following correlations with A-PVT cumulative lapse duration across the 42-hr period of wakefulness: mean (SD) per bout (20-min) coherence between PERCLOS and A-PVT performance lapses was r=0.67(0.26), and the mean (SD) per minute coherence was r=0.48(0.16). A significantly higher correlation between PERCLOS values and V-PVT (r=0.840) performance lapses (described elsewhere) was found compared to the A-PVT ($p>0.05$).

Conclusions: These data illustrate a significant relationship between the occurrence of slow eyelid closures and lapses in auditory vigilance performance. As expected, there was a higher correlation between slow eyelid closures and lapses in visual attention than auditory attention. This may be due to either neurobiological (visual system) or mechanical (the eyelid closing impairs vision) mechanisms. It would appear, however, that slow eyelid closures are a valuable marker of drowsiness, as reflected in increased response times to both auditory and visual stimuli.

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0513.I

Increased Headache Frequency During Chronic Sleep Restriction In Healthy Human Subjects

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Introduction: Chronic sleep restriction and pain are both highly prevalent conditions in our society. Headache is the most common pain-related complaint, with more than 35% of the US population affected by tension-type headache and about 14% suffering from migraine pain each year. Clinicians frequently observe that loss and/or disruption of sleep induces headache but to our knowledge there are no controlled studies examining this phenomenon. As a preliminary investigation, we describe the effects of 9 days of chronic sleep restriction on subjective pain-related symptoms in healthy volunteers.

Methods: Twenty-six young healthy volunteers (age range 21-40 years) were randomly assigned to either 4 or 8 hours of sleep for 12 nights. In both sleep conditions, subjects were permitted to sleep starting at 2300h. In the 8-hour sleep condition, subjects were awakened at 7am, and in the 4-hour condition they were awakened at 3am. During all scheduled wake periods, subjects were continuously monitored by an experimenter to prevent any sleep episodes. On the 2nd baseline day and 10th day of sleep restriction, temperature data, blood, urine, and saliva were collected at regular intervals. On each day of the study, computerized visual analogue scales were presented at two-hour intervals, and subjects were asked to estimate the presence and degree of headache and other pain-related symptoms. We excluded the blood collection days from this analysis and looked at the subjective estimations from baseline through the 9th day of sleep restriction. Subjective estimations of physical state were recorded as the sum of the number of times a symptom was reported in each day, and then analyzed using a Poisson model for repeated measures.

Results: In chronically sleep-restricted subjects, headache frequency was significantly higher than in subjects who slept the regular amount of 8 hours/night (Chi-Sq=4.13; $p<0.05$). Specifically, there was a trend towards a higher headache frequency already after 1 night of reduced sleep compared with the 8 h-sleep condition ($p=0.06$), and thereafter, headache was significantly more frequent following 2 to 8 nights of sleep restriction ($p<0.05$). Across the 9 days of sleep restriction, in 41±8% of the tests headache was present, whereas subjects in the 8 h sleep condition reported headache in 15±9% of the tests ($p<0.05$). Sleep restriction-induced pain was specific to headache: no differences were

observed for other pain-related symptoms, such as muscle pain or generalized body pain.Prostaglandin data are currently being analyzed in urine specimens taken at baseline and day 10 of the experimental protocol.
Conclusions: Sleep restriction to 50% of habitual sleep duration leads to a significant increase in head pain. Our findings demonstrate that chronic sleep loss plays an important role in precipitating headache. Considering that 47 million Americans reported to meet not the minimum sleep amount they need to be fully alert the next day, chronically shortened sleep may be a major factor contributing to the high prevalence of headache observed in population-based surveys.

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0514.I

Recovery Sleep In Flight Crew Spanning 30 Days Of Flight Activity
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Introduction: Research has been conducted to determine the extent of sleep loss and circadian rhythm disruption that occurs during commercial flight operations, especially in those that require crossing time zones. Data collected in survey and field studies have provided some indication that 1-2 days of recovery sleep at home are required after scheduled trips before sleep/wake cycles are stabilized. One goal of this research is to examine the recovery sleep of pilots after successive trip patterns (defined as first flight from home base until returning home), occurring over one month of flight activity in both domestic and international flight operations.
Methods: Captains and first officers from commercial airlines who possessed an Airline Transport Pilot license and active flight schedules participated in the field study. Four domestic pilots (mean age =30) and six international pilots (mean age =47) participated in a 40-day protocol (beginning 5 days prior to the month of flight activity until 5 days after the month). Participants (all male) wore an activity monitor around their non-dominant wrist to measure sleep/wake activity. Digital organizers were used for participants to complete a daily diary of sleep/wake activity. The activity and sleep/wake data were used to examine reported and actigraphy sleep durations up to 3 nights after each trip pattern.
Results: Flight profiles were significantly different by number of trips ($t(8)=5.18$, $p=0.001$) and legs per trip ($t(8)=3.24$, $p=0.012$). Domestic pilots flew more trips ($M=6.25$, $SD=1.26$) and legs per trip pattern ($M=6.87$, $SD=2.64$), crossing 1 time zone than international pilots who flew fewer trips ($M=3.33$, $SD=0.52$) and legs ($M=2.83$, $SD=1.33$), crossing more time zones ($M=10$, $SD=4.10$). Preliminary results suggest that self-reported sleep and sleep measured by actigraphy are significantly correlated ($r=0.859$, $p< 0.001$). Three successive sleep periods after returning home, as measured by actigraphy, were not significantly different for sleep duration ($t(119)=-0.796$, n.s.) or sleep efficiency ($t(116)=-1.88$, n.s.) between domestic ($M=7.86$, $SD=2.01$; $M=79.08$, $SD=7.88$) and international ($M=8.16$, $SD=2.20$; $M=81.95$, $SD=8.51$) pilots, respectively. Similar results were found for self-reported sleep ($t(31)=-0.903$, n.s.) with domestic ($M=7.40$, $SD=1.83$) and international ($M=8.09$, $SD=2.56$) pilots, showing no significant differences. Sleep latency was significantly different ($t(119)=2.29$, $p=0.024$) between domestic ($M=0.38$, $SD=0.48$) and international ($M=0.21$, $SD=0.31$) pilots.
Conclusions: Although the data show that domestic and international flight operations are different in the number of trips per month, legs per trip and time zones crossed, there were no significant differences seen in sleep duration or sleep efficiency for either group. However, the time to fall asleep was significantly different with international pilots having shorter sleep latency than their domestic counterparts. Further analyses will be performed to determine other factors that may affect sleep duration, efficiency, and latency for each recovery sleep period such as age and amount of light exposure prior to sleep.

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0515.I

Comparison of Psychomotor Vigilance and Mood of Interns Following Short Call Versus Long Call Duty
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Introduction: In an effort to improve the performance and mood of internal medicine residents, most training programs have implemented a night float – short call system. An underlying, but unproven, assumption is that residents will perform and feel better after short call than after long call. In order to assess the benefit of short call, we compared psychomotor performance and mood of interns in the days following short call and long call.
Methods: Subjects were 9 medical interns studied for 19 consecutive days during a call duty month in the last trimester of the academic year. The call schedule consisted of a long (24 hour) call alternating with a short (15 hour) call every fourth day. All other days had 9.5 scheduled work hours, with the exception of one day off per week. Over the study period, actual work time averaged 80 hours/week. Total sleep time (TST) was measured by actigraphy and daily sleep logs. Psychomotor vigilance testing (PVT) and the Profile of Mood States (POMS) questionnaire were completed daily between 2.30 and 4.30pm. The PVT is a brief sustained attention visual reaction time task validated to be sensitive to the effects of sleepiness. PVT metrics used were number of lapses and fastest and slowest reaction times. The POMS questionnaire quantifies 6 different mood states: tension-anxiety, depression-dejection, vigor, fatigue, anger-hostility and confusion-bewilderment. Additionally, total time on duty per 24 hours was recorded.
Results: Median TST for the long call night was significantly less than TST on the short call night (1.23 hours vs 4.40 hours; $p<0.0001$) and for the non-call nights ranged between 5.45 and 6.30 hours. Median TST for all nights was 5.2 hours. TST inversely correlated with time on duty ($r = -0.539$, $p<0.0001$). PVT performance did not correlate with TST. Among the 6 mood scales, only tension-anxiety ($p=0.008$) and depression-dejection ($p=0.009$) correlated with TST. PVT metrics were compared after the short call versus long call nights, first post short call versus first post long call nights, etc. and no significant differences were found. Mood scales were compared in the same fashion (short call versus long call, etc.). Interns reported significantly less fatigue ($p=0.02$) and more vigor ($p=0.03$) following the first post short call night compared with the first post long call night. No significant differences were found between the other paired days for any of the mood scales.
Conclusions: Interns displayed no better psychomotor performance on days following short call than on corresponding days following long call. The only improvement noted was in vigor and fatigue following first night post short call versus first night post long call. Although TST increased when time on duty decreased, overall it remained very low. Chronic sleep deprivation likely precludes any significant change in psychomotor performance following a relatively small, although statistically significant, increase in TST.

0516.I

Sleep Satiation I: Effect On Subjective Feelings Of Tiredness
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Introduction: Sleep is regulated by a homeostatic process that is considered to be responsible for the cumulative effect of a daily reduction of total sleep time. This cumulative effect has given rise to the concept of

sleep debt, a debt that is only reduced by extra sleep. It is hypothesized that many people carry a large sleep debt even when they deny feelings of sleepiness. It may also be that these same individuals would freely admit to feelings of tiredness and fatigue.

Methods: Volunteers were fifteen healthy young adults (11 males, 4 females) ranging in age from 18 to 23. Daily sleep was monitored by means of actigraphy and sleep logs. Each subject was asked to obtain their usual sleep for one week and then to obtain as much extra sleep as their circumstances would permit. The typical end point was reached when subjects were unable to sleep more than their putative daily requirement. Each subject had three Multiple Sleep Latency Tests (MSLTs); the first at the end of the "baseline" week, the second after a week of extra sleep, and the third (final) at the end of observations. This report focuses on subjective changes. A special alertness rating scale was devised as follows: Level 1, unambiguously fully alert, absolutely no feelings of tiredness; Level 2, not fully alert, slightly tired; Level 3, unambiguously tired; Level 4, very tired, but definitely not sleepy, no conscious effort required to maintain attentiveness; Level 5, unambiguously sleepy, a conscious effort required to maintain attentiveness and/or avoid falling asleep. Subjects were required to rate their alertness every half hour while awake.

Results: Volunteers continued with their daily lives as students or workers throughout the observations. Baseline MSLT values were generally low. Eight subjects showed peak alertness on final MSLT. Four subjects showed little or no improvement. Three subjects showed unambiguous improvement from basal MSLT, though not >15. Each subject who showed clear-cut improvement in MSLT score had obtained substantial extra sleep. The week of baseline subjective alertness ratings were compared to ratings during the three days preceding final MSLT. Baseline ratings of 1 (peak alertness) were relatively rare and completely absent in several subjects. Ratings of 5 (unambiguously sleepy) were also relatively few. Very clear changes in subjective feelings occurred in subjects who achieved objective alertness. There were almost no ratings of 4 or 5. Compared to baseline, there was a huge increase in ratings of 1 (peak alertness). In subjects with little or no MSLT improvement changes in daytime subjective ratings were inconsistent.

Conclusions: The presence of sleep debt is associated with feeling unambiguously tired throughout the day. Successful reduction of sleep debt is associated with a disappearance or marked reduction of feeling tired while awake. Accordingly, feelings of tiredness and fatigue unaccompanied by feelings of sleepiness in healthy adults may signal substantial sleep deprivation.

0517.J

A Comparison of Auto-adjusting CPAP, Bilevel CPAP, and standard CPAP therapy in Patients with REM Related Obstructive Sleep Apnea

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Introduction: Obstructive sleep apnea (OSA) is a disorder of snoring with the cessation of breathing during sleep. The majority of patients with OSA have apneic events throughout sleep independent of sleep stage. Patients with REM related obstructive sleep apnea (REM OSA) may have apneic events nearly exclusively confined to REM sleep. Many patients with REM OSA may have difficulty with standard CPAP therapy and may subjectively sleep better with auto-adjusting CPAP as it may increase pressure during REM related apneic events and decrease pressure during non REM sleep. Bilevel CPAP was also tested as this may potentially provide some benefit to these patients over standard CPAP. The REMView is a portable sleep recorder that can differentiate whether the patient is awake, in REM or non REM sleep. This was used to correlate REM periods with auto-adjusting CPAP pressure.

Methods: 18 patients completed the study. Patients were randomized for either Bilevel CPAP or auto-adjusting CPAP therapy for one week, followed by standard CPAP for one week, and then the remaining therapy for one week. On each study night the patient used the REMView recorder to determine REM from non REM sleep. The Stanford sleepiness scale was completed by each patient on each morning after therapy. The Epworth sleepiness scale and Functional Outcome of Sleep Questionnaire (FOSQ) were given at the start and after each week of therapy. Total sleep time, REM %, sleep efficiency, FOSQ, and Epworth scores were compared among therapies using a paired t-test . The Stanford score was compared among therapies using repeated measures of variance. Auto-adjusting CPAP pressures were compared to equal time REM and non REM sleep using repeated measures of variance.

Results: Auto-adjusting CPAP pressure during REM sleep was statistically significantly greater than that during non-REM sleep ($p<0.0001$). Stanford scores of auto-adjusting CPAP and standard CPAP were not significantly different from each other ($p=0.339$) but both had significantly lower Stanford scores (less sleepy) than bilevel CPAP ($p=0.0460$ and $p=0.0022$ respectively). No significant differences among Epworth or FOSQ scores were seen among therapies. Increased REM % was nearly significant between auto adjusting CPAP and standard CPAP ($p=0.0708$) and significantly increased between auto-adjusting CPAP and bilevel CPAP ($p=0.0708$). Sleep efficiency demonstrated a significant increase for auto-adjusting CPAP over standard CPAP ($p=0.0346$).

Conclusions: In patients with REM related Obstructive Sleep Apnea, use of auto-adjusting CPAP therapy may result in an increase in REM %, improved sleep efficiency, and less reported sleepiness in the morning following treatment. This may be due to higher pressures delivered during REM related apneic events and lower pressures during non REM sleep where apneic events are less prevalent. Bilevel CPAP therapy does not provide added benefit in these patients.

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0518.J

Tongue Radiofrequency Using a Ventral Route of Application

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Introduction: Tongue Radiofrequency (RFt) has been used applying the needle through the posterior region of the tongue (Stuck et al. Acta Otolaryngol 2002;122:531-6). Using a modified needle architecture we have prospectively studied the effects of an alternate application route (enorally through the floor of the mouth).

Methods: 10 subjects with moderate to severe obstructive sleep apnea syndrome (OSAS) were treated with RFt after full-night polysomnography (PSG). In each subject 2-3 sessions with 3 lesions were performed. Eight weeks after the last session a follow-up PSG was performed. Each subject completed detailed questionnaires on subjective effects, side effects, and the Epworth Sleepiness Scale (ESS) before and after final RFt.

Results: 3 women and 7 men participated in the study. They had a mean age of 49(±14) years, a mean BMI of 26(±3) kg/m2, and a mean preoperative RDI of 47(±29) events/hr. sleep. RFt was able to reduce their mean RDI to 24(±20), (P=0.02). Preoperatively, 10% of the participants had an RDI < 15 while postoperatively this proportion was changed to 50% (P=0.025). The treatment effect was also expressed by a significant change in subjective daytime sleepiness with a reduction of the ESS from baseline 10.2 (±5) to 7.1 (±5), (P=0.0052) postoperatively. No tongue abscess was observed. In comparison to RF application through the tongue surface pain was markedly less using RFt.

Conclusions: RFt is a safe, less painful application procedure for treatment of patients with OSAS. Using RFt virtually no gag reflex was induced in the subjects treated. The therapeutic effects (reduction of disease severity) is comparable to those reported using tonguebase access.

0519.J

The Phonoaudiological Work at Sleep Apnea

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Introduction: People who suffer from Obstructive Sleep Apnea Syndrome (OSAS), frequently exhibits snore, a soft palate increased, a smaller coming-upper aerial space and a wide tongue, among other observations.Our aim, during this research was the direct actuation to the snorer´s oral motricity, having in mind the improvement of OSAS.
Methods: We have worked with 10 (ten) patients with index of light, moderate and severe OSAS, clinically evaluated by the Neurologist and the Otorrinolaringologist. We have also accomplished laboratories, Fibronasofaringolaringoscopy and Polysomnographic tests, before the Phonoaudiological Therapy.The treatment had an average duration of three months with weekly submition for each patient.We have accomplished evaluation from the Stomagnatics functions and from the Oral Motor Sensory System, so that we could guide the exercises to the back dorsum lingual region, soft palate, and facial musculature as well as from masticatory and respiratory functions.Before and after the therapy it was taken pictures from the face and the oral region. It was also required to the patients a Polisomnography, so that we could make the comparison between the first to the second examination.We have considered the index from the American Sleep Disturbs Association, the Scale of Epworth and the statistician test T to the similar samples.Our work requires periodical returning to the Phonoaudiologist because our patients are required to achieve the muscle functional exercises at home. Also we must apply for new Neurological and Otorrinolaringological tests in order to be able of obtaining the results over their lives so that this way we may keep on our research.
Results: Through out the Polysomnographic Test, the Neurologist could observe the improvement before (to) and after (of) the Phonoaudiological Therapeutically Work due to the number of Obstructive Apneas, average (before) 75.10 to (after) 48.60; from the Hipopneas average (before) 36.10 to (after) 11.30; from the apnea and Hipopnea index average (before) 8.15 to (after) 8.54; from the Epworth Scale average (before) 11.00 to (after) 7.60, the other data from Polysonographic didn't change drastically.
Conclusions: The Phonoaudiological Work was significant to the patients that showed light and moderate OSAS, bringing to the enlightenment statistically comproved excellent results.

0520.J

Effect Of Surgically Induced Weight Loss On Obstructive Sleep Apnea In Morbidly Obese Patients

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Introduction: Obstructive Sleep Apnea (OSA) is a frequent syndrome in obese patients. It may resolve after weight reduction. The aim of this study was to evaluate the impact of surgically induced weight loss on OSA in morbidly obese patients.
Methods: Twenty three morbidly obese patients (BMI ≥ 40) with OSA (Apnea/hypopnea Index ≥ 5) who underwent bariatric surgery and accepted to participate in the study were included. Nocturnal polysomnography and the daytime Multiple Sleep Latency Test (MSLT) were performed before and 1-year after surgery. Patients also completed the Sleep Disorders Questionnaire (SDQ) and the Epworth Sleepiness Scale (ESS) the day after polysomnographic evaluation. Pulmonary systolic artery pressure (PSAP) by echocardiogram was also evaluated. Performed surgical procedures were: VBG in 6 patients, RYGBP in 8 patients and distal RYGBP in 9 patients.
Results: There were 10 men and 13 women with a mean age of 39 ± 11 years. One year after surgery, the percentage of excess body weight lost was 64%. Body weight reduction resolved OSA in 44% of the patients (Apnea/Hypopnea Index Before-surgery 45 ± 39; After surgery: Group-without-OSA 2 ± 1, Group-with-OSA 23 ± 25, F=17.2, p<0.006) with a significant improvement in oxygen saturation (Mean % SaO2 in sleep Before-surgery 78 ± 15; After-surgery: Group-without-OSA 90 ± 5, Group-with-OSA 87 ± 4, F=25.6, p<0.001), and a decrease in the level of reported snoring severity (Before-surgery 4 ± 1, After-surgery 3 ± 1, p<0.0001) and reported level of sleepiness (ESS Before-surgery 10.9 ± 7.3, After-surgery 5.5 ± 4.9, p<0.008). One-way ANOVA showed significant improvement of PSAP in the group in whom OSA resolved after surgery: PSAP Before-surgery Group-without-OSA 68 ± 9, Group-with-OSA 50 ± 14; After-surgery Group-without-OSA 43 ± 10, Group-with-OSA 49 ± 14; Group-interaction F=10.7, p<0.02). There was not statistically significant change in objective sleep tendency during the day (MSLT Before-surgery 5.5 ± 4.9 and After-surgery 5.6 ± 5.0, p=ns).
Conclusions: Weight loss induced by surgery eliminates OSA in 44% of morbidly obese patients with an important improvement in oxygen saturation. Pulmonary artery pressure improves only in patients in whom OSA resolved after surgery. Data suggest that daytime sleepiness in obesity might be associated with other factors not associated with sleep-disordered breathing

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0521.J

Oral CPAP for Sleep Apnea: Effectiveness, Patient Preference and Compliance

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Introduction: Nasal continuous positive airway pressure (nCPAP) is the most definitive medical therapy for obstructive sleep apnea (OSA). Many patients have difficulty tolerating nCPAP due to nasal airway problems, mouth leak, and discomfort from the mask and headgear. These limitations may be overcome by an oral interface (OracleTM) that does not require headgear. We performed a study to compare the new oral interface to conventional masks in the effectiveness of CPAP delivery and patient satisfaction and compliance.
Methods: Ninety-eight, consecutive CPAP-naïve, patients diagnosed with OSA by overnight polysomnography (apnea-hypopnea index > 5) were referred for CPAP therapy. All patients were presented with a variety of CPAP masks, including nasal, oro-nasal and the new oral mask, and reasons for mask choice were documented. After 3 weeks acclimatization to the mask of their choice, patients had a CPAP titration sleep study to determine their optimal CPAP level. Two and six months later, a patient questionnaire was completed of CPAP use and effectiveness, mask comfort, and upper airway dryness.
Results: Patients were predominantly male (70%), middle-aged (50.6 ± 11.7 yr) and moderately obese (body mass index 32.5 ± 9.0 kg/m2) with severe OSA (AHI 40.6 ± 25.8 /hr). Patients were divided into 3 groups based on their choice of mask: Nasal (66%), Oral (27%) and Oro-nasal (7%). Baseline characteristics did not differ significantly between groups. Reasons for choosing the oral interface included an appreciation for the lack of headgear (69%), a history of mouth-breathing at night (15%), greater comfort, a sensation of "getting more air" compared to other masks, and a history of chronic sinusitis (16%). Reasons for rejecting the oral interface included that it was too invasive (51%), a sensation of claustrophobia, choking or gagging (18%), a preference for nasal breathing (14%), improper fit, and anticipated dry mouth (17%). Optimal CPAP was not significantly different between mask groups (Nasal:

7.7 ± 2.1 cmHs2sO, Oral: 8.0 ± 2.0 cmHs2sO, Oro-nasal: 9.7 ± 3.2 cmHs2sO, p=0.267). Subjective ratings of compliance, effectiveness, and mask comfort were also similar between groups. However, the Oral group had more complaints of upper airway dryness and "rain-out". The Oro-nasal group had a disproportionately greater number of dropouts from CPAP therapy than the Oral group (57% vs 19%, p=0.046). Nine patients changed from the oral interface to a nasal mask during the study, whereas no patient changed from their nasal or oro-nasal mask.
Conclusions: The oral mask is an effective interface for chronic CPAP therapy in patients with OSA. The main limitations of the mask are upper airway dryness and "rain-out", which may be improved by further technical modifications. The oral mask may be more acceptable than oro-nasal masks for patients who cannot rely exclusively on the nasal airway for CPAP therapy.

Research supported by Fisher & Paykel Healthcare

0522.J

Quality Monitoring of a Split-Protocol Polysomnography
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Introduction: A split-protocol (S-P) institutes a combined diagnostic and therapeutic polysomnography (PSG) on the same night of testing. At our institution, a S-P is applied if within the first two hours of diagnostic sleep an apnea-hypopnea index (AHI) of at least 20 is achieved, or urgent clinical criteria have been met. When accepting of therapy, such patients subsequently undergo a trial of pressurization of the upper airway, which by necessity should sample at least 3 hours of sleep. To assess whether performance of a S-P is consistent with the clinical needs of our patients, we have initiated a continuous quality improvement program. We report on our experience during the first six months of this program.
Methods: PSG's performed from 1/1/02 through 6/30/02 were reviewed. These were categorized as a S-P, "full-study" diagnostic (Dx), or "full-study" titration (T). Data included a pre-test Epworth Sleepiness Scale (ESS), Body Mass Index (BMI, kg/m2) and the diagnostic values for the AHI, nadir sleep oxygen desaturation (SpO2n), and arousal+awakening index (Ar+Aw I) as measured during the S-P and Dx studies. Titration duration (hours) was also analyzed for the S-P and T studies. Unless otherwise stated, data are reported as the mean ± 1 standard deviation.
Results: 1460 PSG's were reviewed. Of these, 203 were S-P; 920 were Dx; 337 were T. The following is noted: ESS= 12.5 ± 5.5 [S-P]; 10.8 ± 5.2 [Dx]; BMI= 37.8 ± 7.2 [S-P]; 32.8 ± 7.4 [Dx]; diagnostic AHI= 48.1 ± 32.7 [S-P], 9.5 ± 13.3 [Dx]; diagnostic SpO2n= 76.2 ± 8.6 [S-P], 85.1 ± 6.8 [Dx]; diagnostic Ar+Aw I= 44.8 ± 27.6 [S-P], 20.0 ± 14.7 [Dx]; and titration duration= 3.7 ± 1.3 hours [S-P], 5.5 ± 1.4 hours [T].
Conclusions: Our staff was effective in selecting for S-P's only those patients with the worst disease severity. Specifically, relative to Dx PSG's, S-P's had a patient population characterized by greater obesity (BMI: 37.8 vs. 32.8), drowsiness (ESS: 12.5 vs. 10.8), sleep-induced hypoxemia (SpO2n= 76.2% vs. 85.1%), fragmented sleep (Ar+Aw I= 44.8 vs. 20.0) and, as expected, much more severe sleep disordered breathing (AHI= 48.1 vs. 9.5). Of note, despite time constraints imposed by a S-P, our staff was still able to achieve a mean titration duration of 3.7 hours of sleep time.Monthly analysis of such data has allowed our service to periodically assess whether performance of a S-P PSG is appropriate in selecting and treating only those patients with moderate-to-severe sleep disordered breathing. It has also provided insight into the clinical and laboratory features that ultimately impact the need for a S-P.

Research supported by the dedicated night time staff of Gaylord Sleep Services

0523.J

Modulation of Inflammation in Obstructive Sleep Apnea (OSA) Patients Treated with Nasal Continuous Positive Airway Pressure (nCPAP)
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Introduction: We hypothesized that nasal continuous positive airway pressure (nCPAP) induces nasal inflammation associated with the nasal side effects of nCPAP.
Methods: Newly diagnosed OSA patients were assigned to one of three groups of allergic rhinitis (AR), non-allergic rhinitis (NAR), or no rhinitis (NR) based on history, physical examination, nasal cytology, and allergy skin testing. Nasal scrapes and lavage were performed before therapy and for three months following initiation of nightly nCPAP. Total nasal airflow (TNA)at -150 Pascals was measured by high resolution anterior rhinomanometry. Cytokines were measured by ELISA. Nasal symptoms and tolerance of nCPAP were scored relative to baseline on a scale of -3 (least symptomatic on nCPAP) to 3 (most symptomatic on nCPAP), with 0 representing baseline.
Results: Twenty eight OSA patients (14 with AR, 10 with NR, 4 with NAR) have completed the study. 69.4% of AR patients, 75% of NR patients and 50% of NAR patients had symptom scores between 0 and -3, reporting either no nasal symptoms or improvement of their symptoms from baseline on nCPAP. At baseline IL-8 levels ranged from 175.3 pg/ml (SD=139) in AR patients compared with 137.4 pg/ml(SD=98)and 96.3 pg/ml (SD=46.5) in NAR and NR patients respectively. During 3 months of nCPAP therapy, IL-8 decreased to 57.5% and 42% of baseline levels in AR and NAR patients respectively, but remained unchanged from baseline in NR patients. Other cytokines remained unchanged from baseline in all groups studied. During the months 2 and 3 of nCPAP therapy TNA increased to 140% and 181% of baseline levels in NR and NAR patients tested, but remained comparable to basal levels in AR patients. All results were subsequently analysed with respect to subgroups of AR, NR, and NAR patients: TNA increased to 156% (SD= 7.05%) and 209% (SEM=68%, n=5) of baseline in subsets of NR and AR patients respectively. In subgroup analysis, IL-8 levels were decreased to 19.4% (SD= 0.35), 47.1% (SD=0.36), and 56.7% (SEM=15.5, n=5) of baseline levels in a subset of NAR, NR, and AR patients respectively. ICAM-1 levels were decreased to 52.7% (SEM=16.9%) and 69.2% (SD=3.2)in subgroups of AR and NR patients respectively. IL-6 levels were decreased to 35.6% (SD=22.4) of baseline in a subgroup of AR patients. IL-13 levels were decreased to 35% (SEM=4.9%) of baseline in a subset of AR patients. In the remaining subgroups of AR, NAR and NR patients the cytokine levels and TNA did not reach statistical significance in comparison to baseline levels.
Conclusions: In subsets of AR, NAR, and NR patients nCPAP therapy modulates paremeters of nasal inflammation.

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0524.J

Screening and Treatment of Obstructive Sleep Apnea in a Brooklyn-Based Minority Sample

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Introduction: Sleep-disordered breathing (SDB) is a major public health problem in the U.S., particularly among the African-American population. Obstructive sleep apnea, the most common form of SDB is associated with hypertension, cardiovascular diseases, pulmonary disorders, stroke, psychosocial consequences, road traffic accidents, and mortality. According to the National Commission on Sleep Disorders Research, which reviewed about a million patient records, only 17 positive diagnoses for sleep disorders were found. These findings emphasize the necessity for adequate screening and timely diagnosis so that effective treatments can be administered to improve sleep and diminish associated risks. The present study sought to ascertain the rate of receipt of a comprehensive assessment of SDB following a referral by a clinician and the efficacy of CPAP treatment in a Brooklyn-based minority sample.

Methods: Data were obtained from a chart audit survey conducted at the Kingsbrook Sleep Center, located in East Flatbush, Brooklyn, New York from November 2001 to June 2002. A total of 271 patients were referred to the clinic, of which 76% were African Americans. Scrutiny was limited to 234 African Americans (average age = 47.71 $\pm$ 17.76 and average BMI = 36.42 $\pm$ 9.65; 57% were female and 43%, male). Upon referral, patients were scheduled for a detailed sleep history by a sleep clinician to determine if laboratory assessment was warranted. To assess SDB polysomnographic assessment was performed using Bio-Logic digital polysomnographs. Standard physiological parameters were monitored including, sleep structure, SaO2, heart rate, respiratory effort, airflow, and EKG- and snoring-related arousals; all parameters were analyzed by a trained technician using standard criteria.

Results: Of the 234 referred patients, 35% (n = 83) complied with the recommendation to undergo a nocturnal polysomnographic evaluation. Of the patients that received a laboratory assessment, 61% received a diagnosis of sleep-disordered breathing using the current nosologic criterion (AHI ³ 5). Of the sample, 36% reported suffering from high blood pressure (HBP); 33%, a family history of HBP; 7%, heart disease; 15%, a family history of heart disease; 24%, depression; 36%, headache; and 15%, stress; 21% reported caffeine consumption; and 21%, tobacco. Significant treatment effects were found for apnea-hypopnea index, number of Sa02 desaturations (34 $\pm$ 35 vs 4 $\pm$ 35, t = 5.47, p < 0.001; 80 $\pm$ 117 vs 31 $\pm$ 49, t = 2.56, p < 0.05) respectively; marginal improvement was noted for total sleep time (4.09 $\pm$ 1.84 vs 4.72 $\pm$ 1.31, t = -1.75, NS).

Conclusions: Strong evidence supports the belief that comprehensive assessment of sleep-disordered breathing, leading to adequate diagnosis and treatment, is necessary to decrease associated morbidity and mortality. The present data show that CPAP is very effective to treat SDB among African-American patients. Interestingly, although national prevalence data show higher rates of SDB for African-Americans our data evidenced that this population may underutilize available sleep assessments. The present study strongly favors the need for educational intervention to increase awareness of sleep-disordered breathing, particularly in African-American communities where sleep complaints may be significantly underreported.

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0525.J

Identifying Patients at High Risk for Postoperative Sleep Apnea

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Introduction: Sleep-related breathing disorders and hypoventilation have been reported in up to 50% of postoperative patients, but most patients do not have apparent adverse outcomes, and the presence of snoring or sleepiness has not been predictive. Patients with obstructive sleep apnea syndrome (OSAS) are predisposed to postoperative apneas by narcotic analgesia, supine position, and by sleep architectural changes such as REM rebound on postoperative days. Case reports describe severe cardiorespiratory complications in some patients with underlying OSAS, and some studies suggest increased hospital morbidity and length of stay. Only about 10% of patients with OSAS are diagnosed at present, so it would be useful to be able to quickly identify patients likely to be at risk for postoperative sleep apnea events.

Methods: Patients scheduled for elective total hip or knee arthroplasty were prospectively recruited to participate in a trial examining the effect of auto-titrating CPAP on postoperative length of stay and complications. Consenting patients were stratified by a clinical prediction model that uses history of habitual snoring, frequent nocturnal choking, gasping, or apneas, hypertension, and measured neck circumference into those with a predicted apnea-hypopnea index (AHI) ³15 (high-risk) and those with predicted AHI < 15 (low risk). Qualifying high-risk patients were then randomized to receive usual care or usual care plus auto-titrating CPAP postoperatively. We recorded blinded overnight oximetry on the first postoperative night and obtained a portable cardiorespiratory sleep study on the night prior to discharge for these high-risk patients. Oximetry and cardiorespiratory data were analyzed after discharge.

Results: Out of 590 contact letters sent to prospective total joint patients, 308 responded, and 91 patients consented to complete the prediction model assessment. 76 had a predicted AHI < 15 (low risk group) or were excluded because of medical exclusion criteria (previously diagnosed OSA, chronic respiratory failure, ACP estimated risk of cardiac complications > 10%, claustrophobia). 15 patients qualified and completed testing (8 auto-CPAP, 7 no-CPAP). During the first postoperative night, all high-risk patients had abnormal oxygen saturation, with mean SaO2, minimum SaO2, and % time with SaO2 < 90% of 91.9 $\pm$ 3.3, 67.9 $\pm$ 14.0, and 27.2 $\pm$ 21.4 respectively (mean $\pm$ SD). Desaturations of at least 4% occurred 12.2 $\pm$ 6.7/hour. At portable cardiorespiratory sleep study, the median AHI was 26.3/hr (range 12.5-71.2, mean 31.7). 3 patients were suspected by their clinicians of having nocturnal hypoxia, and were provided emperic supplemental oxygen.

Conclusions: The clinical prediction model had a 100% positive predictive value in predicting patients that will have an abnormal AHI following total joint arthroplasty. Patients with a predicted AHI ³ 15 had significant postoperative hypoxemia and were documented to have at least mild to moderate AHI abnormalities. If it can be shown that these abnormal cardiorespiratory events are associated with adverse clinical events, this clinical prediction model may be useful in stratifying which patients are at highest risk. A study to determine clinical outcomes and the sensitivity of the model in postoperative patients is needed and is underway.

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0526.J

The Epworth Sleepiness Scale Does Not Measure Perceived Sleepiness In Patients With Sleep Apnea

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Introduction: Patients present clinically with perceived sleepiness.

When sleep apnea is mild to moderate, treatment decisions depend on presence of sleepiness. The Multiple Sleep Latency Test (MSLT) measures ability to fall asleep on demand. The Epworth Sleepiness Scale (ESS) measures tendency to doze off in different circumstances. Does ease of falling asleep measure perceived sleepiness? To further explore this issue, a self-administered questionnaire was designed and administered to consecutive new patients presenting mostly with symptoms of sleep apnea.

Methods: A six-item scale of perceived sleepiness (SPS) was prepared, which asked patients to rate, on a scale of 0 (not at all) to 3 (very much) how much of a problem the following items were for them: sleepiness (SPS1), fatigue (SPS2), tiredness (SPS3), lack of energy (SPS4), lack of attention (SPS5), and memory difficulty (SPS6). Patients also completed an ESS. Patients were administered a polysomnogram (PSG), generally within the next two weeks, followed by an MSLT if clinically indicated. Of forty-nine consecutive patients, one was excluded because of incomplete questionnaire data, and one because the PSG did not occur. 23 patients underwent the MSLT.

Results: The forty-seven patients ranged in age from 17-78 (mean 45.5, SD 12.9). Mean ESS was 11.9 (SD 6.3). Mean (SD) for SPS1 through SPS6 were 1.8 (0.9), 2.1 (1.0), 2.2 (1.0), 2.1 (0.9), 1.4 (.9), and 1.2 (0.9). After Bonferroni correction, SPS1, SPS2, SPS3 and SPS4 were correlated with each other, but not with any of the eight ESS items. Most of the ESS items were correlated with each other. SPS5 and SPS6 were correlated with each other, and with some of the other SPS and ESS items. Factor analysis with varimax rotation using the eight ESS and six SPS items revealed three factors. The eight ESS items loaded highly on Factor 1, the first four SPS items (related to perceived sleepiness/fatigue/tiredness/lack of energy) on factor 2, and the last two SPS items (related to attention/memory) on factor 3. The MSLT did not correlate with the sum of the eight ESS items (ESS), of the first four SPS items (perceived problematic sleepiness), or of the last two SPS items (perceived cognitive problem). The MSLT correlated with sleep latency and negatively with sleep efficiency. Perceived cognitive problems correlated with sleep latency and % stage 1, and negatively with sleep efficiency and % stage 4. ESS and perceived sleepiness did not correlate with any PSG measure.

Conclusions: Perceived problematic sleepiness, fatigue, tiredness, and lack of energy are highly correlated with each other and form a separate factor from the ESS items. Previous studies have shown that the MSLT and MWT are not highly correlated, that the MSLT is most highly correlated with sleep efficiency, and that the MSLT and ESS do not necessarily measure the complaints of sleep apnea patients. Perhaps it is time to rethink our reliance on tests that measure subjective or objective tendency to fall asleep, and to consider replacing these with measures of how problematic patients find their sleepiness (and fatigue, tiredness, lack of energy).

0527.J

ApoE 4 allele Frequency in Japanese Sleep-Disordered Breathing Patients

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Introduction: Apolipoprotein E (ApoE) 4 is a well known risk factor for Alzheimer's and cardiovascular disease. It was reported that ApoE 4 and sleep-disordered breathing (SDB) were associated in middle-aged Wisconsin population (aged 32 to 68 years) but not in elderly Japanese-American samples (aged 79 to 97 years). This discrepancy may be due to difference in age or genetic background. To clarify which may be the case, we are studying the association between SDB and ApoE 4 in middle-aged Japanese population. As a first step, we analyzed ApoE typing in Japanese SDB patients.

Methods: Moderate-to-severe SDB patients (apnea-hypopnea index:AHI ³ 15) were recruited from sleep clinics (male: 98 and female: 2; aged 27 to 76 years, BMI: 28.9 ± 4.05). Nocturnal polysomnography was performed to evaluate AHI. Cholesterol and triglycerides were also measured. ApoE genotypes were determined using sequence analysis.

Results: Allele frequencies for 2, 3 and 4 were 0.043, 0.853 and 0.104, respectively. Total Cholesterol (204 ± 32.0) and triglycerides (249 ± 147) were increased, while HDL (48 ± 14) was normal in these samples.

Conclusions: ApoE 4 allele frequency was slightly higher than that of Japanese general population, which was reported to be 0.093 (n=1328). This control subjects had not been studied for SDB. Up to 9% of middle-aged men in the general population were reported to have an AHI of 15 or more, so it is likely that the control group contained men with SDB. Additional SDB samples and also control subjects with SDB study are needed to perform statistical analysis.

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0528.J

Differences in Antioxidant Intake in Veterans With and Without Obstructive Sleep Apnea

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Introduction: Little, if any, research has been performed on associations between dietary intake and obstructive sleep apnea (OSA) in either veteran or civilian samples. Generally, studies of OSA and nutrition address obesity and body fat distribution, which have been shown to play roles in OSA severity. However, an understanding of the possible relationships between nutrient intake and OSA could lead to novel, high adherence dietary interventions, including the use of metabolic anti-oxidants that could reduce the deleterious effects of oxidative stress that occur with hypoxic events.

Methods: The association of nutrient intake with OSA was investigated in 195 male veterans between 54 and 84 years of age (44% Hispanic; mean age 68±8.0 years). Subjects were recruited from the Southern Arizona VA Health Care System outpatient clinics in Tucson, AZ. Data collection included the Sleep Habits Questionnaire from the multi-center Sleep Heart Health Study, height and weight, and completion of the Arizona Food Frequency Questionnaire (AFFQ). The AFFQ is a validated dietary history form adapted for Southwestern eating patterns that yield macro- and micro-nutrient, caffeine and alcohol intake levels. Chi-square was used for nominal variables. Analysis of variance (ANOVA) was used to determine differences in mean values for antioxidant intake between groups with OSA as the dependent variable.

Results: Of the 195 veterans, 8% of them reported physician diagnosed OSA. Veterans with OSA were significantly more likely to be overweight (BMI=31.9 vs. 27.5, $p<0.01$), and three times more likely to report loud snoring (RR=3.1, $p<0.0001$) compared to veterans without OSA. There were no differences between groups for age, ethnicity, smoking or alcohol consumption. Veterans with OSA had significantly lower Vitamin C intake (135±61.5 mg) compared to those veterans without OSA (197±122.6 mg, $p<0.05$). Borderline significant findings were noted for reduced intake of the B vitamin complex member Folate (382±141 vs. 502±263 mcg, p=0.07), and the lipid soluble carotenoid compounds Lycopene (9,298±2,682 vs. 13,162±9,390 mcg, p=0.097) and Lutein+Zeaxanthin (2,388±1,247 vs. 3,400±2,258 mcg, p=0.07).

Conclusions: Findings suggest that veterans with OSA consume fewer nutrients that contain important antioxidant properties compared to their cohorts without OSA. A reduction in dietary intake of these free radical scavenger nutrients could contribute to greater oxidative stress associated with OSA-related hypoxemia leading to higher rates of cardiovascu-

lar disease (CVD). Further studies using larger samples of subjects with physician diagnosed OSA are required to replicate these findings, and to determine if nutrient intake is associated separately with OSA, with CVD, or in combination with these disorders.

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0529.J

Cardiovascular Mortality in Sleep Laboratory Patients: Excess Risk Associated With Breathing Disorders in Sleep

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Introduction: Sleep disordered breathing is closely associated with cardiovascular morbidity. It is not clear, however, if it is also associated with increased risk of cardiovascular mortality. Here we report mortality data of a large cohort of patients investigated in the Technion Sleep Medicine Center laboratories in Israel.
Methods: During the study period (1985-2000), The Technion Sleep Medicine Center comprised 4 sleep laboratories with a total of 24 recording beds. Between 1 Jan 1985 and 1 Jan 2000 26,872 adults patients were examined. Of these, 949 (3.5%) died by 1 Jan 2000 (examination age: 60.7±13.3, death age: 65.0±13.3). Cause of death was known for 533, of whom 220 (41.3%) died because of cardiovascular/respiratory causes (CVD) and 118 (22.1%) because of malignancies (M). Person years at risk in two age groups 20-59 and >60 yrs were computed using the Israeli general population mortality data for 1996-1997 as a reference group. Comparison of any two specific rates was performed assuming that the number of cardiovascular or malignancy deaths in each subgroup follows a Poisson distribution. A Poisson regression model for aggregate data was performed using SAS procedure PROC GENMOD. Gender specific mortality rates were calculated after patients were stratified according to age (20-59 and >60), RDI (>10 or <10) and BMI (<25: normal weight, 25<BMI<30: overweight, and >30: obese). Mortality risks were calculated separately for cardiovascular and malignancy deaths.
Results: Age 20-59: Significant CVD mortality risk was found for men with RDI>10 in all BMI categories (normal weight:2.86, overweight:1.92, Obese:3.77) but only for "obese" men with BMI<10 (9.25). Significant mortality risk was found for women with RDI>10 in all weight categories (normal weight:7.85, overweight:14.51, obese:17.57) but not for women with RDI<10. A comparable analysis of malignancy deaths did not reveal significant mortality risk for any of the subgroups.Age>60: No significant mortality risk was evident for any of the subgroups of the elderly patients, neither for CVD nor for M deaths. If any, there was a trend toward lower mortality risks than the general population as "normal weight" and "overweight" men with RDI>10 had significantly lower CVD mortality risk (0.62 and 0.66).
Conclusions: Our results demonstrated that breathing disorders in sleep is associated with increased risk of cardiovascular mortality only in patients younger than 60. This was found for all three BMI categories of "normal weight" "over weight" and "obese." Women had considerably higher mortality risk than men in each of the BMI categories.

0530.J

Patient Perceptions of a New Nasal Mask – Results of a Clinical Trial

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Introduction: Patient Perceptions of a New Nasal Mask – Results of a Clinical TrialMansoor Ahmed MD, FACCP, FAASM and Darryl Domenick BS, RRT, RPFT, RPSGTSouthwest Cleveland Sleep Centers, Cleveland, Ohio, Robert Messenger BS, RRT, CPFT Invacare Corporation, Elyria, Ohio.Some of the primary factors that influence compliance with positive airway pressure (PAP) therapy are mask fit and comfort. With this in mind, we sought to determine the impressions of experienced PAP therapy users on the fit and comfort of a new nasal mask prototype. (Twilight Mask, Invacare Corp., Elyria, OH). This mask uses a clear polycarbonate shell, dual walled silicone cushion and adjustable forehead support.
Methods: IRB approval for studies involving human subjects was obtained. 26 Patients from the Sleep Center who were already on PAP therapy that met inclusion criteria were recruited, after the informed consent. Each participant was using PAP therapy ranging from 3 months to 4 years (mean 1.85 ± 1.32 years). Mean nightly PAP use was 6.62 ± 1.02 hours. Participants came to the sleep center where they completed a pretrial questionnaire regarding perceptions of their current nasal mask. Participants were then fitted with the prototype mask.. After receiving instruction on adjustment and cleaning, participants took the mask home and used it as they would their regular mask for a 2-3 week period. At the end of the trial period, participants returned to the sleep center and completed a post-trial questionnaire regarding perception of the study mask. Questions were designed to allow responses along a weighted continuum, allowing for analysis of the responses. These questions required the participant to compare the study mask to their usual mask, and were focused on the silicone seal, vertical and horizontal fit, the exhalation exhaust port(s), swivels, ease of assembly, forehead pads and headgear. Responses were grouped in three categories: 1) inferior, 2) same as, and 3) superior. For questions in which the majority of responses were in the "same as" category, the criteria being evaluated was considered to be similar to that offered by other masks. When the majority of responses were not in the "same as" category then the "same as" responses were dropped and the inferior and superior responses were compared.
Results: 23 of 26 recruited patients completed the study, 2 were dropped due to failure to show for follow-up appointments, and 1 was dropped due to inability to tolerate a nasal mask (a full-face mask was required). Although no single mask type was normally used by all of the participants in the study, several common features of this prototype began to emerge. 78% (14 of 18) rated the comfort of the trial mask to be better than that of their usual mask. Similarly, 70% (16 of 23) rated the fit and overall presence of leakage to be better than that of their usual mask. Also, 59% (10 of 17) found the mask to be quieter, and 93% (13 of 14) identified that the main tubing swivel was better than the mask that they were normally using. However, 2 of the 23 participants indicated that they experienced unintended disengagement of the main tubing swivel, and 48% (11 of 23) identified that they could feel exhaust gas blowing on them or their bed partner. When asked if they would choose to continue using the trial mask if the inequities with the prototype were corrected, 65% (15 of 23) identified that they would continue use.
Conclusions: The new prototype mask seems to meet the comfort and fit requirements of a large portion of PAP users. With correction of the identified deficiencies, this nasal mask should add positive value to the clinician's armamentarium used to promote patient compliance.

0531.J

Are Collegiate Football Players At Risk For OSA?

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Introduction: Collegiate football players strive to become bigger, faster,

and stronger by training and diet. Particular emphasis is placed on thickening and strengthening the neck. Neck circumference has been shown to be predictive of Obstructive Sleep Apnea (OSA). Having a neck circumference of 16.75 inches or more has a 77 to 87% sensitivity, 79 to 82% specificity, and positive predictive value of 66 to 75% for sleep apnea. Neck size is a better predictor of OSA than are traditional clinical symptoms such as snoring and EDS*. Despite the massive body habitus in some athletes and the popularity of sport in today's culture, a Medline Search revealed no data on football players and OSA. We hypothesized that collegiate football players are at increased risk for sleep apnea. *Davis RJ et al. Neck circumference and other clinical features in the diagnosis of the obstructive sleep apnoea syndrome. Thorax 1992; 47: 101-5.

Methods: After obtaining IRB approval and consent from coaches, we asked collegiate football players at the University of Kentucky, West Liberty State College, and Georgetown College to volunteer for the study. Volunteers completed a questionnaire containing the Epworth Sleepiness Scale(ESS)and questions about snoring, witnessed apnea, falling asleep while driving, headache and non-refreshing sleep. We measured neck circumference, blood pressure, height and weight. Variables were compared by 2 tailed, 2 group T test with Bonferroni Adjustment and by linear regression.

Results: We studied 137 collegiate football players, all men. Mean neck circumference was 15.5 inches ($\pm$ 1.3). Mean Body Mass Index (BMI) was 29.8 Kg/m2 ($\pm$ 4.8. Mean ESS was 9.2 ($\pm$ 3.8.Those with neck circumferences of 16.5 inches or more were more likely to snore (p=0.03). There was a linear relationship between neck circumference and BMI. We found no relationship between neck circumference and any of the other symptoms we investigated. Comparing those with the largest necks (neck circumference 17 inches or more, n= 50) to those with the smallest necks (neck circumference 15 inches or less, n=55), we found no relationship between neck size and Epworth Sleepiness Scale score. Of interest was that all athletic trainers had a program in place to address snoring during overnight travel. The most common strategy was segregation of snorers and non-snorers!

Conclusions: Collegiate football players with larger necks are more likely to snore. We did not find a relationship between neck size and Epworth Sleepiness Scale scores, non-restorative sleep, witnessed apneas, moving vehicle accidents, or headaches in this young, fit group. We speculate that the relatively young age and current level of fitness protects collegiate athletes from symptomatic sleep-disordered breathing, despite their large necks. We further speculate that professional football players, being older and heavier, may be more likely to manifest symptoms of sleep-disordered breathing.

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0532.J

Do Two Nights Of CPAP Titration Make A Difference To Patient Compliance?

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Introduction: Continuous Positive Airway Pressure (CPAP) is the preferred method of treating sleep apnea but patient compliance remains less than optimal. A number of factors have been shown to improve patient compliance in using CPAP, one of which is contact time with the sleep clinic technical staff. Recent Medicare guidelines have dictated a reduction in the nights of CPAP titration from two nights to one night. It is not known if CPAP compliance will differ between patients who have had one night versus two nights of titration.

Methods: A chart review of 110 patients from the International Sleep Clinic in Parry Sound, Ontario was conducted. Patients had overnight sleep studies, were diagnosed with sleep apnea, had either one or two nights of CPAP titration and received CPAP machines. In a second arm of the study, the same patients were contacted by telephone for questionnaire interview about their CPAP usage. In this study, CPAP compliance was defined as > 5 hours use per night.

Results: Seventy-eight of the one hundred and ten patients (71% response rate) agreed to be interviewed for the study. First (n=41) and second (n=23) night study data were available for sixty-four of those patients, and of those, fifty-four (84.4%) of patients reported being compliant. On average the patients used their CPAP 6.8 hours per day for about 6 days per week. Sixty-percent of patients stated that their CPAP machine was working well and that they were sleeping much better. The number of hours of machine use did not differ significantly (p=0.86) among those who had either one (6.9 $\pm$ 2.3 hrs) or two (6.8 $\pm$ 2.9 hrs) nights of CPAP titration. The first and second nights yielded similar titration pressures. The only difference noted between the first and second night was a significant improvement ($p<0.001$) in sleep efficiency from the first night (70.6% $\pm$ 16%) to the second (76.3% $\pm$ 14%).

Conclusions: One versus two nights of CPAP titration did not make a difference in CPAP compliance in this population of sleep clinic patients. Of note, sleep efficiency did improve on the second night of titration and an extra titration study may be necessary in the minority of patients who sleep poorly on their first titration night.

0533.J

CSF Hypocretin / Orexin Levels in Patients with Obstructive Sleep Apnea Before Treatment

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Introduction: It has been reported that cerebrospinal fluid (CSF) hypocretin-1 (orexin-A) concentration in the majority of patients with narcolepsy-cataplexy was undetectably low (Nishino 2001). This finding is specific for narcolepsy-cataplexy among various neurological disorders, except for a few Guillain Barre Syndrome (GBS) subjects (Riply 2001). Taken together with the fact that hypocretin levels in the majority of the patients with primary excessive daytime sleepiness (EDS) disorders, such as EDS without cataplexy and idiopathic hypersomnia are in the normal levels (Kanbayashi 2002), measuring CSF hypocretin levels is a promising diagnostic method for narcolepsy-cataplexy among primary EDS diseases. It is however, not known whether CSF hypocretin-1 is altered in patients with secondary EDS disorders. Among secondary EDS disorders, obstructive sleep apnea syndrome (OSA) is the most common disorder. We therefore measured hypocretin-1 in CSF in patients with OSA.

Methods: Sixteen OSA patients were evaluated by complete overnight sleep study, using a computerized polysomnogram system (Night Owl, NoruPro Light Systems, Tokyo, Japan). Patients with an apnea-hypopnea index (AHI) >5 were considered to have OSA. All OSA patients were male and prior to any treatments. For the reference, data of 12 narcolepsy-cataplexy patients and 17 primary EDS without cataplexy patients are presented. Twelve healthy controls (age: 22-67) were also included for CSF hypocretin measurements. The ethnicity of all subjects was Japanese. Demographic data as well as BMI, apnea-hypopnea index (AHI), mean sleep latency by multiple sleep latency tests (MSLT), and HLA typing of patients are summarized. Lumber CSF was collected between 10am to 3pm and samples were kept at -80 C freezer. Hypocretin-1 was measured using radioimmunoassay kits (Phoenix Pharmaceuticals, Belmont, CA) as previously reported (Kanbayashi 2002). This study was approved by the local ethical committee, and all subjects gave

informed consent for the lumbar puncture and hypocretin measurement.
Results: Sixteen subjects with OSA (mean AHI: 34) were compared with other 3 groups. The mean age, AHI and BMI of patients with OSA were significantly higher than other groups. Significant positive correlations between AHI and BMI in OSA patients were observed ($p<0.01$). OSA patients had subjective EDS and a mean sleep latency of 8 patients was confirmed to be shorter than 5 min. The mean sleep latencies were shorter than 5 min and were not significantly different among 3 groups, ie, OSA, narcolepsy-cataplexy and EDS without cataplexy. Mean CSF hypocretin-1 levels in OSA patients (284 ± 74 pg/ml) did not differ from those in the controls (293 ± 63 pg/ml) and EDS without cataplexy (259 ± 57 pg/ml). No significant correlation was found between AHI and hypocretin-1 levels in OSA. All narcolepsy-cataplexy patients with positive HLA DR2 had very low CSF hypocretin-1 levels (<110pg/ml) (Mignot 2002).
Conclusions: We found that a majority of OSA subjects showed normal CSF hypocretin levels. Recently, Mignot et al also reported that normal CSF hypocretin levels in patients with OSA, but these patients were under treatment (Mignot 2002). In our study, all subjects are before treatment and had various degree of AHI. Significant correlation was found between AHI and BMI as previously reported (Browman 1984). The shortened sleep latencies of OSA patients were in the same range of other two primary hypersomnia, such as narcolepsy-cataplexy and EDS without cataplexy. However, significant differences in CSF hypocretin levels were observed among patients with narcolepsy-cataplexy, EDS without cataplexy and OSA.

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0534.J

The Association of Sleep-Disordered Breathing and the Multiple Sleep Latency Test in the Wisconsin Sleep Cohort Study

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Introduction: In clinical populations, sleep-disordered breathing is strongly associated with excessive daytime sleepiness, measured objectively with the multiple sleep latency test (MSLT) or subjectively. However, there is little evidence from population studies that screen-detected sleep-disordered breathing (SDB) is strongly related to excessive sleepiness; data on objectively measured sleepiness is particularly sparse. The aim of this study was to quantify the association of sleep-disordered breathing and MSLT score in the Wisconsin Sleep Cohort Study, a population-based ongoing longitudinal study of men and women ages 30-75 years.
Methods: The sample comprised 850 participants who had undergone a MSLT within 6 months of an overnight protocol. Baseline and up to two 4-year follow-up studies of 377 women and 473 men provided 1105 observations. The categories of sleep-disordered breathing were developed from self-reported habitual snoring and the apnea-hypopnea index (AHI) determined by in-laboratory polysomnography. The association between SDB and MSLT was estimated with both survival analysis and logistic regression, controlling for age, body mass index, smoking status, alcohol use, sleep diary, and caffeine, cigarette use and discomfort on the day of the study. Sleep latency for each nap trial was modeled using survival analysis, which is appropriate because each nap is terminated (censored) if the subject does not fall asleep. Multiple-event survival analysis techniques accounted for differences in the per-nap baseline hazards and correlation among naps. Sudaan software was used to produce robust standard errors which also accounted for within-subject correlation. Separate models were fit for men and women because of differences in sleep latency and sleep disordered breathing. Multiple logistic regression was used to model the association of SDB and a mean MSLT < 5, the usual clinical definition of excessive daytime sleepiness. GEE modeling techniques were used to obtain robust standard errors that account for within-subject correlation.
Results: Using nonhabitual snorers with an AHI < 5 as the reference category, men who were habitual snorers with AHI < 5 (simple snorers) had a hazards ratio of 1.38 (95% CI: 1.13 – 1.70); men with an AHI ³ 15 had a hazards ratio of 1.33 (95% CI: 1.02 – 1.72). Women did not show an increased hazard of falling asleep for any level of SDB.Simple snorers also showed in increased odds ratio (1.80, 95% CI: 1.10 – 3.21) of having a mean MSLT < 5. There were no other significant relationships between the MSLT and SDB for men or women.
Conclusions: Men with sleep-disordered breathing compared to men without have more objectively-measured excessive daytime sleepiness, but there is no apparent dose-response relationship. Both statistical techniques identified habitual snoring as a risk for increased daytime sleepiness as measured by the MSLT. The survival technique also found an association between men with AHI ³ 15 and the hazard of falling asleep during the MSLT.

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0535.J

Improved Alertness in CPAP-treated Patients Not Meeting New Medicare Criteria for CPAP

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Introduction: New Medicare criteria for prescribing continuous positive airway pressure (CPAP) went into effect on April 1, 2002. Part of the new criteria involved re-defining hypopnea as requiring a 4% decline in oxygen saturation. Thus, by Medicare definition, an episode of significant flow limitation terminated by CNS arousal is not a hypopnea. Traditional sleep medicine definitions accept either an arousal or a desaturation event for defining hypopnea. In a previous published report, we found that 41% of patients with an apnea+hypopnea index (AHI) of 20 or less (using a traditional definition for hypopnea) would not qualify for CPAP using the new Medicare guideline. In the present study, we examine CPAP-related changes in alertness in a sample of patients who did not qualify for CPAP under the new Medicare criteria but who nonetheless had a traditionally scored AHI of 20 events per hour, or more.
Methods: All patients were referred for evaluation of sleep-disordered breathing. Epworth Sleepiness Scale (ESS) was administered as part of a larger screening battery during initial consultation. Attended, overnight, comprehensive polysomnography was conducted. Recordings were scored for sleep stages, sleep-disordered breathing, leg-movement activity, and EEG arousals according to standard technique. Two types of hypopnea were scored: (1) traditionally defined hypopnea (i.e., 30% or more decline in airflow associated with an arousal -OR- an oxygen desaturation event) and (2) Medicare defined (must have a 4% or more oxygen desaturation event). The latter type of hypopnea were designated as DHs (desaturating hypopneas) and summarized as apnea + desaturating hypopnea index (ADI).
Results: We identified 25 patients with a traditional AHI of 20, or greater, but who did not qualify for CPAP under Medicare rules because of a low ADI. During follow up at 3-5 weeks post-CPAP therapy, machine utilization was determined and ESS was administered. 18 subjects had been using their machines regularly. Mean ESS for these 18 patients was 14.3 at baseline and had declined to 6.5 at follow up ($p<0.01$).
Conclusions: Our results indicate that patients with significant sleep-disordered breathing who do not qualify for CPAP under the new Medicare Guidelines can nonetheless benefit from treatment with positive airway pressure. Further work is needed to determine if the improved alert-

ness indexed with ESS can be verified using physiological measure of sleepiness (e.g. MWT or MSLT). However, improved alertness indicates that there is therapeutic benefit for these patients.

0536.J

Determinants of Altered Quality of Life in Patients with Sleep-Related Breathing Disorders

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Introduction: Several studies have demonstrated that a large number of patients with sleep-related breathing disorders (SRBD) may have altered health-related quality of life scores using either generic questionnaires such as the Medical Outcome Survey Short Form (SF-36) or disease-specific questionnaires such as the Calgary Sleep Apnea Quality of Life, all showing impairment more frequently in vitality and social functioning. Despite the frequent association between SRBD and altered daily functioning and well-being, no data are available in the literature concerning the mechanisms underlying these psychological disturbances. The primary aim of the study was to determine whether daytime sleepiness, sleep fragmentation, recurrence of breathing disorders or hypoxemia would better predict the degree of changes in quality of life measures in these patients
Methods: 130 patients, 28 females and 102 males, aged 53.6+0.9 years, with a mean body mass index (BMI) of 31.8+0.6 Kg/m2, a mean neck circumference of 41.4+0.3 cm, and a mean AHI of 32.2±2.4, were examined. In all patients daytime sleepiness was assessed by the administration of the Epworth Sleepiness Scale (ESS), Stanford Sleepiness Scale (SSS), Visual Analogic Scale (VAS) and by the Maintenance Wakefulness Test (MWT). Health-related quality of life (HRQL) scores were examined by using the SF-36 questionnaire. For descriptive analysis, an AHI cut-off point of 15 was used to stratify patients in two groups, "snorers": AHI <15 (n:49), and "OSA" AHI >15 (n:81).
Results: SRBD patients had significantly worse mean scores in all dimensions when compared to normative data. The greatest differences were seen for "role physical", "vitality", "social functioning" "role emotional", and "mental health" ($p<0.001$) dimensions, followed by significant differences in the "physical function" and the "general health" scores. OSA patients had worse scores in the "physical functioning", "role physical", "bodily pain" and "general health" dimensions compared to snorers but the differences did not reach statistical significance. BMI correlated negatively with all domains. Minimal nocturnal oxygen saturation, amount of stage 1 and slow wave sleep were correlated mainly with "physical functioning" and "role physical" items, and to a lesser degree with "general health" and "vitality" scores. AHI and number of macroarousals were related to "physical functioning". Subjective perception of daytime sleepiness (ESS, SSS, VAS) contributed significantly to lower scores for all 7 domains. Conversely, objective measurements of daytime sleepiness (MWT) correlated positively with all HRQL scores albeit "role emotional". A stepwise multiple regression analysis including BMI, nocturnal parameters, and indices of daytime sleepiness as independent variables, and successively SF-36 scores as dependent variables, showed that for "physical functioning" a model including BMI, amount of stage 1 and SSS could explain 24% of the variance. Identical significant predictors were found for "role physical" dimension, ESS, BMI and amount of slow wave sleep explaining 15% of the variance. Subjective daytime sleepiness, as defined by the SSS and ESS scores, mostly contributed to the variance of "general health" (14%), "vitality" (15%) and "social functioning" (17%) dimensions.
Conclusions: SRBD patients reported lower social functioning, more limitations in function due to physical and emotional reasons and a lowered sense of well-being for mental health and energy. This predisposition seems to be independent of the AHI and nocturnal hypoxemia as demonstrated by the comparison of patients with and without OSA. While objective assessment of SRDB (hypoxemia, AHI, sleep disruption and sleep fragmentation) appeared to have a small impact on scores relative to physical functioning, obesity and daytime sleepiness contributed more significantly to impairment in all domains of the SF-36 questionnaire.

0537.J

Cephalometric Variables Of Sleep-Disordered Breathing Among Japanese Men And Women In A Sleep Check-up Clinic

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Introduction: Cephalometric abnormalities have been considered to be associated with sleep-disordered breathing (SDB), and recently craniofacial morphology and body mass index (BMI) accounted equally for one half of the total variance in apnea-hypopnea index in male subjects with the entire continuum of SDB. However, the protective effect of gender on SDB in respect of craniofacial structure was not analyzed, and previous studies have shown that SDB was disproportionally severe in non-obese Asian patients compared to the Caucasians due to characteristic craniofacial morphology. We analyzed our cephalometric data in relation to overnight oxymetry among Japanese men and women.
Methods: We studied consecutive people (184 men and 65 women) who came to our sleep check-up clinic between Nov. 2001 - Nov. 2002. This sleep check-up clinic was aiming at screening moderate to severe SDB by using home pulse oxymetry (Minolta Pulsox 3i wrist oxymeter). One man and three women were excluded due to technical errors of cephalometric radiography, so we studied 183 men and 62 women (mean age: M 53.4±13.0, W 54.3±11.8, mean BMI: M 25.9±3.6, W 22.9±3.5). All subjects completed lateral facial cephalometric radiographs, comprehensive sleep questionnaire, and overnight pulse oxymetry at home. We determined the oxygen desaturation index (ODI) as the number of desaturations ±3% per hour of recording time from the baseline. We measured seven cephalometric dimensions (SNA, SNB, ANB, SN, PNS-P, H-MP, IAS) that had been already reported to be associated with the severity of SDB. Data was analyzed using ANOVA, stepwise regression, and multiple logistic regression.
Results: The mean ODI was 20.0±20.7 in men, and 6.9±9.3 in women. In men, BMI, H-MP, SN, PNS-P, and SNB accounted for 43.0% of the total variance in ODI. BMI was the most influential variable, accounting for 33.7%. There is great difference between men and women in probability of showing high ODI. For men the probability of having ODI of 15 or more increased 6.5 fold (95%CI :2.4±22.0; BMI and age adjusted) or 5.4 fold (95%:1.7±21.0; BMI, age, H-MP, SN, PNS-P, and SNB adjusted). There was a menopausal effect on ODI between pre- (n=15) and post-menopausal women (n=44). After BMI, age and cephalometric parameters were adjusted, mean ODI of the former was 0.99, and the latter 8.60 ($p<0.03$).
Conclusions: BMI and four simple cephalometric measures accounted for 43.0% of the variation in ODI among Japanese subjects. Men showed stronger probability to have SDB, pre- menopausal women were a most SDB-free group. Our study provides a new picture of the cephalometric and gender analysis of SDB in the Japanese.

0538.J

CPAP Decreases Blood Pressure In Sleep Apnea Patients With Hypertension

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Introduction: Sleep apnea is being aggressively studied as a risk factor for hypertension. This observational chart review was conducted in order to determine the long term effects of Continuous Positive Airway Pressure (CPAP) on blood pressure in a sample of sleep apnea patients from urban and rural populations.
Methods: This study was conducted using data from one hundred seventy-eight clinical charts from the years1995-2002 from patients seen in an urban (Toronto) and rural (Parry Sound) sleep clinic. Patients were identified as hypertensive (systemic blood pressure >140 mmHg) or normotensive. The final recording of blood pressure was obtained from their follow-up appointments.
Results: Thirty-two percent of the patients diagnosed with sleep apnea were found to have hypertension (mean systolic = 164.4 ± 20.3 mmHg, mean diastolic = 96.9 ± 5.3 mmHg). The average use of CPAP was 12.1 ± 22.4 months. The hypertensive group showed a significant reduction in blood pressure: systolic blood pressure dropped by an average of 21.1 mmHg (p=3.7 X 10-5) and diastolic blood pressure dropped by an average of 11.8 mmHg (p= 0.002). Blood pressure in the normotensive group did not significantly decrease after CPAP treatment. Among the patients with sleep apnea, 58% of those with hypertension became normotensive after CPAP treatment.
Conclusions: Our results confirm that the prevalence of hypertension is increased among sleep apnea patients. The long term use of CPAP in hypertensive patients with sleep apnea is associated with a significant decrease in blood pressure to levels such that their cardiovascular risk decreases considerably. In this study, CPAP treatment was shown to reduce blood pressure to normotensive levels in over half of our patients with sleep apnea.

0539.J

Time-dependent Impairment Of Spatial Working Memory Following Chronic Intermittent Hypoxia (CIH) In The Rat

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Introduction: Exposure to CIH, such as occurs in Obstructive Sleep Apnea (OSA), is associated with substantial impairments in spatial reference memory in rodents, which are preceded by neurodegenerative changes in the CA1 region of the hippocampus (HPC) and cortex. However, OSA patients show a pattern of executive dysfunction that is consistent with prefrontal cortex (PFC) damage and/or impaired function, suggesting that disruption of hippocampal prefronto-cortical circuits plays an important role in the neurocognitive deficits observed with OSA patients. In the rodent, both PFC and HPC are required for intact spatial working memory (SWM), suggesting that working memory deficits may be more severe in animals exposed to intermittent hypoxia.
Methods: To examine the effect of CIH on SWM, a delayed matching to place (DMP) task in the water-maze was used in 16 male rats (8 weeks of age; 175-200g). During each daily training session, rats were required to locate a submerged platform hidden in a novel location on the first trial (acquisition trial), and then retain that position 10 min later (test trial). Rats were exposed to Room Air (RA, n=8) or CIH (n=8) consisting of alternating 90 second epochs of 21% O2 and 10% O2. SWM was assessed at 1, 5-7, and 12-14 days of CIH exposure. To assess working memory performance during DMP training, mean escape latencies and swim distances were derived from trial 1 (acquisition trial) and trial 2 (retention trial) of each training session and the differences (T1 – T2) were analyzed by one-way repeated measures ANOVA. A p value <0.05 was considered statistically significant.
Results: Peak impairment of working memory occurred at 5-7 days of CIH exposure (p<.001 and p<.029 for pathlength and latency, respectively), with partial functional recovery observed at 12-14 days (p<.006 and p<.046 for pathlength and latency, respectively). No significant group differences emerged after 1 day of CIH exposure, and no significant differences in swim speeds, latency, and pathlength to locate a cued platform were present, indicating that SWM differences were not due to sensorimotor impairments.
Conclusions: Exposure to CIH results in substantial impairment of spatial working memory which is time-dependent. Thus, CIH-induced disruption of hippocampal prefronto-cortical circuits is likely to play an important role in the cognitive deficits associated with OSA.

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0540.J

Control of Upper Airway Muscle Activity During Sleep Onset

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Introduction: During wakefulness, upper airway muscle activation is driven both by central pattern (CPG) generator input and local activation via a negative pressure reflex (NPR) mechanism. During passive negative pressure ventilation (NPV) in an iron-lung, (with markedly decreased or absent CPG input), upper airway muscle activation is maintained during wakefulness via the NPR. Therefore, the amount of muscle activation (GGEMG) is directly proportional to the level of epiglottic negative pressure, and the slope of this relationship (GGEMG/Pepi) is constant between different breathing conditions. While it is known that this reflex is largely lost during stable NREM sleep, the time course over which this occurs is not well understood.
Methods: We studied 12 normal subjects (7 males) during passive NPV and during basal breathing (BB). We measured genioglossal (GGEMG) and diaphragm (DiEMG) EMG, airflow and pharyngeal resistance during multiple transitions from wakefulness to sleep (a-)under both breathing conditions. Breaths were scored as a (wake) or (sleep) and defined by their position relative to the state transition. The effect of breathing condition on the state-related changes in upper airway muscle activity were then compared.
Results: Peak GGEMG was higher during a during NPV compared to BB (47.4 vs. 29.7 AU, $p < 0.05$) due to more negative airway pressure. The fall in GGEMG at the a-transition was also substantially greater during NPV (13.44 ± 3.0 vs. 4.0 ± 0.9 AU, $p < 0.01$) compared with BB. However, peak GGEMG remained slightly greater at breath 2 following the transition during NPV. Pharyngeal resistance was greater during NPV awake (2.99 vs. 1.82 cmH2O/l/s, $p < 0.01$) and rose to a greater degree at the a-transition (1.04 vs. 0.17 cmH2O/l/s, $p < 0.05$).
Conclusions: These results suggest that there is an abrupt reduction of the negative pressure reflex at sleep onset, thus removing an important protective mechanism for defending upper airway patency. However, the fact that peak GGEMG was still slightly higher during NPV in the immediate post-transition period suggests that some NPR remains at this time point.

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0541.J

Central Sleep Apneas and Supine Dependency

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Introduction: Obstructive sleep apneas are most frequent in the supine position but the impact of body position on central sleep apneas is unknown. We aimed to study the effect of body position on central apneas and to compare such effect to that of obstructive. A second objective was to study the effect of sleep stages on central and obstructive sleep apneas.
Methods: One hundred and ninety-three consecutive over-night polysomnographies including body position measurements were retrospectively examined. Central sleep apnea was defined as a central apnea-hypopnea index (AHI) >15 together with obstructive AHI <5. Obstructive sleep apnea was defined as obstructive AHI >15 together with central AHI <5.
Results: Central sleep apnea was found in 28 patients. The central AHI among them was 41.7 ±16.0 in the supine position and 23.6 ±16.3 in non-supine positions (p<0.001). Central sleep apneas were most frequent in sleep stage 1 and 2 (p<0.001). Obstructive sleep apnea was observed in another 34 patients. The obstructive AHI among them was 47.1 ±22.5 in the supine position and 26.9 ±17.0 in non-supine positions (p<0.001). Obstructive apneas were most frequent in sleep stage 1, but rare in slow wave sleep (p<0.001).
Conclusions: Central sleep apneas occur more frequently in the supine position than in the lateral and prone positions. The effect of the supine position for the generation of sleep apneas is, in fact, as high for central apneas as for obstructive. Both central and obstructive sleep apneas are most frequent in sleep stage 1 and 2. Obstructive apneas are rare in slow wave sleep.

0542.J

Depressive Symptoms Predict Fatigue More Than Disease Severity In Obstructive Sleep Apnea (OSA)

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Introduction: We have previously reported that various OSA sequelae are more strongly associated with patient characteristics (age, body mass index (BMI), blood pressure, coping, mood) than with the OSA itself. More specifically, we recently observed that fatigue in OSA patients appears to be driven by depressive symptoms, not OSA severity (as measured by respiratory disturbance or blood O2 saturation (SaO2)). Here, we attempt to replicate and expand on this finding using a new dataset and multiple measures of fatigue.
Methods: OSA patients (n=52) were recruited by advertisement and word of mouth, were 100-150% of ideal body weight and free of major illness other than OSA. Patients were studied for two nights with polysomnography. OSA was defined as an apnea-hypopnea index (AHI) >=15 (mean=63; SD=32, range=16-136). Percent of time SaO2<90% was computed (mean=7%; SD=12%; range=0-49%). Patients completed the POMS, Medical Outcomes Studies Functioning and Wellbeing (MOS), Multidimensional Fatigue Symptom Inventory (MFSI), and Center for Epidemiological Studies—Depression (CES-D) scales. Data were analyzed using SPSS 10.1 correlation and multiple regression. CES-D scores >=16 indicate the probability of a diagnosable mood disorder. Therefore, we also used multivariate analysis of covariance (MANCOVA) to determine the degree to which fatigue differs in OSA patients likely/not likely to have a clinical mood disorder.
Results: Significant correlations were observed for POMS Fatigue with BMI (r=.40, p=.003), SaO2<90% (r=.35, p=.011), and AHI (r=.29, p=.037); therefore, these three variables were included as covariates in the analyses. In multiple regression (R2=.42, F=8.65, p<.001), SaO2<90% (B=9.53, t=1.21, p=.23), AHI (B=-.02, t=-0.45, p=.65) and BMI (B=.27, t=1.63, p=.11) explained 19% and CES-D (B=.38, t=4.34, p<.001) another 23% of variance in POMS Fatigue. In MANCOVA, the Hi CES-D group reported 60% higher POMS Fatigue than the Lo CES-D group (13.9 vs. 8.8, p=.008). Similar results were obtained using MOS Energy/Fatigue and MFSI scales instead of POMS Fatigue.
Conclusions: Depressive symptoms account for more fatigue than OSA severity. Patients likely to have a mood disorder report considerably higher fatigue than other OSA patients. These associations remained remarkably robust across three commonly-used measures of fatigue. Assessment and treatment of mood, not just the disordered breathing itself, might reduce the fatigue experienced in OSA.

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0543.J

Is Snoring In the Ear of the Beholder?

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Introduction: Patients who claim that they snore so much that they wish to undergo surgery are usually, without any testing, classified as habitual snorers. To test whether this assumption is correct we investigated patients demanding treatment for snoring from a private ENT surgeon.
Methods: 368 patients, 108 women and 260 men, were investigated overnight with digital home recordings (Apnolog®) including respiration movements, ear oximetry, body position and snoring sounds (dB). Snoring sounds were recorded by a dB-meter placed at a bed partner's distance. The average dB-level of the entire sleep period was compared with the dB-level of the 5% of the night when the sound was most loud. Snoring was graded into four levels: no snoring (1-2 dB difference), slight snoring in periods (3-5 dB difference), continuous snoring of intermediate loudness (6-9 dB difference), loud continuous snoring (>10 dB difference). The recordings were also checked manually for artifacts and estimation of time during which the patient snored and periodic breathing time. Oxygen Desaturation Index (ODI) was calculated by the soft-ware.
Results: 82 patients (22% of the entire group) were classified as non-snorers. The rest were snoring; 51 patients (14%) slightly, 77 patients (21%) moderately and 158 patients (43%) loudly. There was no significant difference between men and women concerning prevalence of snoring, nor between degree of snoring and age or Body Mass Index (BMI). Obstructive Sleep Apnea (OSA) was diagnosed in 59 cases (ODI >6, >40% periodic breathing), and another 43 cases were borderline. None of these were silent. ODI was significantly correlated to degree of snoring (r= 0.41, p=0.0002).
Conclusions: 22% of patients who claimed that they snored to such an extent that they wanted surgical treatment were silent throughout one night of objective sound recording. These results indicate that snoring quite often can be placed in the ear of the beholder and no where else. The reason for the discrepancy between subjective and objective findings remains unclear. In some cases the recording night might have been unusually good, perhaps due to lack of alcohol or nasal congestion, but if so it can be argued that the patients were not habitual snorers. In some other cases, partner interviews made it obvious that there were other kind of marital problems than snoring, prompting a wish for separate bedrooms. On basis of our results we advocate that objective sound recordings should be made prior to surgical treatment.Our results also indicate that there is a positive correlation between degree of snoring and respiratory distress, which has previously been questioned.

0544.J

Percentages of Sleep Stages 3/4 and REM in Relation to the Respiratory Disturbance Index (RDI) in Men and Women

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Introduction: Studies that have examined sleep architecture in patients with sleep apnea syndrome (SAS) compared to controls have noted decreases in sleep stages 3/4 and REM. However, none have examined changes in sleep architecture systematically with increasing apnea severity on a large patient population. In the present study, changes in sleep stages 3/4 and REM with increasing respiratory disturbance indices (RDI) are reported for men and women.
Methods: Data from 4678 consecutive patients who were referred to the Technion Sleep Laboratories between 1994-2000 for overnight polysomnography due to suspected SAS were retrospectively studied. Patients included 3784 men aged 20-89 (mean age 48±12) and 894 women aged 20-84 (mean age 52.5±12). Sleep stages and RDI were determined by traditional scoring criteria. Sleep stages 3/4 and REM in minutes were transformed to percentages of total sleep time (TST) and normalized by ranking. RDI was categorized (CRDI) into 7 levels: 0-9, 10-19, 20-29, 30-39, 40-49, 50-59, =>60. A multivariate general linear model (GLM) was performed by gender, with CRDI as the independent variable, ranked percentages of sleep stages 3/4 and REM as dependent variables, and age (categorized by decades) as a covariate. Planned contrasts were performed between each two successive CRDI levels.
Results: Percentages of stages 3/4 and REM decreased between lowest and highest CRDI levels on average by 19% and 5% in men and by 20% and 8% in women respectively. The GLM model was significant ($p<0.001$) for ranked percentages of stages 3/4 ($F=266.2$, $F=51.4$) and REM ($F=33.9$, $F=14.4$) for men and women respectively. Planned contrasts revealed significant differences between each two successive CRDI levels for ranked percentages of stages 3/4 ($p<0.01$ for men and $p<0.05$ for women) and REM ($p<0.05$, excluding levels 2 vs. 1 for men and levels 2 vs. 1 and 3 vs. 2 for women).
Conclusions: In the present study we have demonstrated on a large patient sample systematic declines of sleep stages 3/4 and REM with gradual increases in RDI. The particularly striking declines in stages 3/4 with increased apnea severity may be the underlying factor for pathological daytime somnolence.

0545.J

Prevalence of Sleep Apnea Syndrome and it's Association with Quality of Life after Kidney Transplantation

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Introduction: A high prevalence of sleep disorders has been reported in patients on maintenance dialysis. Sleep disorders may impair quality of life (QoL) of the patients. The estimated prevalence of Sleep Apnea Syndrome (SAS) is 21-47% in this population and it also contributes to the cardiovascular comorbidity of patients with chronic renal failure (CRF). It is not known, however, if successful kidney transplantation would reduce the prevalence of SAS in patients with CRF. The aim of our study was to estimate the prevalence of SAS and examine the association between the health-related quality of life and presence of SAS after kidney transplantation.
Methods: Here we report data obtained in 398 patients living with a functioning kidney graft followed at the transplant center of the Semmelweis University, Budapest. The mean age of the patients was 47±13 years (18-78 years), 57% male, 16% diabetics. The mean serum creatinine level was 156±75 micromol/l, mean hemoglobin level was 135±45 g/l. The patients were administered a battery of questionnaires including the Berlin Questionnaire (Netzer NC. et al., 1999) to estimate the risk for SAS. Also included in the battery was the "Kidney Disease Quality of Life Questionnaire" (KDQoL) (Hays et al, 1995), a modular, kidney disease-specific, self-administered questionnaire that contains the SF-36, a widely used generic QoL instrument. KDQoL scales measure between 0-100 points, the higher suggesting a better QoL. We also recorded laboratory data, disease history, and medications.
Results: 22.6% of the patients scored high risk for SAS on the Berlin questionnaire. The serum creatinine level of patients with high risk for SAS was significantly higher than the rest of the population (174.9±89.4 micromol/l vs. 146.1±61.3 micromol/l, $p<0.01$) while serum albumin and also the hemoglobin concentration were similar between the groups. There was, however, a statistically and clinically significant difference in numerous QoL domains between patients with high versus low risk for SAS. The SF-12 Physical Composite score was 39.8±9.8 in patients with high versus 44.8±10.3 in patients with lower risk for SAS ($P<0.001$). Similarly the SF-12 Mental Composite score (46.5±11.6 vs. 50.7±11.2, $p=0.04$), the "energy/fatigue" score (54.5±22.2 vs. 68.7±22.7, $p<0.001$) and also the "sleep" score (67±17.8 vs. 75.4±16.8, $p<0.001$) were significantly lower in patients with high risk for SAS, suggesting poorer quality of life.
Conclusions: The prevalence of SAS as estimated by the Berlin questionnaire was somewhat lower in our kidney transplant patients than published previously for patients on maintenance dialysis. High risk of sleep apnea syndrome was associated with poorer quality of life.

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0546.J

Prevalence of Glaucoma in Patients with Obstructive Sleep Apnea-A Prospective Case-Series

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Introduction: It has been previously suggested that patients with obstructive sleep apnea (OSA) are at risk of developing glaucoma. Mojon et al (Ophthalmology 1999; 106:1009) reported the presence of glaucoma in 7.2% (5 of 69) of patients referred for polysomnographic examination.
Methods: We report an ongoing, prospective case-series that has examined 46 consecutive patients with confirmed OSA [apena-hypopnea index (AHI) > 15] for the presence of glaucoma. All patients were evaluated with a complete ophthalmologic examination, which included a direct measurement of intraocular pressure (IOP) via goinoscopy, visual field indices, and direct visualization to identify the presence of glaucomatous optic disk changes. A single glaucoma specialist performed all exams. Pertinent variables such as age, sex, body-mass index (BMI), AHI, IOP, and positive diagnoses of glaucoma were tabulated and analyzed for correlation in all patients.
Results: Sixteen of 46 patients were females. The median age and BMI (body-mass index) of the study group were 60 and 34, respectively. 19 of 46 [41% (95% confidence intervals =28.3-57.8)] patients were confirmed to have glaucoma with the presence of glaucomatous optic disk changes and elevated IOPs. The mean AHI and IOP in glaucoma patients were 49 (SD =26.2) and 17 (SD=4.3), respectively as compared to non-glaucoma patients' median AHI and IOP of 51 (SD=27.6) and 15

(SD=2.5), respectively. The AHI did not correlate with the diagnosis of glaucoma (p=0.6). However, there was a slight trend towards the presence of glaucoma or high IOP with an abnormal AHI.
Conclusions: Patients with OSA have a risk of associated glaucoma and should be screened for this disease.

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0547.J

Proteomic Approaches Reveal Differential Urinary Protein Expression In Patients With Sleep-Disordered Breathing

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Introduction: Patients with sleep-disordered breathing (SDB) are at risk for cardiovascular morbidity, particularly hypertension. Based on differential expression of kidney proteins in a rodent model of SDB, we hypothesized that analysis of proteins in human urine may provide reliable non-invasive biomarkers for the presence of SDB.
Methods: Adult male subjects referred for suspected SDB underwent overnight polysomnography. They were considered to have SDB if their AHI was >30. Conversely, they were assigned to the control group if the AHI was <5. Urine samples were collected in the morning after the sleep study. Proteins were isolated by acetone precipitation and separated by two-dimensional polyacrylamide gel electrophoresis (2D-PAGE), and identified by matrix-assisted laser desorption ionization-time-of-flight (MALDI-TOF) mass spectrometry followed by peptide mass fingerprinting.
Results: Thus far, 3 control subjects and 5 patients with SDB have been analyzed. The human urinary proteome includes a total of 67 protein forms from which 47 proteins have been conclusively identified. Of these, one protein so far has been identified as being distinctly and consistently over-excreted in patients with SDB compared to controls. Indeed, urinary levels of alpha-1B-glycoprotein were 19958±7554 densitometry units (DU) in SDB patients vs. 2252±402 DU in controls ($p < 0.03$).
Conclusions: The increased expression of alpha-1B-glycoprotein in the urine samples from patients with SDB suggests that some degree of glomerular and/or tubular insult has occurred in these patients, and that the kidney is yet another organ adversely affected by the processes underlying tissue injury in SDB.

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0548.J

The Role of Ventilatory Instability in Obstructive Sleep Apnea

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Introduction: It is unclear if obstructive sleep apnea (OSA) is predominantly a disease of abnormal pharyngeal anatomy, or whether abnormal anatomy simply acts to exacerbate an underlying disorder in ventilatory control. We hypothesized that both factors play a contributing role, and that the primary mechanism may be different depending on the individual. We began testing this hypothesis by measuring both passive pharyngeal anatomy [pharyngeal critical closing pressure (Pcrit)] and ventilatory control stability [loop gain (LG)] in a group of OSA patients. LG, an engineering term, is used to describe the inherent instability in a system controlled by feedback loops, like respiration. Mathematically, it is the ratio of a corrective response (hyperpnea) to a disturbance (apnea). If the corrective response is greater than the disturbance (LG >1), ventilation will oscillate (periodic breathing) following even small disturbances. Proportional assist ventilation (PAV) increases the numerator in the LG ratio (by amplifying respiratory effort) and thus can delineate how susceptible a subject is to periodic breathing; individuals requiring large amounts of PAV to bring LG to > 1 (periodic breathing) have a low LG (close to zero), and vice-versa.
Methods: First, LG was measured by progressively increasing the amount of PAV support until either periodic breathing or awakening occurred. The amount by which PAV amplified a patient's intrinsic LG was quantified from the tidal volume amplification factor [(VTAF) assisted tidal volume/unassisted tidal volume]. LG was then calculated as the inverse of the VTAF occurring at the assist level immediately preceding the emergence of periodic breathing (when LG x VTAF = 1). Second, Pcrit was measured by intermittently dropping nasal pressure for 3 breaths to successively lower levels from an optimum level (the pressure that abolished flow limitation). The third breath in each pressure drop was analyzed for flow limitation (using visual criteria of the pneumotach flow tracing) and used to construct a pressure-flow regression line. Pcrit was taken as the x-intercept of this line, which is the nasal pressure at which flow stopped. Last, apnea severity was measured with the AHI determined from supine, NREM sleep.
Results: 5 subjects have completed the study to date. LG, Pcrit, and AHI in all 5 subjects are as follows. Subject 1: 0.32, +1.91, 73. Subject 2: 0.41, -4.47, 14. Subject 3: 0.31, +1.4, 32. Subject 4: <0.45, -0.16, 37. Subject 5: 0.38, +1.08, 80. Both Pcrit and LG correlated poorly with AHI (R-square values 0.54 and 0.10, respectively) in univariable models. This correlation improved (R-square 0.64) when both variables were considered together.
Conclusions: We were able to explain 64% of the variance in AHI using both Pcrit and LG in this small study. However, more subjects with a broader range of LG's will need to be studied in order to draw firm conclusions about the role of ventilatory instability in OSA.

0549.J

Racial Differences in Sleep Apnea Severity in a University Based Sleep Disorders Center

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Introduction: Sleep apnea is a serious problem that may be more severe in African-American (AA) patients than in Caucasians (C). This could have implications for resource requirements in sleep centers serving populations with larger proportion of AA patients. We compared sleep apnea severity in patients presenting to the sleep center at the University of Maryland to determine if in fact sleep apnea is more severe in AA patients presenting to a sleep center than in C.
Methods: The University of Maryland Medical Center is a large urban medical center serving a mixed racial population in downtown Baltimore and the state of Maryland. We analyzed 141 patients presenting with symptoms of sleep apnea to our Sleep Disorders Center. All patients were referred for symptoms of excessive somnolence and snoring, and all carried medical insurance. All were evaluated by the same team of physicians. Polysomnography for diagnosis of Sleep Apnea was carried out using standard techniques for gathering and scoring data. The degree of excessive daytime somnolence was assessed with the Epworth Sleepiness Scale (ESS).
Results: 53.9% of the patients were male. 51.7% were AA. AA were younger than C (41.6±14.7 vs 50.8±13.3 yrs; p<.0001). Body Mass Index (BMI) was greater in AA than C (41.6±11.2 vs 34.2±11.7; p<.0009) as were Respiratory Disturbance Index (RDI) (42.1±39.4 vs 30.5±23.7; p<.04) and REM RDI (47.5±31.7 vs 30.8±23.9; p<.0008). However, ESS scores were similar in AA and C (13.8±6.2 vs 12.2±5.1;

NS). Sleep architecture (Sleep latency, TST, % SWS and %REM) were also not different between the groups. Percent of the night with O2 saturation less than 90% (T90) was greater in AA than C (20.6±30.3 vs 11.1±22.0%; p<.011). When we adjusted for differences in BMI (ANCOVA), the racial difference in overall RDI was reduced to borderline significance (p<.054), while the difference in REM RDI was still highly significant (p<.0003).

Conclusions: In this population, both AA and C patients presented with similar symptom severity (ESS). AA were younger, heavier and had more severe disease. When adjusted for BMI, REM RDI was still greater in AA. This may indicate racial differences in facial structure, upper airway muscle tone or respiratory control in AA, especially during REM sleep, each of which could increase apnea severity.

0550.J

Differentially Regulated Genes in Peripheral Blood of Children with Obstructive Sleep Apnea

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Introduction: Obstructive sleep apnea syndrome (OSAS) is characterized by episodic hypoxemia, hypercapnia, and arousal during sleep, and is associated with significant cardiovascular and neurocognitive deficits in children. However, the mechanisms underlying such morbidity are currently unknown.

Methods: To identify gene expression patterns that characterize OSAS, we analyzed peripheral blood RNA from children with and without OSAS using oligonucleotide micorarrays. Total RNA was extracted from whole blood of 4 children with OSAS, 3 primary snorers and 2 healthy controls. Purified mRNA was used as template for double stranded DNA synthesis, and c-RNA transcription. Labeled probe was hybridized with Affymetrix Human Genome U133A oligonucleotide microarrays that allow the simultaneous profiling of approximately 20,000 genes. For data clustering and visualization we used publicly available software packages such as Treeview, GeneCluster, and Click. For statistical analysis we used non-parametric scoring methods, TnoM, and Info, all available in Scoregene Package.

Results: Of the 20,000 genes represented on the array, expression levels for 194 genes were significantly higher and 178 genes were lower in the OSAS group compared to the non-OSAS group. This was higher (>2-fold) than predicted by the null hypothesis. Subset gene analyses permitted identification of multiple regulated genes that did not overlap between OSAS and non-OSAS children. Among these genes (approximately 150), the following functional categories were primarily represented: cell survival, cytoarchitectural integrity and modulation of apoptosis, regulation of metabolism, immune system, neuronal interaction and synaptic transmission, and endocrine/cardiovascular function.

Conclusions: OSAS children exhibit distinct gene expression patterns in their peripheral blood. These include alterations in multiple functional groups of genes that may represent both adaptive and injury-related pathways elicited by the disease process. Expansion of these findings to a larger cohort for additional confirmatory purposes is currently underway.

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0551.J

Gender Differences in Clinical Presentation of Patients Diagnosed with Obstructive Sleep Apnea

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Introduction: Obstructive sleep apnea syndrome (OSAS) is characterized by recurrent episodes of breathing cessation, followed by awakenings from sleep resulting in daytime sleepiness. OSAS patients have a higher prevalence of cardiovascular disease, decreased memory, concentration, and more motor vehicle crashes. Population based epidemiological studies have shown that OSAS is more prevalent in males compared to females (4% vs 2% or a 2:1 ratio). Previous studies have explored gender-related differences in upper airway anatomy and function, hormonal physiology and polysomnographic findings. To date, little information has been published about differences in clinical presentation between females and males with OSAS.

Methods: Information obtained from our sleep questionnaire/initial patient assessment of 130 OSAS/upper airway resistance syndrome gender pairs matched for age, body mass index (BMI), apnea/hypopnea index (AHI), and Epworth Sleepiness scale (ESS) was analyzed.

Results: There were no differences between genders for age (48.0 ± 1.1 years [mean±SEM] for females vs 47.6 ± 1.0 years for males (p=.14)), BMI (40.4 ± 0.66 for females vs 40.0 ± 0.62 for males (p=.24)), AHI (36.8 ± 3.3 for females vs 36.0 ± 3.0 for males (p=.11)) or ESS (12.5 ± 0.53 for females vs 12.8 ± 0.47 for males (p=.60)). On initial presentation, females were found to have a statistically significant higher incidence of depression (Odds ratio - OR:4.60; 95% Confidence Interval:[CI] 1.711 to 15.489), history of thyroid disease (OR:5.60; 95%CI: 2.135 to 18.574), history of asthma/allergies (OR:1.90; 95%CI: 1.058 to 3.497), use of psychiatric medications (OR:3.88; 95%CI: 1.742 to 9.756), thyroid medications (OR:4.33; 95%CI: 1.744 to 12.873), asthma/allergy medications (OR:2.63; 95%CI: 1.117 to 6.853), and hormone replacement therapy (OR:10.5; 95%CI: 2.567 to 92.373). Females more commonly described their main presenting symptoms as insomnia (OR:4.2; 95%CI: 1.541 to 14.256), complained more often of heart palpitations (OR:2.5; 95%CI: 1.321 to 4.838) or noticed presence of ankle edema (OR:2.71; 95%CI: 1.522 to 5.035). Females presented less often with known witnessed apneic episodes (OR:0.6: 95%CI: 0.308 to 0.966), subjectively slept more hours/night (8.0 hours vs 7.6 hours in males; p=.01), consumed substantially less caffeine/day (3.3 cups vs 5.2 in males; p=.0001) and admitted much less often to alcohol consumption (OR:0.36; 95%CI: 0.176 to 0.697).

Conclusions: There are some differences in the clinical presentation of sleep breathing disorders between genders. Especially striking is the previous history of depression and thyroid disease in females. Female patients are more likely than males to complain of insomnia, heart palpitations and ankle edema. Males were more likely to have a history of known witnessed apneic episodes, less total hours of sleep per night, consume more caffeinated beverages per day and admit to more alcohol consumption. Based on these findings, clinicians should appreciate that a higher degree of suspicion of sleep apnea is needed in females, as females may present clinically differently from males.

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0552.J

Evidence for Lipids Peroxidation in Obstructive Sleep Apnea

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Introduction: Obstructive sleep apnea syndrome (OSA) is associated

with increased cardiovascular morbidity. Although several mechanisms have been proposed to explain this association, its exact nature is yet to be determined. We hypothesized that the repeated apnea-related hypoxic events in OSA in a similar manner to hyoxia/reperfusion injury, initiate oxidative stress which results in lipids peroxidation. To investigate this hypothesis we determined plasma levels of Thiobarbituric Acid Reactive Substances (TBARS) and lipid peroxides (PD) which are biomarkers of lipids peroxidation, and paraxonase-1 (PON-1), an enzyme protecting Low and High Density Lipoproteins against oxidation, in sleep apnea patients.

Methods: We investigated fasting levels of TBARS, PD and PON1 in 105 untreated OSA patients, 24 OSA patients treated with CPAP and in 103 non-OSA controls. Stepwise regression analysis was used to determine the independent contribution of sleep apnea severity variables (RDI and percent time below 90% oxygen saturation) to the lipids' oxidation biomarkers.

Results: Untreated sleep apnea patients had higher levels of TBARS and PD (17.7±7.4 nmol/ml, 907.4±113.9 nmol/ml) than both controls (13.4±3.6 nmol/ml; 803.5±114.9 nmol/ml) and CPAP treated patients (15.7±3.9 nmol/ml, 858.6±107.3 nmol/ml), and lower levels of PON1 (84.8±16.3, 90.3±15.8, 91.3±11.5 U/ml/minute for OSA, controls and treated OSA, respectively). Stepwise regression analysis using the following variables: gender, existence of: ischemic heart disease, s/p MI, CVA, hypertension, diabetes mellitus, chronic obstructive lung disease, asthma, usage of drugs, smoking, hyprcholestrolemia, "being sick lately," age, BMI, RDI, percent time below 90% arterial oxygen saturation, creatinine, cholesterol, HDL, LDL, triglycerides, and glucose levels, revealed that TBARS concentration was prediceted by RDI, age and COPD (total explained variance: 24% RDI predicted 15%), PD was predicted by RDI, gender, HDL and triglycerides (total explained variance: 29%, RDI predicted 15%), and PON1 was predicted by RDI and BMI (total explained variance: 13%, RDI predicted 11%).

Conclusions: Patients with obstructive sleep apnea have increased rate of lipids peroxidation which contributes to the cardiovascular sequelae of the syndrome.

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0553.J

The Relationship Between Micro Arousals And Pulse Rate Changes During Sleep In Sleep-Disordered Breathing

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Introduction: Apnea-hypopnea index (AHI) has been generally used for evaluation of severity of obstructive sleep apnea-hypopnea syndrome (OSAHS). We have reported that the degrees of desaturation during sleep are well evaluated by AHI, but AHI is insufficient to detect the whole pathophysiology in OSAHS patients.There are possible risks in evaluation of OSAHS using only AHI, such as overlooking upper airway resistance syndrome (UARS) or underestimation of sleep disturbance in mild to moderate OSAHS patients, because AHI doesn't reflect the degree of micro arousals.The aim of this study was to explore the value of transient increase of pulse rate non-invasively measured by pulse oximetry that reflects autonomic arousals as an index of sleep fragmentation during sleep studies on patients suspected of having OSA, evaluating the relationship with EEG micro arousals.

Methods: Twenty-eight consecutive patients (age 25-69 years, mean 47.6±12.1 years) were investigated for sleep related breathing disorders. Polysomnograpy, including pulse oximetry measurement, was performed in all cases. The main outcome measurements in this assessment were: Total arousal index (T-ArI) and PRRI*. Spearman fs rank correlation was used to examine the relationships between T-ArI and PRRI.*: PRRI (Pulse Rate Rising Index); defined as the number of pulse rate rises per hour during sleep, which is calculated by the DS-M software (Minolta, Osaka, Japan). Forexample, PRRI-3 is the number of 3 pulse rate rises per hour during sleep. (X=3 `12)

Results: There was statistically significant correlations between T-ArI and PRRI-X (X=3 `12) which ranged from r=0.558 to r=0.724. The PRRI-4 was the most related to the T-ArI (r=0.724, P=0.0002). It was shown that the PRRIs (especially from PRRI-3 `5) were rather useful for assessment of degrees of EEG micro arousals during sleep. More, our results suggest that autonomic arousals and EEG micro arousals correlate well with each other.

Conclusions: Analyzing the PRRI during sleep, it is possible to evaluate the sleep disturbance in OSAHS, especially in mild to moderate cases which are underestimated frequently by using AHI alone as the diagnostic index. This study has demonstrated that EEG micro arousals and PRRI correlate well. It indicates that PRRI can be a valuable screening marker in evaluation of sleep distrubance of OSAHS, and autonomic arousals may provide a useful alternative to manualscoring of EEG micro arousals according to criteria in American Sleep Disorders Association.

0554.J

Atypical Clinical Presentations Of Sleep-Disordered Breathing Among Trauma Survivors

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Introduction: Many trauma survivors suffer from a common medical disorder, sleep-disordered breathing (SDB)—a known aggravator of insomnia and a potential key factor in posttraumatic sleep disturbance.. Recognition of SDB in trauma survivors may be obscured because they often present without the classic combination of snoring and sleepiness complaints, which may prompt some sleep specialists to forego polysomnography (PSG) for these patients. We investigated SDB clinical presentations among trauma survivors by comparing objective sleep data and medical signs and symptoms between crime victims (CV) and sleep clinic (SC) patients.

Methods: Matching for age and sex, 178 adult patients—all with SDB—were selected from a group of sleep clinic patientsts (SC=89) and a group of crime victims (CV=89), each comprised of 78 women and 11 men with a mean age of 41 years. A Sleep Medicine History was administered to collect presenting sleep complaints, insomnia profiles and severity, cognitive-affective symptom severity, sleep breathing symptoms, and peripheral SDB symptoms (morning dry mouth, morning headache, nocturia). SDB was confirmed on PSG or a portable monitor, which provided data on obstructive sleep apnea (OSA) or upper airway resistance syndrome (UARS) diagnoses, presence or absence of snoring, and apnea-hypopnea index (AHI). Body-mass index (BMI) was calculated for each patient.

Results: CV patients with SDB presented with more complaints of insomnia, nightmares, leg jerks, and poor sleep quality (P<.0001), whereas SC patients presented with more complaints of sleep apnea and loud snoring (P<.0001). Insomnia profiles and severity and cognitive-affective symptoms were all worse in CV (mean d=.94, P<.0001), whereas SC reported worse sleep breathing symptoms (d=.76, P<.0001). CV reported less snoring than SC (21% vs. 63%, P<.0001), but objectively observed snoring rates were equivalent (72% vs. 74%). SDB diagnoses in CV were equally distributed between OSA (52%) and UARS (48%) in contrast to SC (OSA=82%, UARS=18%) (P=.0001). Due to SDB diagnostic types, AHI(SD) differed markedly between groups [CV=9.5(12.6) vs SC=41.0(46.7) P=.0001]. CV were barely overweight

compared to marked obesity in SC (BMI=26.96 vs. 34.47, P<.0001). In contrast to their marked clinical differences, both groups reported high rates of fatigue or sleepiness (CV=83%; SC=76%) as well as nocturia (CV=63%, SC=54%), dry mouth upon awakening (62% vs. 49%), and morning headache (45% vs. 38%).
Conclusions: Mental health professionals as well as sleep specialists may think of posttraumatic sleep disturbance solely as a psychiatric disorder, whereas recent evidence indicates that trauma survivors often suffer from co-morbid SDB. Therefore, algorithms must be developed to enhance detection of this physiological disorder of respiration among posttraumatic stress disorder patients. In the current study, crime victims presented with both atypical (insomnia, fewer snoring reports, less obesity, more UARS) and typical (fatigue or sleepiness, peripheral medical symptoms) SDB features, the combination of which might serve to reliably identify trauma survivors requiring PSG.

Research supported by New Mexico Crime Victims Reparation Commission, Frost Foundation

0555.J

Aggravation Of Sleep Apnea By The Use Of Occlusal Stabilization Splint In Apneic Patients: A Pilot Study

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Introduction: Single dental arch oral splints are frequently used in the North American population for the management of temporomandibular disorder and bruxism (3.6 millions fabricated per year in USA; Pierce et al., J. Am. Dent. Ass., 1995). However, the influence of occlusal splints on sleep apnea has not been studied. This study was designed to assess the effect of using an occlusal stabilization splint on respiratory parameters during the sleep of mild to moderate apneic patients, whose diagnosis is often unknown.
Methods: Ten patients (3 females and 7 males) with a sleep laboratory diagnosis of sleep apnea (mean $\pm$ SE apnea-hypopnea index of 21.3 $\pm$ 3.2 [10.5-43.1]) and snoring were included in the study. This sample size provided a power of 80% to detect a variation of 42% in the apnea-hypopnea index at an alpha level of 0.05. The mean age was 49.0 $\pm$ 2.7 [31-59]. Patients spent 2 nights in the sleep laboratory; the first for baseline monitoring and the second using an upper maxillary splint, following an adaptation period of at least 2 weeks. The following principal outcome variables were analyzed under blind conditions: total sleep time, sleep efficiency, number of awakenings, number of micro-arousals per hour of sleep, number of apnea and hypopnea per hour of sleep (AP & HYP) and percentage of sleep time with snoring. Paired t tests and Wilcoxon signed rank tests were used when appropriate.
Results: There was no difference between the two sleeping conditions for total sleep time, sleep efficiency, number of awakenings and number of micro-arousals per hour. The median AP & HYP index was not different between baseline (20.1 [10.5-43.1]) and splint (20.9 [11.8-85.0]) nights. However, 6 of the 10 patients showed a rise in their AP & HYP index with the splint: 2 went from light to moderate, 2 from moderate to severe. The increase in the AP & HYP index was more than 50% in 5 of the 10 patients. The percentage of sleep time with snoring increased by 40% with the splint compared to the baseline night (p=0.04). An increase was observed in 9 out of 10 patients. The sleep time with snoring was prolonged by more than 50% in 4 of the 10 patients. Finally, all patients showed an increase in the index of respiratory events (apnea + hypopnea + resistance) that occurred in a non-supine position (4.3 [1.5-58.4] and 18.3 [4.2-81.3] for baseline and splint nights; p=0.005).
Conclusions: These preliminary results suggest that it may be relevant to question patients about snoring and sleep apnea before using an occlusal splint since it may aggravate sleep respiratory disturbances. However, a study with a larger sample size is needed to confirm this recommendation.

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0556.J

The Use of the Sleep Apnea Scale of the Sleep Disorders Questionnaire in Patients with Epilepsy

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Introduction: Obstructive sleep apnea (OSA) commonly coexists with epilepsy, and its treatment may improve seizure control and daytime sleepiness. The Sleep Apnea Scale of the Sleep Disorders Questionnaire (SA-SDQ) may be useful in screening epilepsy patients for OSA. We present data including receiver-operator curves (ROC) that provide optimal cutoffs in the University of Michigan epilepsy population.
Methods: 125 adult subjects with epilepsy completed a survey about their sleep, including the 12-item SA-SDQ scale. All subjects underwent routine polysomnography (PSG) for either clinical or research indications. We defined OSA as 5 or more apneas or hypopneas per hour of sleep. We constructed ROC curves for men and women separately using SDQ scores and OSA status on PSG. We determined optimal cutoffs based on the calculated sensitivities and specificities derived from the ROC curves. We also examined each item comprising the SA-SDQ to compare responses in subjects with and without OSA. The purpose of this item analysis was to determine whether omitting any individual questions from the SA-SDQ would maximize the overall sensitivity and specificity of the instrument. Significance was set at $p < 0.05$.
Results: The sample consisted of 70 men and 55 women. Forty-four men (63%) and 25 women (45%) had OSA; these relatively high percentages reflect that a proportion of subjects studied had been referred for PSGs for clinical indications. The area under the curve was 0.744 for men and 0.788 for women. For men, a SA-SDQ score of 29 provided a sensitivity of 75% and a specificity of 65%. For women, a SA-SDQ score of 26 provided a sensitivity of 80% and a specificity of 67%. Questions that were significant or showed a positive trend related to loud snoring ($p = 0.0001$), witnessed apnea ($p = 0.003$), worsening of snoring/breathing in supine sleep ($p = 0.001$), worsening of snoring/breathing with alcohol ($p = 0.088$), history of hypertension ($p = 0.081$), and also age ($p = 0.0001$), weight ($p = 0.0001$), and BMI ($p = 0.0001$). Questions that were not significant related to awakening gasping for breath ($p = 0.206$), nighttime sweating ($p = 0.334$), nasal congestion ($p = 0.137$), and also cigarette smoking ($p = 0.354$). Omitting the non-significant questions from our analysis as well as weight (which is specified within the BMI) only slightly improved the area under the ROC curve to 0.773 for men and 0.804 for women.
Conclusions: In our population of epilepsy patients, the SA-SDQ is a useful screening tool for OSA, with reasonable sensitivities and specificities in both men and women. Based on these results, we have chosen to use cutoffs of 29 in men and 26 in women in screening subjects for inclusion in an ongoing pilot clinical trial of the effects of treating obstructive sleep apnea in patients with epilepsy. Our findings will require further validation in larger samples of subjects.

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0557.J

Quantification of Adipose Tissue in the Head and Neck in Apneic and Normal Patients: A Comparative Analysis

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Introduction: Obesity, defined as a BMI > 28, is a known risk factor for obstructive sleep apnea. Neck size is also an important risk factor for sleep apnea. Therefore it has been hypothesized that the amount of adipose tissue (AT) surrounding the upper airway in patients with sleep apnea is greater than that for normal subjects. We have shown that magnetic resonance imaging is an accurate and reliable method to quantify adipose tissue in humans, and this technique was used to quantify the visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) surrounding the upper airway in normals and apneics.
Methods: We studied apneics, siblings of apneics, controls, and siblings of controls. Each apneic (RDI > 15) and his/her sibling were matched with a control (RDI < 5) and his/her sibling according to residence, gender, age, and race. Awake axial T-1 images were obtained using a 1.5 Tesla magnetic resonance scanner. The volume of the visceral and subcutaneous adipose tissue in the head and neck region was objectively quantified using a validated computerized software program (Volumetric Image Display Analysis {VIDA}). Thresholding was used to differentiate adipose tissue from surrounding tissues, and visceral adipose tissue was differentiated from subcutaneous adipose tissue by anatomical relationships. We quantified upper airway adipose tissue from the level of the hard palate to the base of the epiglottis.
Results: We studied a total of 196 subjects: 48 apneics (age:45.3 $\pm$ 9.7 yr., BMI:36.2 $\pm$ 8.8 kg/m2super, RDI:45.4 ± 26.0 events/hr), 48 apneic siblings (age: 44.6 ± 10.7 yr., BMI:29.6 ± 6.0 kg/m\super2, RDI:11.8 $\pm$ 17.0 events/hr), 48 controls (age:41.3 $\pm$ 10.5 yr., BMI:25.9 $\pm$ 4.8 kg/m2, RDI:2.0 $\pm$ 1.6 events/hr), and 48 control siblings (age:39.2 $\pm$ 11.7 yr., BMI:25.9 $\pm$ 4.5 kg/m2, RDI:4.3 $\pm$ 4.2 events/hr). The mean volume of visceral adipose tissue was found to be the greatest in the patients with sleep apnea (VAT: 175,000 + 44,000), and when compared with the controls, there was a significant difference in visceral fat (VAT: 57,000 $\pm$ 50,000, p<0.01) between the two groups. The apneic siblings had the second highest mean volume of visceral adipose tissue (VAT: 147,000 $\pm$ 51,000) and also showed a significant difference in visceral fat volume (p<0.01) when compared to the siblings of the control group. The volumetric data for the subcutaneous fat followed the same trend, with the apneics having the highest mean volume, the proband siblings the second highest, and the controls and control siblings having the smallest mean volumes. There were no significant differences in either visceral or subcutaneous fat between the controls and control siblings.
Conclusions: Our data indicate that visceral and subcutaneous adipose tissue is greatest in patients with sleep apnea, next largest in siblings of patients with sleep apnea and smallest in normals and their siblings. The controls and siblings of the controls were BMI matched and had similar volumes of adipose tissue. Such data suggests that the amount of upper airway adipose tissue may be heritable.

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0558.J

Relationships Between Upper Airway Anatomy and Dilator Muscle Activation in Obstructive Sleep Apnea

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Introduction: The patency of the human upper airway is dependent upon its passive anatomical characteristics and the activation of the pharyngeal dilator muscles. During wakefulness, the more collapsible upper airway of patients with obstructive sleep apnea (OSA) is associated with increased activity of the pharyngeal dilator muscles. This is thought to occur primarily via activation of a locally mediated negative pressure reflex (NPR) and represents a neuromuscular compensatory mechanism for this more collapsible airway. We thus hypothesized that there would be a direct relationship between the closing pressure of the passive upper airway (Pcrit during NREM sleep) as a measure of passive anatomy, and EMG activity of the dilator muscles genioglossus (GGEMG) and Tensor Palatini (TPEMG) during wakefulness. As the reflex component of muscle activation is lost asleep, we also hypothesized that the reduction in muscle activity at sleep onset(amount of reflex lost) would correlate with Pcrit.
Methods: We studied 9 male subjects with moderate to severe OSA (age 49.2 $\pm$ 5.1 yrs, BMI 36.3 $\pm$ 8.6). Pcrit was measured during NREM sleep on nasal CPAP using brief (3-breath) reductions in mask pressure. GGEMG and TPEMG were measured using intramuscular electrodes: (a) during quiet breathing awake, (b)as the fall in activation during nasal CPAP application awake and (c)at sleep onset. Muscle activation is reported as % maximal activation.
Results: We found that a number of measures of muscle activation directly correlated with Pcrit. These included peak and phasic GGEMG during wakefulness ($r = 0.71$ and 0.76, $p < 0.05$) as well the % change in tonic GGEMG at sleep onset ($r= 0.81$, $p <0.01$). There was also a correlation with TPEMG phasic reduction at sleep onset ($r = 0.74$, $p < 0.05$). No relationship waking muscle activation and pharyngeal resistance was seen.
Conclusions: These data suggest that upper airway muscle activity is directly proportional to passive upper airway anatomy. With sleep onset, this compensation is lost, again in proportion to the compensatory copmponent.

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0559.J

The Effects of Oral Appliance Therapy on Occlusal Function in Patients with Obstructive Sleep Apnea: A Preliminary Study

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Introduction: Oral appliances (OAs) reduce the severity of Obstructive Sleep Apnea (OSA) and have been used as a treatment option for OSA especially in mild to moderate cases. Since most OAs are designed to advance the mandible, which forces the patient to keep their jaw in a forward position during the entire night, they may cause side effects related to the patient's occlusal function. This preliminary study was designed to determine the potential effect of OAs on occlusal function in terms of objective variables such as occlusal contact area (OCA; mm2) and bite force (Bf; Newton). We compared morning and evening values in patients prior to the initiation of treatment (pre-treatment) and in patients after titration of the OA (post-titration). Our hypothesis is that OA usage could alter the OCA and Bf in the morning due to difficulty in biting and possible differences in bite position.
Methods: Two pre-treatment patients and two post-titration patients with OA (KlearwayTM) use of more than five years were invited to participate in the study. An Occluzer (FPD703, GC, Tokyo, Japan) was used which consists of pressure-sensitive sheets and an image scanner to measure OCA and Bf as indicators of occlusal function. The sheet contains microcapsules which release staining granules for a colour-developing chemical reaction when the sheet is bitten. The image scanner detects the degree of colouring and the extent of the coloured area and a microprocessor determines values for OCA and Bf. Each patient was given one

pair of sheets which matched the size of his/her dental arch prior to the study and asked to bite the sheet as hard as possible for 5 seconds in their habitual bite position in the morning and again in the evening before inserting the OA. Results of OCA and Bf are given as a percentage of change of the value measured in the morning in relation to the value measured in the evening, (morning value - evening value) / evening value x 100. A minus value indicates an OCA or Bf decrease in the morning.

Results: One pre-treatment patient had an OCA of -14.1% and a Bf of -2.9%. The other revealed an OCA of +25.7% and a Bf of -11.26%. One post-titration patient showed an OCA of +14.6% and a Bf of -9.9% . The other patient had an OCA of -44.1% and a Bf of -42.9%.

Conclusions: This study suggests that OCA and Bf measurements with the Occluzer may objectively measure the effect of OA treatment on occlusal function. Although this was a preliminary study, we found one post-titration patient with large decreases in OCA and Bf in the morning as compared to the evening recording which suggests that forward jaw position during sleep could have an effect on occlusal function.

0560.J

The High Incidence of Daytime Pulmonary Hypertension in Patients with Severe Sleep Apnea-Hypopnea Syndrome

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Introduction: Transient and repetitive elevations of pulmonary artery pressure (PAP) during nocturnal sleep have been reported in association with obstructive sleep apneas. We have reported a case of primary pulmonary hypertension with central sleep apneas (Jpn Circ J 2002). The present study was undertaken to clarify the prevalence of daytime pulmonary hypertension(PH) as a complication of sleep apnea-hypopnea syndrome (SAHS).

Methods: The subjects consisted of 54 patients, 50 men and 4 women with a mean age of 46.3±13.1 years, who admitted to our Sleep Disorders Center for heavy snoring and/or excessive daytime sleepiness. Patients with coronary artery disease, renal and liver failure, and known lung disease were excluded from the study. We investigated PAP in all subjects by Doppler echocardiography during the day after a full overnight polysomnography (PSG).

Results: Sixteen of the 54 SAHS patients (29.6%) had daytime PH. All of the patients with daytime PH had severe obstructive sleep apneas with an apnea-hypopnea index (AHI; /hr) „30, and the incidence of daytime PH in patients with severe obstructive SAHS (OSAHS) was 40.0%(16/40), while patients with mild or moderate OSAHS had no daytime PH.

Conclusions: We conclude that investigations of PH by Doppler echocardiography, which is easily performed, are necessary in severe OSAHS patients. It seems that the involvement of PH and/or right-sided heart failure influences the mortality in severe OSAHS case such as obesity hypoventilation syndrome.

0561.J

Depressive Symptoms in Patients with OSA and the Impact of Nasal CPAP Treatment

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Introduction: Depressive symptoms are observed in up to one third of patients with obstructive sleep apnea (OSA). It is unclear whether a causal relationship exists between OSA and depression as studies investigating whether treatment of OSA alleviates depression show discordant results. In a consecutive case series of OSA patients, we attempted to determine to what extent OSA patients are affected by depression, if depression decreases with nasal continuous positive airway pressure (nCPAP) treatment, and who is most likely to benefit from such treatment.

Methods: All patients seeking sleep care at our sleep center routinely complete a Beck Depression Inventory (BDI) before diagnosis and treatment. They also complete a general questionnaire on demographics, health information, sleep habits, and symptoms of sleep disorders including the Epworth Sleepiness Scale (ESS). Subjects diagnosed with OSA based on one night of standard polysomnography and subsequently treated with nCPAP are asked to complete a second BDI after 3 months of treatment. With IRB approval, all patient data from 2001 meeting these criteria were analyzed.

Results: A total of 104 patients (66m, 38f, age 57.49±14.2 yrs) completed a BDI before and after three months of CPAP treatment. The mean BMI was 31.8±7.8, the Respiratory Disturbance Index (RDI) 49.5±28.5, and the ESS score 11.17±5.39. Participants had 3.2±1.8 comorbid conditions and were taking 4.7±4.2 medications. A total of 32 individuals (30.8%) were on antidepressants.The average BDI score at baseline was 8.77±7.58 with a total of 28 subjects (26.9%) having a score of ³14, which is indicative of depression. Depression did not correlate with the baseline RDI or any sleep parameter (e.g. REM latency). Depressed subjects (BDI³14), however, had a significantly higher BMI (35.9 vs. 30.3), higher scores on the Epworth Sleepiness Scale (13.0 vs. 10.5) and more co-morbid conditions (3.0 vs. 2.0) than non-depressed participants (BDI<14).After three months of CPAP treatment, the mean BDI score decreased from 8.77±7.58 to 4.97±7.14 reflecting a significant decline in depression (p>0.01). The percentage of subjects having a BDI³14 declined from 26.9% to 15.4%. A stepwise regression was performed to evaluate which baseline factors best predicted improvement of depression after treatment. Two factors were significant: baseline BDI (r=0.34, r2=0.11, F to Enter = 13.05) and RDI (r=0.43, r2=0.18, F to Enter=9.12). The baseline BDI accounts for 11% of the variability of the improvement in mood, the pre-treatment RDI accounts for 7% of the residual variance.

Conclusions: This study shows significant reduction of depressive symptoms in OSA patients after CPAP treatment. Mood is most improved in patients with high depression scores and RDIs.

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0562.J

Prevalence of Hyperuricemia in Patients with Obstructive Sleep Apnea-Hypopnea Syndrome

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Introduction: Obstructive sleep apnea-hypopnea syndrome (OSAHS) is associated with multiple coronary risk factors, such as hypertension, diabetes mellitus, and hyperlipdemia, which are related to obesity. Because little has been reported about hyperuricemia in patients with OSAHS, we investigated prevalence of hyperuricemia in OSAHS patietns and examined whether or not continuous airway positive pressure (CPAP) has the effect on the value of serum uric acid (UA).

Methods: The subjects consist of 78 controls (AHI<5/hr) and 510 patients(456 men and 54 women) diagnosed with OSAHS, referred to Sleep Disorders Center, Aichi Medical University Hospital. They underwent overnight polysomnography by the conventional method. The patients were divided into three groups, according to the severity of apnea-hypopnea index; AHI(/hr). Blood sample test was done to controls and all patients at the time of the early morning hunger after the

polysomnographic study. We examined the prevalence of hyperuricemia in all of the subjects. In addition, we compared the serum uric acid before and after CPAP therapy of the 45 cases.
Results: Two hundred and nineteen of the 510 (42.9%) patients with OSAHS had hyperuricemia. The prevalence of hyperuricemia was 33.1% for the 43 patients with mild OSAHS patients, 39.4% for the 50 patients with moderate OSAHS patients, and 49.8% for the 126 severe patients. When compared with the controls (33.3%), the patients with severe OSAHS had significantly higher prevalence of hyperuricemia ($P<0.05$). The diffrence of the serum uric acid between before and after CPAP therapy was not statistically significant (6.1±1.9 vs 5.9±1.8mg/dl).
Conclusions: The prevalence of hyperuricemia in patients with OSAHS was 42.9%. Severe OSAHS patients had a higher prevalence of hyperuricemia. It seems that CPAP therapy had no effect on the serum uric acid.

0563.J

Efficacy Of Kampo Herbal Medicine And Dopamine Agonists
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Introduction: Sleep apnea syndrome (SAS) is the most important of all sleep disorders (Guilleminault et al.). Two current treatments for obstructive sleep apnea were both introduced in 1981. These are continuous positive airway pressure (CPAP) treatment applied through the nostrils (Denderian et al., 1988; Millman et al., 1989) and a surgical procedure. However, the long term use of nasal CPAP requires considerable cooperation and commitment on the part of the patient. Recently, a variety of dental appliances have been developed for the treatment of obstructive sleep apnea. One of the authors found that some Kampo herbal medicines are effective for the treatment of patients of excessive snoring and sleep apnea.(Inanaga, K. 1996) The rationale of applying the Kampo herbal medicines, for example Dai-sai-ko-to to patients with excessive snoring and SAS is as follows. Excessive snoring is often observed to in vigorous, robust and obese patients, who are prone to hypertension and cardiovascular disease. Dai-sai-ko-to has been traditionally prescribed these robust and obese subjects for insomnia, obesity, constipation, hypertension and so on. When Dai-sai-ko-to was used for the first time in a patient with insomnia, it was found that both insomnia and excessive snoring were improved. Based on this observation, it was considered that Dai-sai-ko-to might be able to cure both excessive snoring and sleep apnea.
Methods: In some patients with excessive snoring, a respimonitor (TN 1110 Techno Industry) was used to measure respiration. Nasal respiration was measured using a thermister, which measures thermal change as a result of nasal airflow, and abdominal respiration was measured as the electro-static capacity change on the abdominal wall. The time and duration of apnea, as well as the position and the number of apneic events per hour were measured. Patients used these devices while sleeping in their beds at home or in hospitals beds to ensure that their sleep conditions were otherwise unchanged. An apnea index above 5 was diagnosed as sleep apnea syndrome.First, a study was performed to ascertain the effectiveness of Dai-sai-ko-to on excessive snoring in 60 subjects. They consisted of 24 outpatients and 36 inpatients being treated in 9 psychiatric institutions. There were 40 male and 20 female patients, with an average age of 51.7 years old. Patients received medicine orally, 7.5g daily in three divided doses for one month. An overall evaluation of efficacy was made in all subjects. Secondly, we have treated 20 patients with SAS by the administration of Dai-sai-ko-to. Furthermore, two patients with Parkinson's disease were treated with several anti-parkinson drugs for seven years and excessive snoring disappeared after the additional administration of talipexole (a dopamine agonist, Domin).
Results: Kampo herbal medicineA study was performed to ascertain the effectiveness of Dai-sai-ko-to on excessive snoring in 60 patients. Excessive snoring was almost completely cured in 22 patients (36.7%), and moderately cured so that it no longer disturbed the bed partner's sleep in 16 patients (26.7%) The onset of efficacy was observed within one week in 30 subjects among 51 markedly and moderately improved cases. The efficacy differed between the two groups. The group under treatment with psychotropic medications showed a poor response, compared with that shown by the group without psychotropic medications. This result suggests a snoring inducing effect of psychotropic medications. Traditional herbal prescriptions are based on a very complex interaction of numerous herbs contained in the formula. The total extent of this synergistic action is still not fully understood, although great progress has been made in the chemical and pharmacological analysis of individual herbs contained in each prescription. Bupleuri Radix, which is a component of Dai-sai-ko-to, has been shown to have hepatoprotective and anti-inflammatory properties. Saikosaponin, one of the main constituents of Buplerei Radix, was shown to be effective in both chemically-induced and immunologically-induced hepatitis. Herbal prescriptions that contain Bupleuri Radix seem to be effective for snoring and SAS based on our clinical experiences. We have treated 20 patients with SAS by the administration of Kampo medicine.Dopamine AgonistsA 70-year-old male patient with Parkinson's disease had been treated with several antiparkinson drugs for seven years and excessive snoring was to disappear after the addition of talipexole (a dopamine agonist, Domin). This serendipitous observation suggested a trial administration of some dopamine agonists to treat excessive snoring and sleep apnea. Dopamine agonists that have been used are talipexole, carbergolin, and pergolide. Patients with excessive snoring were treated with one of these dopamine agonists, which were found to be effective for excessive snoring in 8 cases. The effective doses of these three drugs were lower than the doses used to treat Parkinson's disease.

0564.J

Evaluation Of Head MRI Findings In Sleep Apnea Syndrome
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Introduction: Sleep apnea syndrome (SAS) not only disturbs the patient's daily life due to excessive sleepiness during the daytime and insomnia during the nighttime but also is considered to be a cause of polycythemia and sudden death not only in infants but also adults as well as circulatory disorders such as hypertension, ischemic heart disease, and arrhythmia. The relationship between SAS and cerebrovascular diseases has been reported, and SAS is considered to be a risk factor for cerebrovascular diseases following hypertension, arrhythmia, and aging. In this study, we evaluated the cause-effect relationship between SAS and cerebrovascular diseases by head MRI examination.
Methods: Head MRI was performed in 28 patients (23 males and 5 females; mean age 49.4±12.0 years) who consulted our sleep disorder clinic, underwent the PSG test for possible SAS, and consented to be enrolled after oral and written explanation about the purpose of this study. According to PSG, SAS was regarded as being severe when the apnea-hypo index (AHI) was 30 or greater, moderate when AHI was 15 or greater and less than 30, and mild when AHI was 5 or greater and less than 15, and MRI findings, clinical symptoms, and patients' characteristics were compared between the 14 patients with severe SAS (mean AHI 52.0±22.6, mean age 46.8±12.4 years) and the 14 patients with moderate or mild SAS (mean AHI 14.2±8.8, mean age 53.4±13.5 years).
Results: 12 of the 14 patients with severe SAS and 12 of the 14 patients with moderate or mild SAS complained of sleepiness during the daytime. Insomnia during the nighttime was observed in 6 of the first group and 6 of the latter group, a heavy feeling of head was reported by 7 and 6, respectively, routine alcohol intake was observed in 10 and 5, smoking was noted in 3 and 1, hypertension was present in 4 and 2, and diabetes mellitus was present in 1 and 2. BMI was 27.1±5.4 in the first group and 26.1±3.7 in the latter group. On MRI, high signal areas were

observed in the white matter in 2 and 0, and around the posterior horns in 2 and 5, respectively. Mild to moderate subcortical atrophy was noted in 11 and 8, respectively. Moreover, while 5 of the patients of the former group who showed subcortical atrophy were aged less than 50 years, all patients of the latter group who showed atrophy were aged 50 years or above.
Conclusions: No difference was observed in clinical symptoms or BMI between the two groups. Concerning complications, hypertension tended to be observed more frequently in the severe SAS group. On MRI, no clear difference was observed in high-signal areas, which suggest cerebrovascular lesions, between the two groups. However, when the mean age of the patients (51.5±12.8 years in males and 43.8±14.6 years in females) was considered, patients with severe SAS appeared likely to develop atrophy of the cerebral cortex.

0565.J

Overnight Increase in Respiratory Chemoreflex Sensitivity of Patients with Obstructive Sleep Apnoea Syndrome

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Introduction: Patients with obstructive sleep apnoea (OSA) are exposed to numerous bouts of hypoxia, hypercapnia and arousal nightly. We attempted to identify how such disturbances affect respiratory control by measuring ventilatory chemoreflex responses before and immediately after a night of sleep.
Methods: Using a rebreathing technique we obtained estimates of CO2 threshold and CO2 sensitivity of the peripheral and central respiratory chemoreflexes. Ten patients with severe OSA were compared to 12 with few or no apnoeas during sleep.
Results: The severe OSA group had an average apnoea/hypopnoea index (AHI) of 57.6 (range 30 to 111) while the control group had an average AHI of 2.9 (range 0 to 9). There were no remarkable overnight changes in any chemoreflex response parameters in the control group. The OSA group, similarly to controls, demonstrated no change in CO2 threshold. Also, prior to sleep, OSA patients were no different than controls. However, the OSA group was distinguished by a large overnight increase in chemoreflex sensitivity. In rebreathing tests performed while hypoxic, CO2 sensitivity increased from 5.7 to 8.4 l/min/mmHg ($p<0.05$) and while hyperoxic, increased from 2.6 to 3.2 l/min/mmHg ($p<0.05$).
Conclusions: We conclude that the disturbances associated with severe OSA result in a general increase in the sensitivity of the ventilatory response of the peripheral and central respiratory chemoreflexes.

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0566.J

An Observational 24 Months Compliance Study of Patients with Sleep Apnea Hypopnea Syndrome with nCPAP Treatment in Japan

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Introduction: CPAP therapy is the first line non-invasive treatment for with sleep apnea hypopnea syndrome (OSAHS), however its efficiency mainly depends on long-term effective use, because OSAHS is usually a lifelong condition. It is in 1998 that CPAP therapy has been firstly authorized by national health insurance system in Japan, and especially in our country, patients must come to hospital at least once a month to continue their therapy by social insurance. However, there are few studies in Japan regarding sleep apnea and the use of CPAP. Our aim is to show semi-long term 24 months (24M) use of CPAP of Japanese patients with OSAHS to examine a correlation between terms of CPAP usage and symptom (subjective sleepiness) and disease severity of starting point.
Methods: N= 528 patients, race; all Japanese of our institute from 1998 to 2001. All patients were diagnosed with OSAHS and also were titrated on CPAP on polysommnography. All patients were divided into four groups according as their symptoms (Epworth sleepiness score; ESS) and seriousness of disease (Apnea Hypopnea Index;AHI) of therapy starting point, as , Group1(n=204 AHI>=31,ESS>=11) Group2(n=202 AHI>=31,ESS<10) Group3(n=81 31>AHI>=20,ESS>=11)and Group4(n=41 31>AHI>=20,ESS<10).The method of survival analysis (Kaplan-Meier) were used and additionally univariate analyses (log-rank test) were used to appear statistical correlations and differences among four groups.
Results: Each ratio of usage of CPAP after 24 M was 83.8%(group1), 77.6%(group2),85.4%(group3) and 78.8%(group4). There were statistically significant differences between group1 and 2, and between group 1 and 4($p<0.01$ each). Next to clarify which index was better between ESS and AHI for the purpose of predicting compliance after 24 M, first we compared higher AHI group(1 plus 2) with lower AHI group(3 plus 4),but no significant difference was appeared($p>0.05$). Second we compared between high ESS group (1 plus 3) and low ESS group (2 plus 4), and significant difference was obtained ($p<0.01$). Then we considered CPAP compliance after 24 M was predicted by using ESS more than AHI.
Conclusions: 1) 24 months CPAP compliance impacts on more subjective sleepiness (ESS) than disease severity (AHI) of starting point of therapy. 2) The ratio of 24 M CPAP usage of group 4 (31>AHI>=20,ESS<10) was 78.8% which was higher than we have supposed. We consider there are many other subjective and objective factors to continue to use CPAP, which cannot be explained only by ESS or AHI, such as recognition of sensation of alertness in the morning and partially may be due to the quite intensive follow up system of our country that gall those who use CPAP gmust come to institute every month.

0567.J

Changes in off-CPAP Apnea-Hypopnea Index (AHI) Over Time in Women CPAP Users

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Introduction: Some studies of sleep apnea patients have shown that off-CPAP AHIs of CPAP users after long-term CPAP therapy are reduced, suggesting a sustained improvement in sleep-disordered breathing. However, others have shown no significant difference in AHI from pre-treatment to a single post-treatment off-CPAP Nocturnal Polysomnogram (NPSG). One explanation for this discrepancy is that a "first night effect" exists where the pre-treatment AHI is artifactually high because of disrupted sleep, leading to reduced values at follow-up. In addition, a single baseline or follow-up measurement may fail to reflect sleep-disordered breathing status, due to intra-subject variation. Our aim for this analysis was to use multiple measures of AHI over time to examine the effect of CPAP use on off-CPAP AHIs. We also examined weight changes over time, theorizing that CPAP users might have health benefits leading to weight loss as part of a natural reinforcement cycle.
Methods: Our study population consists of 186 female participants in the Women's Sleep Study (WSS) a subset of the Wisconsin Sleep Cohort Study (WSCS), contributing up to seven in-home sleep studies each. For each study, CPAP users are asked to sleep without CPAP. All NPSGs were performed using Compumedics, Inc. P-Series portable sleep recording equipment, at approximately 6-month intervals. Women who have used CPAP (N=17) have contributed 92 sleep studies and the remaining 169 Non-users have contributed 795 sleep studies for this analysis.
Results: We found that the average AHIs of both the CPAP Users (off-

CPAP) and Non-users did not vary significantly over time. The average change in AHI over 6-month intervals among CPAP users was -0.12 events/hour of sleep compared to an average change in AHI among Non-users of 0.11 (NS). The average change in weight over 6-month intervals among CPAP users (0.61 Kg) versus Non-users (-0.056 Kg) was marginally statistically significantly different (p=0.07).
Conclusions: CPAP use did not result in significantly lower AHIs over time. The use of CPAP did not appear to be associated with weight loss. In fact, the CPAP users were slightly more likely to gain weight during each 6-month interval than Non-users.

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0568.J

Comparison in CPAP Adherence Among UARS Patients - Split Versus Full Night Positive Airway Pressure Titration

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Introduction: Split night studies have been introduced into routine practice to reduce the cost of polysomnography (PSG). In a split night study, the first part of the night is used to make the diagnosis and the second part to achieve an appropriate level of continuous positive airway pressure (CPAP). The objective of this study is to compare the compliance from CPAP treatment among upper airway resistance syndrome (UARS) patients who had split versus full night PSG.
Methods: Five patients diagnosed with UARS by split night were matched in severity based from RERA index with patients who had traditional full night PSG and titration. All patients received 16 channel PSG including esophageal manometry using Gaeltec multiport catheter. Respiratory effort related arousals (RERAs) indices were obtained by dividing the number of RERAs with total sleep time and expressed as events per hour. RERA was defined as progressive negative esophageal pressure (Pes) deflections of at least –12 cm H20 in association with arousal or microarousal. RERAs also include interspersed arousals or microarousals during continuous abnormal negative inspiratory pressures of at least –12 cm H20. A diagnosis of UARS was made with RERA index greater than 10/hour. Patients who underwent split night were based on observed RERAs greater than 20/hour . The decision to split was done by the technician in attendance after a minimum of two hours of sleep time. The CPAP compliance downloaded from smart card of Remstar Pro CPAP device during their follow up visit was compared. Parameters for CPAP compliance obtained from downloaded data include percent of days greater than 4 hours, average hours of use and percent of days with the device. Independent sample T-test were used to compare equality of means. All values were expressed as the mean + standard deviation.
Results: There were no differences in CPAP adherence but an increasing trend in CPAP compliance with full night PSG was observed. Percent of days with CPAP use > 4 hours (54.4 vs 63.0 (p=0.67)), Average hours of use (3.7 vs 4.5 (p=0.43)) and percentage of days with device (65.3 vs 71 (p=0.47) were not statistically different between the split night and full night studies respectively.
Conclusions: We conclude that CPAP adherence among UARS patients was not significantly different whether split or full night titration protocol was applied. Utilizing split nightprotocol may lead to important savings in money, time and increased availability of services.

0569.J

A Retrospective Correlation Study Examining Heart rate, Stroke Volume, Cardiac Output and Obstructive Sleep Apnea Severity

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Introduction: Obstructive sleep apnea causes fluctuations in cardiac hemodynamics during individual apneic episodes. There is evidence that during the obstructive portion of the apnea, heart rate decreases slightly, then abruptly increases at the resumption of breathing. Stroke volume decreases in a compensatory manner while cardiac output is maintained. The stability of cardiac output throughout the apnea cycle has been debated and may be dependent on sleep stage. The purpose of this study is to examine average heart rate, stroke volume and cardiac output during the total night in relation to obstructive sleep apnea severity.
Methods: Data from sixty-five patients (48 male, 17 female) seen for routine polysomnography to rule out obstructive sleep apnea was analyzed. Heart rate, cardiac output and stoke volume values were obtained through non-invasive impedance cardiography (BioZ.com) at a collection rate of once per minute. Mean heart rate, stroke volume and cardiac output was calculated from total time in bed. Apnea/hypopnea index was calculated during total sleep time, during NREM sleep and during REM sleep. Individual partial correlations were performed controlling for weight. The mean age of the group was 47.7 (SD = 11.47) and mean weight was 242.2 kg. (SD = 53.36).
Results: The apnea/hypopnea index frequency distributions revealed negatively skewed data. The total apnea/hypopnea index mean was 38.3 (SD = 33.23), NREM apnea/hypopnea index mean was 37.4 (SD = 35.19) and REM apnea/hypopnea index mean was 41.8 (SD = 28.64). Heart rate, stroke volume and cardiac output frequency distributions revealed normally distributed data. Mean heart rate was 90.7 (SD = 8.81) beats/minute, mean stroke volume was 78.7 (SD = 16.8) ml, and mean cardiac output was 5.33 (SD = 1.03) l/min. There was a significant positive correlation between heart rate and total apnea/hypopnea index (partial correlation = .3521 P <0.01), NREM apnea/hypopnea index (partial correlation = .3394 P <0.01) and REM apnea/hypopnea index (partial correlation = .3602 P < 0.01). There was a significant negative correlation between stroke volume and total apnea/hypopnea index (partial correlation = -.3811 P < 0.01), NREM apnea/hypopnea index (partial correlation = -.3391 P <0.01) and REM apnea/hypopnea index (partial correlation = -.5201 P < 0.001). There was a significant negative correlation with cardiac output only when correlated with REM apnea/hypopnea index (partial correlation = -.3610 P <0.01).
Conclusions: Fluctuations in cardiac hemodynamics were related to obstructive sleep apnea severity. Patients with more severe sleep apnea had a higher average heart rate and lower average stroke volume with stable cardiac output. Average cardiac output was lower only with increased REM apnea/hypopnea index. The compensatory effect in stroke volume to maintain a stable cardiac output during individual apneas could disturb the averaged values in individuals with obstructive sleep apnea syndrome and this compensatory effect is not maintained during REM sleep.

0570.J

Gender Differences in Early CPAP Use: Are Women Really from Venus and Men from Mars?

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Introduction: The effectiveness of CPAP therapy in obstructive sleep apnea is related to patient acceptance and compliance. These factors may

pose an obstacle in establishing CPAP therapy, as patients may perceive treatment as obtrusive or cumbersome. Age and OSA severity do not seem to influence long- term compliance. However gender differences in CPAP acceptance and compliance have not been evaluated. We studied the gender differences in CPAP-related problems and compliance.
Methods: We retrospectively reviewed case records of patients with obstructive sleep apnea (OSA) treated with CPAP from April 2002 to October 2002 in an accredited Sleep Disorders Center. We randomly selected 39 patients, 21 males and 18 females (mean age 53 years, range 35 to 77 years). All patients had outpatient diagnostic polysomnography with documented OSA. Patients had an initial outpatient CPAP orientation followed by overnight CPAP titration and appropriate CPAP prescription. They were seen in our outpatient sleep clinic after approximately 1 month of CPAP use. All patients were asked about overall CPAP satisfaction (good / moderate / poor) as well as CPAP-related difficulties (e.g. nasal symptoms (Sx), pressure and mask related problems) and residual excessive daytime sleepiness (EDS). Respiratory disturbance index (RDI), CPAP pressure used, and periodic limb movement index (PLMI) were obtained from their initial sleep study. Gender differences were compared for each of these variables. Data were analyzed with a Fisher exact test for discrete variables and Student t test for continuous variables.
Results: Overall CPAP compliance was good. Treatment was tolerated similarly in men and women. The specific distribution of CPAP satisfaction score, tabulated by gender, was as follows: males—62% good, 19% moderate, 19% poor versus females—44% good, 39% moderate, 16% poor (p = ns). No correlation between CPAP pressure and compliance were seen (r = ns). The mean RDI, CPAP pressure, and PMLI in this group were in males 41±18, 10.2 ±3, 12±14 versus females 35±20, 9.1±3, and 12±19. Mean compliance (night/week) in males 6.3±1.6 versus in females 6.0±2.1; and mean compliance (hours/night) in males 5.6±2.2 versus females 4.8±2.0. CPAP difficulties occurred in males and females respectively, as follows: nasal symptoms 10 and 4, pressure symptoms 5 and 5, and mask related problems 6 and 10. Residual EDS occurred in 8 male and 13 female subjects. Gender differences for all of the above variables were not significant (p> 0.05), although EDS in females was approaching significance (p = 0.05)
Conclusions: We did not find gender differences in early reported CPAP compliance and CPAP-related difficulties. Trends towards more nasal symptoms in males, mask-related symptoms and residual sleepiness in females were seen in our sample, which were not statistically significant.

0571.J

Continuous Positive Airway Pressure Does Not Reverse Hypercortisolism, Hypercytokinemia, or Insulin Resistance Associated With Sleep Apnea

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Introduction: We have shown that obstructive sleep apnea (OSA) is associated with hypercytokinemia, insulin resistance, and visceral obesity, and we have proposed a bi-directional, feedforward, pernicious association between sleep apnea, sleepiness, inflammation, and insulin resistance, all promoting atherosclerosis and cardiovascular disease. The objective of this study was to characterize further these metabolic alterations and to test whether these abnormalities are reversed after the use of continuous positive airway pressure (CPAP).
Methods: Our study included three groups: obese middle-aged men with sleep apnea; nonapneic age- and body mass index obese controls and age-matched lean controls. To qualify for the study, apneic patients had to have an apnea/hypopnea index (A/HI) of more than 20 events/h of sleep plus excessive daytime sleepiness and/or the presence of cardiovascular abnormalities. Control subjects had an A/HI < 5. All subjects were monitored in the sleep laboratory for 4 consecutive nights. During the fourth day, serial 24h plasma measures of IL-6, TNFa and cortisol were obtained, and daytime sleepiness was assessed with the multiple sleep latency test (MSLT). Also, single measures of fasting blood sugar and insulin were obtained. The patients with sleep apnea were reassessed with the same protocol after at least 3 months of closely monitored nightly use of CPAP.
Results: Preliminary analyses of 6 sleep apneics (pre- and post-CPAP), 6 obese controls, and 7 lean controls indicated that sleep apneics pre-CPAP had a higher mean value of 24-h cortisol secretion compared to obese and lean controls (both P < 0.1); this difference was significant for the daytime levels (0800-2200) (P < 0.05). Also, IL-6 levels in the morning (nadir point of IL-6 secretion) were highest in the sleep apneics, intermediate in obese controls, and lowest in lean men (both P < 0.05). Furthermore, insulin levels were highest in sleep apneics, intermediate in obese controls, and lowest in lean men (both P < 0.05). The use of CPAP was associated with a slight nonsignificant decrease of cortisol compared to baseline, whereas IL-6 and insulin levels remained unchanged. Following CPAP, objective sleepiness was nonsignificantly improved (P = 0.1).
Conclusions: Sleep apnea is associated with hypercortisolism, hypercytokinemia, and hyperinsulinemia that appears not to be reversed with the currently most common therapeutic modality, i.e., CPAP. These data suggest that although CPAP may provide some symptomatic relief in patients with OSA, it does not protect from the long-term consequences of hypercortisolism, "low grade" inflammation, and insulin resistance i.e., cardiovascular abnormalities, diabetes, and decreased longevity. New treatments with a focus on the correction of metabolic aberrations associated with sleep apnea are needed.

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0572.J

Detection of Sleep Disordered Breathing Using Implanted Cardiac Pacemakers

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Introduction: Recent studies have demonstrated that sleep disordered breathing (SDB) is prevalent in patients with cardiovascular disease. Increasingly, implanted cardiac pacemakers are used to manage a variety of cardiovascular disorders. In the US, approximately 170,000 new pacemakers are implanted annually with a total prevalence of 600,000 implanted patients. These pacemakers are typically implanted in the anterior chest wall, and modern pacemakers can measure trans-thoracic impedance to determine a number of respiratory parameters, including rate, tidal volume and minute ventilation. Thoracic impedance is a widely used respiratory signal in portable diagnostic sleep apnea monitors. In this study, we tested the performance of an algorithm to automatically detect sleep disordered breathing from the pacemaker's trans-thoracic impedance signal.
Methods: Forty male patients (age 70 ± 13 years) with a previously implanted PULSAR MAX I or II pacemaker (Guidant Corporation) were recruited from a pacemaker clinic by their cardiologist and screened for SDB risk with the Berlin Questionnaire. Fifteen of the 40 patients with positive questionnaire responses for snoring, wake-time sleepiness, and presence of obesity or hypertension participated in overnight full polysomnography (PSG). The pacemaker's trans-thoracic signal was simultaneously recorded with the PSG. Sleep stages were scored with Rechtschaffen & Kales criteria. Apneas were manually scored using standard criteria. Hypopneas were manually scored in 2 ways: with a 30% airflow reduction and 4% desaturation rule (Method 1) and with a 30% reduction in airflow without a desaturation criterion

(Method 2). An algorithm was developed to automatically detect SDB events from the pacemaker's trans-thoracic impedance signal alone. The accuracy of this algorithm was compared to technician scored PSG.
Results: Of the 40 patients screened, 33 (83%) were identified by the Berlin questionnaire to be at high risk for SDB. PSGs showed that 8 of 15 (53%) had an apnea-hypopnea index (AHI)5 and a mean AHI of 12 ± 12 when the hypopneas were defined using Method 1. When Method 2 was used to define hypopneas, all 15 patients had an AHI 15, with a mean AHI of 60 ± 20. The automated algorithm detected SDB events from the impedance signal with a sensitivity of 80 ± 6% and specificity of 65 ± 15%, compared to the technician scored PSG using Method 2. Presence of congestive heart failure or chronic obstructive pulmonary disease did not affect the sensitivity or specificity.
Conclusions: Sleep-disordered breathing is highly prevalent in patients with cardiac pacemakers. Implanted pacemakers with trans-thoracic impedance sensors may be able to accurately characterize sleep disordered breathing when compared to standard PSG. Pacemakers may represent a new method to screen and provide long-term assessment of sleep disordered breathing in high-risk patients.

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0573.J

Long QT Syndrome and Obstructive Sleep Apnea

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Introduction: Patients with obstructive sleep apnea (OSA) are considered to be at increased risk for sudden cardiac death. The long QT syndrome (LQTS) is associated with polymorphic ventricular tachycardia and is a known cause of sudden cardiac death. The present study was undertaken to determine if there is a relationship between OSA and the LQTS.
Methods: Case-control study based on a random sample of the general population and a group of patients from our Sleep Disorders Clinic. A total of 633 subjects were selected for this study. The first group included 140 consecutive patients evaluated in our Sleep Disorders Clinic for OSA (clinic OSA) with an apnea/hypopnea index (A/HI)³ 15 and a recommendation for CPAP. The second group included 87 subjects from the random sample of the general population (general population OSA), who had an A/HI³ 10 + daytime sleepiness, hypertension or other cardiovascular disorder. The control group included 400 subjects without OSA (A/HI=0) that were selected from the same random sample and matched for age and body mass index (BMI) to the clinic OSA group. The QT interval was measured manually and the corrected QT (QTc) was calculated (Bazett formula). LQTS was considered if QTc was greater than 0.45 seconds for males and 0.47 seconds for females. Odds ratio (OR), logistic regression and ANOVA (controlling for age and BMI) were used for statistical analysis.
Results: The prevalence of LQTS was highest in the clinic OSA (11.8%), intermediate in the general population OSA (6.9%), and lowest in the control (1.8%). OR of LQTS in the clinic OSA versus the control group was 7.4 (3.0,18.5), P<0.001 and in the general population OSA versus the control group was 4.1(1.4,12.6), P=0 .02. Using logistic regression to control for age and BMI, OR was 2.3(1.4, 3.9), P=0.002 and 2.6(0.8, 8.8), P = 0.11 respectively. The mean QTc intervals for the control group was 0.403±0.001 seconds compared to 0.430±0.002 seconds for the clinic OSA group (P<0.001) and 0.412±0.003 seconds for the general population OSA (P=0.02).
Conclusions: The prevalence of LQTS in patients with OSA was significantly greater than in control subjects. An increase in the sudden cardiac death in patients with OSA might be related to a LQTS leading to ventricular tachyarrythmias. In the OSA patients an electrocardiogram should be performed to screen for LQTS and special precautions need to be taken with medications that may prolong the QTc interval.

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0574.J

Prevalence of Sleep-Disordered Breathing in Patients with Acute Coronary Syndrome

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Introduction: There are known associations between myocardial infarction and sleep apnea, yet acute coronary syndrome (ACS) itself is associated with physiologic instability, which might also produce apneas. The purposes of the study are: a) to identify the prevalence of sleep-disordered breathing (SDB) in patients admitted with an ACS, and b) to validate the utility of a sleep questionnaire to identify which of these patients might be at risk for sleep-disordered breathing.
Methods: Consecutive patients admitted to the VA Hospital with an ACS were invited to participate. After informed consent, demographic data was gathered and the Cleveland Sleep Habits Survey (CSHS) was administered. The CSHS incorporates the Berlin Questionnaire criteria, providing a pre-test probability for sleep apnea, with additional questions to address symptoms of insomnia, leg jerks during sleep, strange sensations in legs, and drop or weakness attacks, during wakefulness. Scoring of these questions was performed as to possible risk of a sleep disorder based upon the presence of persistent symptoms (3-4 times a week or more) and sleepiness (as assessed on the Berlin questionnaire). A portable sleep study (Eden Trace II System) was done within 72 hours of admission. Study was scored for recording time, Apnea-Hyponea Index (AHI), and Oxygen Desaturation Index (ODI).
Results: 59 patients (96% male) and 50 completed sleep studies comprise the analysis. The mean age (SD) was 61.3 ± 11.1 years; BMI, 30.1± 5.6 kg/m2; mean arterial pressure was 96.7±15.8 mmHg and ejection fraction, 46.1±13.9%. According to the CSHS, 58% had high pre-test probability for sleep apnea, 42% for insomnia, 14% for restless legs, and 1% for narcolepsy. 72% of the patients had an AHI > 5/hr; 24%, an AHI>30. The most prevalent pattern appeared obstructive in nature (66%). However, there was no correlation between AHI and a pre-test probability for OSAS (p= 0.472) or the degree of subjective sleepiness (p= 0.503), as measured by Epworth Sleepiness Scale. A high AHI was more often present in patients with hypertension (23 vs. 10%), diabetes mellitus (25% vs. 18%), or known coronary artery disease (22% vs. 12%).
Conclusions: In the setting of ACS, the prevalence of SDB is high, and not detected by standardized questionnaires for sleepiness or composite risk for SDB. Also, SDB in ACS is more common in the presence of known cardiovascular co-morbidity.

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0575.J

Abnormal Cardiovascular Responses to Non-Respiratory Arousals in Obstructive Sleep Apnea Syndrome

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Introduction: Elevated sympathetic drive and impaired parasympathetic cardiac control during wakefulness and sleep may contribute to increased risk for systemic hypertension and cardiovascular disease in

patients with obstructive sleep apnea syndrome (OSAS). These abnormalities in autonomic control likely result from long-term exposure to nocturnal episodic hypoxia and repetitive arousal from sleep. Recent studies have found that hypoxia does not produce peripheral vasodilation in OSAS as it does in normals; as well, the vascular responses to alpha- and beta-adrenoreceptor stimulation are impaired. We hypothesized that the cardiovascular response to transient arousal from sleep may also be different in OSAS subjects relative to normals.

Methods: 16 volunteers participated in overnight sleep studies following informed consent. These subjects consisted of 8 untreated normotensive OSAS patients (AHI>20, 48.0±3.1 years, BMI 34.0±1.6 kg/m2) and 8 healthy controls (AHI<5, 41.8±6.0 years, BMI 26.3±1.7 kg/m2). ECG, continuous blood pressure (by applanation tonometry) and respiratory airflow were recorded during acoustically-induced arousals from NREM sleep. The acoustic stimulus consisted of a binaural tone of frequency 1 kHz, lasting 0.5 s with amplitude ranging from 50 to 115 dB. CPAP was applied at individually titrated levels to regularize respiration in the OSAS subjects. An adaptive filtering algorithm was used to estimate the time-varying changes in the spectra associated with heart rate variability and blood pressure variability during arousal. From the low-frequency and high-frequency bands of these spectra, we computed various indices related to sympathetic (LFPRR, LFPSBP and MLHR) and parasympathetic (HFPRR,GRSA) activity (Am J Respir Crit Care Med 164:807-812, 2001). Repeated-measures analysis of variance was performed to determine the significance of responses relative to pre-arousal baseline as well as between subject groups.

Results: Arousal-induced changes in RR and SBP were substantially larger in controls vs OSAS (P<0.05). None of the parasympathetic-related parameters (HFPRR, GRSA) showed any change with arousal (P>0.05) in OSAS, whereas HFPRR in controls decreased (P<0.001). The lack of change in GRSA suggests that the changes in HFPRR were secondary to primary changes in respiration. On the other hand, all parameters related with sympathetic activity increased (P<0.001) in both groups following arousal. In controls, LFPRR, MLHR and LFPSBP were significantly higher than baseline from t~6.5s to t~32.5s. However, the changes in MLHR and LFPRR were larger in controls vs OSAS (2-way RMANOVA time X group interaction, P<0.001), whereas the magnitude and time-course of LFPSBP was similar between the 2 groups.

Conclusions: The OSAS patients displayed a diminished cardiac sympathetic response to transient arousal from sleep: changes in heart rate, blood pressure and low-frequency heart rate variability were smaller relative to normals. However, the similarity in changes of low-frequency blood pressure variability in both groups suggests that the vascular response to arousal remains intact in OSAS.

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0576.J

Treatment With Recombinant Growth Hormone Attenuates the Cognitive Impairments Associated With Chronic Intermittent Hypoxia (CIH) In Rats

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Introduction: Exposure to CIH, but not sustained hypoxia (SH) of similar magnitude, is associated with cognitive impairments and increased neuronal apoptosis in brain regions involved in learning and memory in the rat. Recent evidence suggests that growth hormone (GH) is produced by neurons, and may provide an endogenous neuroprotective and/or regenerative mechanism in response to neuronal injury. CIH for up to a week has no effect on GH mRNA expression. However, SH elicits marked increases in the neural tissue expression of GH mRNA in rats. We therefore hypothesized that treatment with GH may prevent the cognitive impairments associated with CIH.

Methods: 72 young adult male rats (175-200g) were exposed to 7 days of Room Air (RA, n=36) or CIH (n=36; 90 sec alternations between 10% and 21% O2). Each group was further subdivided and received an injection of 1mg/kg/day recombinant GH (n=18) or vehicle (V; n=18) throughout the duration of the experiment. Behavioral testing consisted of a standard place-training reference memory task in the water maze. Rats were trained to locate a hidden, submerged platform using only distal, spatial cues. On each trial, the rat was placed into the pool from quasirandom start points and allowed a maximum of 90 seconds to escape to the platform, where it was allowed to remain for 15 seconds. Training consisted of two daily 2 trial training sessions, separated by 4 hours, for 3 days. The position of the platform remained constant across trials. To assess performance during place training, mean escape latencies, swim distances, and swim speeds were analyzed by a two-way (hypoxic condition x treatment) repeated measures analysis of variance. A p value <0.05 was considered statistically significant.

Results: V-IH rats were found to require significantly longer times (latency) and distances (pathlength) to locate the hidden platform (p<.002 for both latency and pathlength), than V-RA, GH-RA, and GH-IH animals. Post-hoc analyses showed that GH-RA and GH-IH animals were not significantly different from controls on the latency and pathlength to locate the hidden platform. No significant differences were found between groups in regards to swim speeds or on the latency and pathlength to locate a cued platform, indicating that group differences were not due to sensorimotor impairments.

Conclusions: GH treatment prevents the spatial learning impairments associated with exposure to CIH. We speculate that these effects may be due to GH-induced protective mechanisms within vulnerable neurons. The mechanisms underlying such protection are currently unknown.

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0577.J

Bulky Inferior Tongue and Elongated Pharyngeal Airway in Men Compared to Women Evidence from A Cephalometric Study

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Introduction: Epidemiological studies have suggested a strong male predominance of obstructive sleep apnea syndrome (OSAS). The possible reasons may be multifactorial and have not yet been fully elucidated. This study explores the mechanisms underlying the female advantage in the maintenance of pharyngeal patency by cephalometric analysis.

Methods: Ninety-four male and 28 female subjects were recruited from a university hospital clinic and hospital staff. Selection criteria include (1) AHI<5/hr; (2) BMI<25Kg/m2; (3) no any symptoms suggesting OSAS; and (4) no any chronic diseases. An overnight polysomnographic (PSG) study was performed and a lateral cephalogram was obtained for each subject. Thirty-four cephalometric variables representing soft tissues, bony structures and upper airway were measured. The methods for PSG study, cephalometric picture-taking and analysis were the same as described earlier (Sakakibara H, Tong M, Matsushita K, et al. Cephalometric abnormalities in non-obese and obese patients with obstructive sleep apnoea. Eur Respir J, 1999; 13:403-410).

Results: No differences were found in BMI (22.3±2.1 vs 21.7±2.4, NS) and AHI (1.7±1.3 vs 1.7±1.3, NS) between men and women. There were

significant differences between groups in most of the cephalometric variables measured. To clarify if these differences were just a function of the difference in body size, a normalization strategy was employed. After normalized for SN (the length of the cranial base), significant differences were still observed between male and female groups in 4 bony structure variables, i.e., N-ANS (0.83±0.05, vs 0.80±0.08, p<0.05), S-Go (1.28±0.10 vs 1.21±0.09, p<0.001), S-Ar (0.57±0.06 vs 0.52±0.06, p<0.001), Ar-Go (0.78±0.08 vs 0.74±0.08, p<0.05), 6 soft tissue variables, i.e., MP-H (0.23±0.10 vs 0.16±0.09, p<0.001), H-VL (0.56±0.06 vs 0.52±0.08, p<0.001), MPT (0.15±.0.04 vs 0.12±0.03, p<0.01), TGL (1.16±0.10 vs 1.07±0.06, p<0.001), Ton (0.67±0.09 vs 0.61±0.07, p<0.01), Ton2 (0.13±0.05 vs 0.09±0.04, p<0.001) and pharyngeal airway length, i.e., PNS-V (1.16±0.10 vs 1.07±0.06, p<0.001). These results suggest that compared to women, men have (1) a longer face; (2) a greater tongue volume, especially inferior tongue volume; (3) a thicker soft palate; (4) a more inferiorly located hyoid bone; and (5) a longer pharyngeal airway.

Conclusions: Our results clearly indicate that significant differences exist in craniofacial structures between men and women, which may contribute to the explanation of the gender difference in OSAS prevalence and expression. Strikingly and interestingly, in comparison to those of women, the cephalometric features in men observed in this study highly resemble those of a patient with OSAS. Thus, an elongated pharyngeal airway in men is more likely subjected to compression by the surrounding soft tissues. Bulky inferior tongue volume loaded against an elongated pharyngeal airway may well be the night evil leading to repeated upper airway obstruction during sleep.

0578.J

T99m HMPAO rCBF SPECT Findings In OSAS Patients

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Introduction: Beside excessive daytime sleepiness, OSAS patients develop mild cerebral impairment syndrome including deficits in memory, attention and executive functions as well. Some SPECT studies referred to higher frequency of frontal and/or parietal hypofixation (hypoperfusion) in untreated OSAS patients. The present long term follow-up study was designed to improve our understanding upon the characteristics of local cerebral perfusion developed by OSAS pts. and upon its possible alteration caused by adequat CPAP treatment

Methods: Patients: males, age < 60 yrs., RDI: between 15 and 50, Epworth < 10, htc < 0.5, stroke free patient's history and negative CDS finding, right handedness. Protocol: Complete sleep lab examination, vascular laboratory tests, CDS, CT, HMPAO SPECT performed right after a polisonmnografically controlled night sleep, neurophysiological examination based on internationally accepted test battery. Protocol was repeated at the end of each 6-month period of controlled CPAP/BiPAP treatment

Results: Until this time 39 pts. have undegone the first(A) ,22 pts. the secon (B) and 4 pts. the third(C) steps of control. A. HMPAO SPECT showed 4 types of regional hypoperfusion: frontal in 17 pts. (in 14 pts. on the right side), right frontoparietal in 11 pts., bifrontal left parietal in 8 pts., left parietal in 1 pt. , normal finding in 3 pts. B. All cases with frontal hypoperfusion (inlcuded right and bifrontal cases) had been completely normalized by effective CPAP treatment . Right parietal hypoperfusion returned to normal in 9 of 11 pts while left parietal hypoperfusion remained unchanged in 4 of 9 pts. CT and MRI revealed lacunar emollitions in 6 cases of parietal and in 1 case of frontal-frontoparietal pts.

Conclusions: Our study demonstrates the significance of the HMPAO SPECT examinations in the diagnostic protocol of OSAS and proves the early vulnerability of the frontal lobe in OSAS. Frontal hypoperfusion detected in the morning with HMPAO SPECT seems to occure in majority of OSAS pts. and turnes to normal in almost all pts. treated with CPAP. As a result of CPAP treatment parietal hypoperfusion (in particular the left ones) seems to be less susceptible to relief.

0579.J

Sleep Related - Breathing Disorders and Rehabilitation Outcome of Stroke Patients: A Prospective Study

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Introduction: Sleep-Related Breathing Disorder (SRBD) is more prevalent in stroke patients than in age-sex matched controls, but the relationship between SRBD, functional levels on admission, and subsequent recovery is unclear. We evaluated patients after a first stroke to determine the prevalence of SRBD and the influence of SRBD on the recovery of discharge functional status after a rehabilitation program.

Methods: In a prospective study, 30 stroke patients were studied by Continuous Overnight Pulse Oximetry during sleep for the presence of desaturation events (fall of arterial saturation > 4% from the baseline). The Respiratory Disturbance Index (RDI) was defined as number of desaturations per sleep hour. Functional assessment was done on admission using the Functional Independent Measures (FIM) score. The patients were asked about total hours of sleep and the presence or absence of habitual snoring before and after the stroke. The outcome measure on discharge was the FIM score.

Results: On linear regression, after including the FIM score on admission, in the model, the RDI score was negatively correlated with the FIM gain (coefficient = - 0.635±0.27, p = 0.025) and together the variables explained 20.9% of the total variance (adjusted r-squared). All patients with an admission FIM of 70 or more (only mild functional impairment) had a good outcome (FIM > 100 on discharge). However, only 2 of 6 of those with a FIM < 70 with SRBD (defined as and RDI score of > 10) had significant improvement (at least 30 points), whereas this occurred in 7 of 9 of those without SRBD (Prevalence ratio = 0.43, 95% CI, 0.13-1.40, p = 0.085)

Conclusions: Even after adjusting for the admission functional status, the presence of desaturation events during sleep predicts a poorer recovery, especially in those with poor function on admission

0580.J

Mouse as an Animal Model of Sleep Apnea

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Introduction: Several animal models of sleep apnea have been described during the last two decades. To our knowledge, however, sleep apnea in mice without artificial maneuvers has not been documented. Identification of sleep apnea in mice will subsequently allow understanding of the molecular basis of sleep apnea, because these animals are frequently used in genetic engineering. We aimed (1) to examine whether normal mice develop apnea during sleep, and if so, (2) to examine the relationship between types of sleep apneas and sleep stages, and (3) to examine the effect of respiratory chemostimulation on sleep apnea.

Methods: Ventilation in male adult 129/Sv mice (n=5) was recorded by whole body plethysmography concomitantly with electroencephalograms (EEGs) and neck electromyograms (EMGs). The chamber was continuously flushed with a gas mixture at rate of 500 ml/min; using either room air (RA), hypoxic (15% O2 balance with N2), hyperoxic (100% O2), or normoxic hypercapnic (5% CO2-21 %O2-N2 balance)

gas mixtures. All the recordings were performed from 10:00 to 16:00. During the entire recording period, the mouse was allowed to move freely in the chamber. Quiet wakefulness (QW) was defined by the presence of high-frequency (8-30 Hz) low-amplitude EEG with relatively high EMG tone. Active wakefulness (AW) was defined by very high amplitude EMG volleys. Slow wave sleep (SWS) was defined by a low frequency (0.25-4 Hz) high-amplitude EEG. Rapid-eye-movement (REM) sleep was defined by a mixed-frequency (4-8 and 8-30 Hz) low-amplitude EEG associated with weak or no EMG activity. Apnea was defined as cessation of plethysmographic signals for at least two respiratory cycles. Apnea occurrence index, defined as the number of apneic episodes per hour, was separately calculated for each apnea type during each stage of sleep.

Results: (1) While breathing room air, 32.3±6.9 (mean±SEM, n=5) apneas were observed during sleep but not in QW periods. Two types of sleep apneas, post-sigh and spontaneous apneas, were observed. Apneas were classified as post-sigh if the preceding breath was at least 25% above the average amplitude during the preceding 10 seconds. Apnea without a preceding sigh was defined as spontaneous. (2) Post-sigh apneas occurred exclusively during SWS while spontaneous apneas arose during both SWS and REM sleep. (3) Compared with room air (9.1±1.4/hr of SWS), post-sigh apneas were more frequent in hypoxia (13.7±2.1) and less frequent in hyperoxia (3.6±1.7) and hypercapnia (2.8±2.1).

Conclusions: Our data indicated that significant sleep apneas occur in normal adult mice and suggested that the mouse could be a promising experimental model with which to study the genetic and molecular basis of respiratory regulation during sleep.

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0581.J

Uvulopalatopharyngoplasty for Obstructive Sleep Apnea: 15-year Review of Complications

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Introduction: Since uvulopalatopharyngoplasty (UPPP) was first introduced as a treatment for obstructive sleep apnea in this country, its potential for serious complications has dictated post-operative management. Initially, most patients underwent tracheotomies to stabilize the airway and were observed for days in the intensive care unit, whereas now, very few undergo concomitant tracheotomies and many are observed overnight on the general surgical ward. The purpose of this study is to review all complications of UPPP at this institution to evaluate if there are clinical parameters that may be identified as pre-operative risk factors for complications.

Methods: Patients that underwent UPPP and associated procedures were reviewed from 1996-2001, evaluating for age, gender, comorbidities, body-mass index, neck circumference, respiratory disturbance index, apnea index, lowest pre-operative oxygen saturation (LSAT), number and type of concomitant surgeries performed, complications, and total hospital days. Complication data was generated for this cohort and compared to a prior study from the same institution from 1987-1995 to generate a 15 year review of all UPPP complications.

Results: 307 charts were reviewed (257 male, 50 female) from the 1996-2001 cohort. The prior study reviewed 347 patients. There were 32 total complications over the 15 years (4.8%), and 18 complications during the past 6 years(5.8%). Specific complications were related to airway (1.8%), bleeding (1.8%), and other (1.2%). No patient suffered a myocardial infarction, cerebrovascular accident, or death. Those patients that had any complication had a statistically significantly lower LSAT than those without a complication (72.5% vs. 80%, p=0.0198). All other variables were similar. Those patients with complications mandating overnight hospital admission were also found to have a significant lower LSAT (66% vs. 80%, p=0.0120).

Conclusions: UPPP is a safe operation with a total complication rate of approximately 5%. The majority of these complications were not life-threatening. Our data supports stratifying the following patients as low-risk for complications: RDI £ 38, AI £ 22, LSAT ³ 80%, and £ 3 concurrent surgical procedures. Given the data from the earlier cohort, there is a higher risk for complications in those patients with a pre-operative LSAT less than 80% and those patients undergoing 4 or more independent procedures.

0582.J

Imaged-based Modeling of Upper Airway Resistance in Children with Obstructive Sleep Apnea Syndrome

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Introduction: Obstructive sleep apnea syndrome (OSAS) may affect up to 2% of children, and is associated with lymphoid hyperplasia, craniofacial anomalies, and neurological disorders. Recently we have shown that children with OSAS but no apparent craniofacial or neurological disorders have decreased upper airway volume, and decreased mean and minimum airway cross-sectional areas, compared to controls. The physiological significance of these anatomic differences is explored using image-based flow modeling.

Methods: 20 OSAS children were recruited through the Sleep Disorders Center after OSAS was diagnosed by polysomnography and compared to 20 matched controls. MRI was performed with a 1.5 T scanner. Sequential T2 spin-echo axial sections were obtained along the airway from the orbital cavity to the larynx. The airway dimensions were determined after segmentation and 3D reconstruction using 3DVIEWNIX (MIPG Dept., University of Pennsylvania). Computational fluid dynamics software (CFD) was used to calculate the effects of airway anatomical differences on flow resistance and pressure drop at peak inspiratory flow rates. Area-length curves of the airway from the nasopharynx through the epiglottis were used to generate axisymmetric flow models. Velocity, pressure, and turbulence fields were calculated at peak inspiration flow, using a commercial software package (Fluent 6/Gambit 2, Fluent, Inc). Endpoints were maximum pressure drop through the upper airway, and flow resistance ((change in pressure)/(change in flow) at peak flow).

Results: Area profiles based on the average of 20 OSAS subjects had approximately 10-fold higher pressure drop than area profiles from controls, and concomitant 10-fold increase in resistance. Segment pressure drop in OSAS subjects was comparable to critical airway closure pressures reported in the literature. A three-dimensional model of the airway showed additional resistance when elliptical airway cross-sections and airway curvatures were added.

Conclusions: Anatomical differences between upper airways lead to significantly higher airway resistance in OSAS children compared to children with normal airway anatomy. Future work will study the effects of more complex, deformable airway geometries on flows, resistance, and airway stability.

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0583.J

Electrodermal Activity in a Sleep Clinic Population: Its Relation to Stress, Sleep Quality and EEG Arousals

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Introduction: The study of electrodermal activity (EDA) began over a century ago, and it has been linked to many aspects of emotion, arousal and attention. A subset of studies has focused on the occurrence of EDA in sleep (EDAS). These investigations have defined when EDA is most and least likely to occur during the sleep cycle, and have found that at least moderate stress tends to increase EDAS. The latter studies, though intriguing, have fallen short methodologically. The aims of the present study were: (a) to investigate the relation of negative affect and stress to EDAS and to determine the extent to which these variables are predictive of EDAS; (b) to explore the utility of EDAS as an index of sympathetic nervous system arousal and of sleep quality; and (c) to assess for possible relations between apnea severity and central and autonomic arousal variables.
Methods: Participants were 70 referrals to a sleep disorders center (mean age = 50.7 $\pm$ 11.9; mean Apnea-Hypopnea Index [AHI] = 26.9 $\pm$ 28.4). Subjects completed a demographic profile, Profile of Mood States, Penn State Worry Questionnaire, and Derogatis Stress Profile prior to their diagnostic polysomnography, and a sleep diary the following morning. Participants also underwent skin potential response (SPR) measurement throughout the polysomnography. SPRs were scored as spontaneous, respiratory-event related (RE-SPR) or periodic limb movement related (PLM-SPR).
Results: Pearson product-moment correlations revealed no significant correlations between the questionnaire measures and EDAS. Multiple regression analyses indicated that none of the self-report measures reliably predicted overall EDAS or EDA during slow wave sleep; however, study type (i.e., split-/full-night PSG), and self-report of mood disturbance and stress reliably predicted EDA during rapid eye movement (REM) sleep, accounting for 13% of the total variance. Further, EDAS variables were not significantly correlated with or predictive of subjective sleep quality. AHI was positively correlated with both RE-SPR ($r = .74$; $p < .01$) and respiratory-event arousals ($r = .95$; $p < .01$), and RE-SPR and respiratory-event arousals were positively correlated with each other ($r = .71$; $p < .01$). A similar relation between periodic limb movement arousals and PLM-SPR also emerged ($r = .91$; $p < .01$). A multiple regression analysis found that RE-SPR and respiratory-event arousal indices were significant predictors of AHI, accounting for 91% of the total variance.
Conclusions: Weak relations exist between negative affect, worry, and stress and EDAS, and these variables are largely ineffective in predicting EDAS in a sleep-disordered population. Further, EDAS had no relation to self-reported sleep quality in this sample. Additional analyses found significant associations between apneic and periodic limb movement events and both central (EEG) and autonomic arousals (EDAS). These data suggest that a combination of both central and autonomic arousal variables might provide a better indicator of the amount of sleep disturbance present.

0584.J

The Effect Of CPAP On Exercise Performance In OSA Subjects

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Introduction: Recent studies have demonstrated adverse cardiovascular effects of OSA. The impact of these adverse effects on exercise performance of OSA patients is largely unknown. It is also not known whether treatment of OSA with CPAP has any beneficial effects on exercise performance. This study was designed to examine: 1. exercise performance in OSA patients; and 2. the impact of three-month therapy with CPAP on exercise performance in OSA.
Methods: Ten adult male subjects (age: 44.7±12 yrs, BMI: 34.3±6.5) diagnosed with OSA (AHI: 36.7±36.9, Epworth Score 12.9±3.8) were studied. Subjects with history of cardiovascular, respiratory or musculoskeletal disease were excluded. All subjects had normal resting pulmonary function. Subjects underwent two baseline maximum, incremental, symptom-limited exercise studies on a stationary bicycle ergometer. Minute ventilation (VE), oxygen consumption (VO2), heart rate (HR), respiratory rate (RR), and Borg scale for dyspnea and leg fatigue were measured at rest and during exercise. Inspiratory capacity (IC) maneuvers were obtained at rest and at maximum exercise and were used to estimate end-expiratory lung volume (EELV =TLC–IC). Subjects were prescribed CPAP at a pressure determined during the titration PSG. Three months later a follow-up PSG and exercise study was performed with identical measurements. CPAP compliance was downloaded after three months. Pre- and post-CPAP variables were compared using paired t-testing.
Results: Average CPAP compliance was 3.7±3.1 hrs/night. OSA subjects had a mild reduction in exercise performance (peak workload 189.5±22.3 W, 88.1% predicted; peak VO2 2.50±0.4L/min, 88.0% predicted). In all subjects leg fatigue limited exercise (peak Borg scale of 5.3±2.4 for dyspnea and 7.0±1.9 for leg fatigue). There were no significant differences in exercise duration (575 vs. 580 sec; p=0.84), peak workload (197±31 vs. 203±43 W; p = 0.50), peak VO2 (2.67 ±0.58 L/min vs. 2.41±0.32 L/min, p=0.22), peak heart rate (156±13 vs. 156±11 bpm; p= 0.93), or dyspnea/leg fatigue scores after CPAP therapy (n=4). End expiratory volume increased in subjects with OSA during exercise, but CPAP had no effect on this increase. In none of the subjects was there evidence of respiratory limitation to exercise.
Conclusions: 1. OSA patients have mildly reduced exercise performance, likely secondary to obesity and de-conditioning; 2. There is no evidence the respiratory system plays a role in limiting exercise in these patients; 3. Short-term (three-months) treatment with CPAP has no effect on cardiovascular or respiratory responses to exercise.

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0585.J

The Understudied Epidemic: The Actual Incidence Of Polysomnography Versus The Presumed Prevalence of Obstructive Sleep Apnea In A Major VA Population

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Introduction: The community prevalence of obstructive sleep apnea (OSA), defined by an RDI of 5 or more events per hour has been estimated to be approximately 9% in women and 24% in men. The prevalence is much higher among the elderly and among those with hypertension and/or congestive heart failure (CHF). OSA is associated with substantial subsequent morbidity, and the cost of untreated apnea has recently been estimated at $3.4 billion annually. Since 1995, the VA has been charged with providing not just medical care but the highest quality preventive care available to population that is older and has more chronic illness than the general population. In VA VISN-8 (Florida and South Georgia), wait times for a sleep study can exceed 6-12 months. The utilization of polysomnography and CPAP in this population has not been reported.

Methods: Data was extracted for all outpatient services from 1999-2002 in VA VISN-8. We tabulated the number and percent of polysomnography, CPAP procedures, and apnea diagnoses among all patients and among patients with CHF and/or hypertension. To evaluate the extent of lack of resources for diagnosis and treatment, we calculated standardized morbidity ratios for each year, using preliminary community OSA prevalence rates reported in the literature.
Results: The number of patients who underwent polysomnography in VISN 8 in 2002 was 510 out of about 330,000 patients seen. Based on the number of VA with documented heart failure and or hypertension, the estimated number of patients that may need diagnosis and treatment for OSA is approximately 61,000. We estimate that less than one in every thousand patients who may have clinically important OSA are being diagnosed and treated in this VA population.
Conclusions: Our data indicates that significant measures need to be taken to address this serious shortfall in the availability of diagnostic and treatment services for OSA.

This research was supported by the Patient Safety Center at the James A. Haley VA Hospital in Tampa, FL.

0586.J

Personality and Initial Doctor Contact for Patients Diagnosed with Obstructive Sleep Apnea

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Introduction: We hypothesized that whether an obstructive sleep apnea (OSA) patient or their partner first initiated doctor contact would be related to their internal-external scores on Health Locus of Control (HLOC). HLOC is a personality measure with three subscales assessing the degree to which one believes that one's health is 1) under one's own control (high score indicates internal LOC-I), 2) under the control of powerful others (i.e. health professionals; high score indicates external LOC-PO), and 3) a matter of chance (high score indicates external LOC-C). Norman and Bennett (1996, in M.Conner and P.Norman, (Eds.) Predicting Health Behaviour. Open University Press) write that individuals who act to promote their health, such as by exercise, or stopping smoking, are more likely to have an internal locus of control. Once ill, however, people who have belief in the power of others may be more likely to engage in health promoting behavior, such as going to the doctor.
Methods: 45 OSA patients (41 males, 4 females, mean age 57.9 years, range 37 – 82 years), with 4% dip rate > 10 per h and Epworth Sleepiness Score > 10, and their partners, were studied. Patients and partners completed questionnaires asking: 1) demographic details, 2) who initiated contact with their doctor (5-point scale: 5 = self, 4 = mainly self, 3 = jointly self and partner, 2 = mainly partner, 1 = partner), 3) 3 questions to assess each of the LOC subscales, and 4) 4 questions to assess degree of valuing health.
Results: The 5-point contact initiation scales of each couple were combined to provide an agreed initiation score, high scores meaning initiation by the patient: mean score = 3.00 (SD = 1.22). Initiation by the patient was more likely if they had a high LOC belief in Powerful Others ($r=.30$, $p<.05$). This correlation was smaller for OSA sufferers with (median-split defined) low value of health scores ($r=.24$, n.s.) than for those who value health highly ($r=.43$, $p<.05$). Partners were more likely to have initiated the contact if they are low (external) in LOC-I ($r=.32$, $p<.05$); this correlation was smaller in partners with low value of health score ($r=.20$, n.s.) than in those who value health highly ($r=.49$, $p<.05$). Contact initiation was not predicted by ESS scores (patient or partner).
Conclusions: People with OSA who believe in the abilities of the medical profession play a greater role than their partner in deciding initially to see a doctor about their condition. It may therefore be necessary to target individuals who do not in general have faith in the medical profession with information about specific treatments for OSA if they are to be encouraged to decide to see their doctor. However, this will only be effective for people who already value their health.

0587.J

Impact of the Nasal Surgery on Obstructive Sleep Apnea

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Introduction: Nasal continuous positive airway pressure (CPAP) is now established treatment for obstructive sleep apnea syndrome (OSAS). If the nasal cavity is obstructed, the treatment of CPAP for OSAS has a high possibility of a cessation. In the case of the complaint of nasal obstruction which resist medical treatment with CPAP failure , patients may require corrective surgery for an obstructive lesion such as polyps, marked mucousal thiking, or deviated septum. The purpose of this study was to assess the effectiveness of nasal surgery for CPAP failure in patients with severe OSAS and nasal obstruction.
Methods: Subjects were 8 male patients diagnosed as OSAS (ages 55.2 pm 8.3 years). CPAP failure was defined as the use for less than 4 hours per night on 70% of night and/or lack of symptomatic improvement due to the complaint of nasal obstruction. Sleep parameters were evaluated using standard polysomnography before and after nasal surgery. We also performed the rinomanometry to the degree of nasal obstruction before and after nasal surgery.
Results: After the nasal surgery, nasal resistance remarkably decreased (0.60pm0.29 /Pa/cm3/sec vs 0.17pm0.03 /Pa/cm3/sec,P f0.01). The lowest SpO2 significantly increased from (67pm11 % to 74pm8 % ,P f0.05) , but AHI did not show significant changes. The 3 patients (60%)who could not use both bilevel positive airway pressure (BiPAP)and CPAP before nasal surgery, but they could after surgery. @With using CPAP or BiPAP, AHI significantly decreased (50pm14 / hr vs 6.1pm2.5/ hr, P f0.01). The value of CPAP decreased in 3 cases from 17 cmH2O @to 13 cmH2O , from 17 cmH2O to 12 cmH2O, from 17 cmH2O to 12 cmH2O respectively.
Conclusions: Nasal surgery could improve the ability to tolerate CPAP as well as the severity of OSAS. Increased nasal resistance might contribute to CPAP failure. Hence, the correction of severe nasal obstruction is considered an important component in CPAP treatment for OSAS.

0588.J

REM Rebound Phenomena in OSA Patients

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Introduction: Obstructive sleep apnoea syndrome (OSA) disrupts the sleep structure, leading in most cases to deprivation of slow wave sleep (SWS) and rapid eye movement period (REM). The abnormal sleep architecture causes the accumulation of sleep deficit and related significant reduction of daytime performance. Polysomnography is the major method for complete diagnosis of OSA and nasal continuous positive pressure (nCPAP) has become the mainstay of therapy. Optimal nCPAP pressure is determined by a polysomnography. It is known that there is increase in REM with CPAP therapy, especially during the split-night and next few days (REM rebound phenomenon).The aim of the study was to evaluate the relationship between severity of sleep disturbances in OSA patients and occurrence of REM rebound.
Methods: A retrospective study of 30 male patients, within the period 2000 – 2002 year, was reviewed. All of the patients were referred to our sleep laboratory due to suspected OSA with mean Epworth sleep scale

(ESS) 13.2 [6-21] points. The mean age of the patients was 53 [38-69] years and the body mass index (BMI) was in range 26.8 – 49. A split-night with nCPAP titration with 16-channel polysomnographic system for evaluation of sleep and breathing disturbances was performed.
Results: 28 of the patients were evaluated for OSA. 2 had only habitual snoring with respiratory disturbances index (RDI) below 20 per hour. During the first part of the split-night without CPAP the mean RDI for the OSA patients was 50.1 [23-76] per hour and the mean arousal index (number of arousals per hour) was 63.59 [20-120]. There were no registration of SWS – III and IV stage of NREM sleep and lack of REM sleep. Total sleep time period (TST) was between 298.5 and 532.5 minutes; the mean sleep time without CPAP was between 46 and 95 minutes. A REM rebound phenomenon was found during the second part of the split-night with nCPAP titration in 14 patients (50%) - first group. The percent of REM sleep referred to TST was between 18.48% and 55.49%; and the mean RDI was 66.17 [23-76] per hour. The rest of the patients (second group) showed REM percent between 8.99% and 17.6%; mean RDI – 45.58 [18.5-72] per hour. 2 of the patients from the second group (14.29%) had significantly high RDI (65 and 72 per hour) and 3 of the patients from the first group (21.43%) had RDI between 23 and 26 per hour.
Conclusions: REM rebound phenomenon is registered in almost 50% of the patients with OSA. The severity of OSA (high level of RDI and arousal index) in most of the patients is associated with the percent of REM rebound. The accumulated sleep deficit contributes to higher percent of REM.

0589.J

Sleep Related Breathing Disorders in Veteran Beneficiaries
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Introduction: Sleep-related breathing disorders (SRBD) are serious; potentially life threatening conditions. SRBD prevalence among veterans very likely exceeds current estimates drawn from the general population because of the high amount of risk factors and comorbidities. We undertook analysis of the available VA databases to identify the prevalence of the diagnosed SRBD and some of the associated comorbidities.
Methods: This is a retrospective cohort study for fiscal years of 1998 to 2000 on all Veterans Affairs (VA) beneficiaries with a VA Outpatient Clinic File (OCF) and/or a VA Patient Treatment File (PTF) diagnosis of SRBD using ICD9-CM codes 780.53 and 780.51. PTF contains the records of hospitalizations among veterans. OCF contains all diagnoses documented during outpatient encounters in veterans. PTF contains information related to inpatient health encounter. Individual patients identified in the PTF can be tracked through the different files of the PTF and OCF by their unique identifiers (social security numbers) to obtain a complete record of encounters in the system.
Results: Total of 77,038 (from 3,243,039 individuals) in 1998 had SRBD diagnosis in their medical record. This number increased to 90,877 (out of 3,397,693) in 1999 and 110,960 (out of 3,647,328) in 2000. Prevalence of the SRBD was 2.38% for 1998, 2.67% for 1999, and 3.04% for 2000. Mean age at diagnosis was 58. 7 (SD + 14). 38% of subjects were 65 years or older. Some of comorbid diagnoses in this group included: Obesity 28%, Diabetes 28%, Hypertension 65%, and coronary artery disease (including MI and angina) 21%.
Conclusions: SRBD is a prevalent disease in this population. According to a study by Young (Sleep 1997), our data may be an underestimation of the true SRBD prevalence in this population. On the basis of Young's report, true prevalence of SRBD in VA beneficiaries may be well above 16%. This preliminary data also shows increase in diagnosed cases of SRBD in each of the successive years. This change may reflect increasing awareness of medical community about SRBD. In addition, as shown in above data, the cardiovascular comorbidities, diabetes mellitus, and obesity are common in this population. High prevalence of SRBD and accompanying comorbidities in VA beneficiaries indicate a need for increased sleep resources in the VA health care system.

0590.J

The Effects of nCPAP Therapy and Aerobic Exercise on Daytime Heart Rate Variability in Patients with Obstructive Sleep Apnea
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Introduction: Blunted heart rate variability (HRV) has received considerable attention in recent years as a potential indicator of risk for adverse cardiovascular events. Recent evidence indicates that HRV is altered during sleep in patients with obstructive sleep apnea (OSA). However, typical HRV protocols use 24-hr sampling that includes the acute effects of repetitive apneas. Our first objective was to assess HRV only during wakeful periods in newly diagnosed OSA patients with no other diagnosed cardiovascular comorbid conditions. The second objective was to assess effects of short-term nCPAP therapy, with or without aerobic exercise, on daytime HRV in these same patients.
Methods: Fourteen OSA patients [8 male, 6 female; age = 42.6 $\pm$ 11.9 yr; respiratory disturbance index (RDI) = 29.1 $\pm$ 12.3; Body Mass Index (BMI) = 35.8 $\pm$ 7.6 kg/m2] and 7 sedentary, apparently healthy controls (5 male, 2 female; age = 39.7 $\pm$ 9.0 yr; BMI = 31.6 $\pm$ 3.3 kg/m2) completed daytime measures of HRV at baseline and 6 weeks. HRV was assessed from precise ($\pm$ 1 ms) heart rate records of 8-hour waking periods in which subjects wore a small battery powered single-lead ECG recorder. After correcting the data for ECG artifact and extrasystoles, HRV was analyzed as the standard deviation of all normal R-R intervals (SDNN). All OSA patients were fitted with a ResMed (Poway, CA) AutoSet T™ nCPAP device. In addition, 7 of these treated OSA patients were randomized to a moderate-intensity (50-60% of VO2pk) aerobic exercise training program 3 days/wk.
Results: Mean nCPAP usage reported was 5.9 hr/night. At baseline, HRV (SDNN) was significantly higher in controls compared to the OSA group ($P = 0.03$). After 6 weeks, controls exhibited a 5.0% decrease in HRV, whereas the OSA group HRV increased by 130% ($P = 0.04$). At 6-wk, HRV was not different for OSA vs. control groups ($P > 0.05$) and the OSA subgroup receiving nCPAP therapy alone exhibited HRV increases that were not different ($P > 0.05$) than the subgroup receiving nCPAP combined with aerobic exercise. These findings show improved cardiovascular sympathovagal balance after nCPAP treatment and may be attributable to a reduction in apneic/hypoxemic events and associated surges in autonomic sympathetic activity.
Conclusions: Short-term nCPAP treatment increases daytime HRV in OSA patients who adhere to nCPAP therapy. Future studies should consider the potential beneficial effects of aerobic exercise to augment the effects of nCPAP treatment. Moreover, the addition of aerobic exercise training may be an effective intervention for reducing coronary risk factors, e.g., obesity and hypertension, in OSA patients.

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0591.J

Prevalence of Obstructive Sleep Apnoea Amongst Adult Mâori and non-Mâori in a New Zealand Community Sample

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Introduction: Effective diagnosis and treatment of obstructive sleep apnoea syndrome (OSAS) is currently hindered in New Zealand due to insufficient resource allocation, a lack of awareness amongst health care professionals and the public, and a lack of accurate prevalence information. This study aimed to estimate the prevalence of OSA in Mâori (indigenous people of New Zealand) and non-Mâori adults in the Wellington region, specifically addressing reported clinical differences in prevalence between Mâori and non-Mâori patients.
Methods: Between August 1999 and May 2001, letters and information packs were mailed to a stratified random sample of 1,200 people (600 of Mâori and 600 non-Mâori descent) aged between 30-60 years selected from the Wellington electoral rolls. Participants completed an unattended MESAMIV sleep monitoring study in their home and a pre-piloted questionnaire documenting sleep complaints and risk factors for OSA (body mass index, neck circumference, age and gender). MESAMIV studies were manually edited and scored blindly according to a validated method to estimate a respiratory disturbance index (RDI).
Results: Of 786 (65%) subjects contacted by phone, 364 (Mâori=169, non-Mâori=195) agreed to an overnight MESAMIV sleep study. A further 341 (Mâori=137, non-Mâori=204) answered the questionnaire only over the phone. Non-responders (questionnaire only, refusal, non-contactable) were not different to responders in terms of ethnicity, gender or age. The mean neck size for Mâori men was significantly larger than mean neck size for non-Mâori men (40.96 cm vs. 39.91 cm, difference=1.05, p=0.03). Similarly, there was a significant difference between Mâori and non-Mâori women (35.86 cm vs. 34.18 cm, difference=1.68, p<0.0001). Mâori were three times more likely to have 10 or more respiratory disturbances per hour during the night than non-Mâori (OR 2.97, 95% CI 1.27-6.94, p=0.01). Logistic regression analyses identified neck size, BMI and gender as independent predictors of an RDI/geq10. After controlling for these factors, ethnicity (Mâori vs. non-Mâori) no longer predicted an RDI/geq10.
Conclusions: In this preliminary analysis of an adult Wellington population sample, OSA was more prevalent and severe amongst Mâori, which concurs with clinic reports. The higher risk among Mâori for OSA appears to be due to well-recognised risk factors such as BMI, gender and neck circumference. A questionnaire-based multivariate predictive index for OSA will be developed combining this community sample (n=358) with a clinic sample (n=510) referred for suspected OSA. This will also be applied to the national survey (n=7048) of sleep habits and risk factors for OSA, to attain an estimate of OSA prevalence amongst New Zealand adults.

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0592.J

Nocturnal Angina Caused By OSA With Symptoms Relieved By Positive Airway Pressure

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Introduction: Nocturnal angina is traditionally thought to be due to coronary vasospasm. We present two cases of nocturnal angina which were caused by obstructive sleep apnea and were completely relieved by positive airway pressure. In both cases, return of symptoms indicated a need to alter treatment pressures which, when accomplished, abolished nocturnal angina again.
Methods: Two patients with known severe coronary artery disease on maximal medical therapy had angina occurring only at night. Both patients underwent full sleep evaluation including NPSGs. We present results of their studies and treatment.
Results: Case #1- A 71 y.o. male with known severe coronary artery disease (CAD), s/p CABG who had residual non-operable lesions. The patient had no daytime angina but was regularly awakened from dream sleep with typical angina relieved by nitrates. A NPSG revealed an AHI of 46 with O2 desaturations to 81%. The patient was treated with autotitratable CPAP and ultimately with BiPAP at pressures of 14/11 cm. H2O and had complete resolution of angina for more than a year. Repeat nocturnal symptoms prompted another study which showed return of OSA. Pressures were adjusted upward to 20/14 and both OSA and angina were abolished.Case #2- A 77 y.o. male with triple vessel CAD who had angioplasty of his LAD with residual disease in his RCA and Diagonal vessels. A NPSG was performed because of snoring and narrowed oropharynx and revealed an AHI of 35 with O2 desaturations only to 93%. The patient was intolerant of CPAP and was given an oral appliance. A NPSG evaluation of the oral appliance showed worse OSA with an AHI of 50.9 and desaturations to 70%. This was primarily due to greater amounts of REM sleep (77 minutes vs. 5 minutes in the original study). He was treated with BiPAP which resolved his SDB. The patient did well, lost 11 pounds and returned with recurrent angina awakening him from sleep early in the morning. A further study showed OSA that, after weight loss, BiPAP improved sleep fragmentation in non-REM sleep allowing transition to REM, more REM associated apnea and precipitation of angina. He was treated with greater BiPAP pressures and had resolution of his angina.
Conclusions: Nocturnal angina is a sign of OSA. Return of symptoms, after initial abolition with treatment, is an indication that positive airway pressures may need to be adjusted.

0593.J

Effect of Selective Serotonin Reuptake Inhibitors in Patients with Obstructive Sleep Apnea Syndrome and Depression

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Introduction: Animal studies have suggested that serotonin is important in the maintenance of upper airway patency. Serotonergic neurons exert an excitatory effect on upper airway dilator motorneurons. Abnormalities in brain serotonergic activity have been implicated in psychiatric disorders, including depression. This study examined how depressive symptoms and antidepressants such as selective seratonin reuptake inhibitors (SSRIs) affect sleep architecture, severity of obstructive sleep apnea syndrome (OSAS), and periodic leg movements.
Methods: The polysomnogram reports from July 2002 to November 2002 of 190 subjects (115 men , mean age 51.6, 75 women, mean age 51.4) with OSAS were reviewed retrospectively. Subjects were divided into depressive and non-depressive groups based on the Beck depression index (BDI) score (BDI<10: no depression, BDI>=10: depression). These two groups were further divided into SSRI and non-SSRI groups based on the medication history (Group 1 : OSAS without depression and SSRI, 51 men and 30 women, Group 2 : OSAS without depression and with SSRI, 9 men and 3 women, Group 3 : OSAS with depression without SSRI, 36 men and 28 women, Group 4 : OSAS with depression and SSRI, 19 men and 14 women). We excluded subjects who received antipsychotic, antianxiety, and hypnotic medications. Objective data such as age, sex, Epworth Sleepiness Scale (ESS), Body Mass Index (BMI), respiratory data (AHI, Back index, REM index), periodic leg movement index (PLM-I), periodic leg movement arousal index (PLM-AI), and sleep architecture (total sleep time:TST, sleep efficiency:SL,

sleep latency:SL, REM latency: REML, arousal index: AI, % of desaturation:%DESA) were collected. OSAS severity was grouped into mild (AHI: 5-20), moderate (>20-40), and severe (>40).
Results: 45 subjects (28 men, 17 women / 12 without depression, 33 with depression) among 190 subjects with OSAS were found to be taking SSRIs. The types of SSRIs were Zoloft, Paxil, Prozac, Celexa. Among the 4 groups, there were no differences in the sleep architecture, PLM-I and PLM-AI. Group 4 had higher ESS scores than Group 1 (13.1 vs 9.4, P=0.034,). Group 4 had a significantly lower AHI and Back index than Group 1 (AHI: 17.4 vs 34.7, P=0.020, Back index: 20.1 vs 40.6, P=0.026). There was a difference in the severity of OSA between group 1 and group 4. (group 1=42% mild, 22% moderate, 36% severe vs group 4=76% mild, 12% moderate, 12% severe). A reduction in AHI was seen during NREM sleep and while in the supine position, not during REM sleep.
Conclusions: This study suggests that depression symptoms did not affect the sleep architecture, severity of obstructive sleep apnea, and periodic leg movements seen in patients with OSAS. Enhanced serotonergic transmission may be more beneficial to patients with OSAS and depression than patients with OSAS without depression.

0594.J

Upper Airway Reflexes in Wakefulness to Sleep: Gender Differences
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Introduction: Although anatomical differences exist between genders, the mechanisms underlying the increased risk of OSA in men versus women remains unclear. One mechanism critical to OSA pathogenesis is the loss of protective upper airway reflexes in transitioning from wakefulness to sleep. To investigate this further we have studied 23 normal men and 18 normal women.
Methods: Each subject was instrumented to measure ventilation, pharyngeal mechanics (Millar catheters), and intramuscular upper airway muscle EMGs (genioglossus and tensor palatini) during basal breathing and negative pressure pulses (-10cmH2O at the choana) in both wakefulness and stable NREM sleep.
Results: We observed:1) No important differences between genders during basal breathing awake or asleep.2) Similar negative pressure reflexes between genders during wakefulness for both the GG and TP.3) Relatively preserved reflexes in women compared with men, in particular for the TP.4) The decrement in reflex from wake to sleep was more marked in men, especially for the TP.5) In 50% of the women, an actual increase in TP reflex response to negative pressure was observed.
Conclusions: We conclude that state-dependent gender differences in upper airway reflexes are present in normals and may explain some of the male predisposition to pharyngeal collapse.

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0595.J

Genioglossal Activity in Young and Middle-Aged Men During Normal Ventilation and CPAP Application
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Introduction: Genioglossal activity (gg EMG) is believed to be responsive to upper airway (UA) negative pressure. During wakefulness, gg EMG is elevated when airway resistance, and thus negative pressure, are high, as occurs in OSA patients. However, during established sleep gg responsiveness to negative pressure is reduced. At sleep onset gg activity shows a transitory fall, followed by a rapid recruitment, suggesting that early in sleep, in contrast to later in sleep, reflex activation of the muscle is present. To evaluate this hypothesis we studied airway resistance and gg EMG activity at sleep onset in two groups of subjects.
Methods: Eight middle-aged (MA, high resistance) and 12 young (Y, low resistance) men, with BMIs of 23.7 ($\pm$2.03) and 23.7 ($\pm$1.21) respectively, were studied supine for one night under two conditions, normal ventilation and CPAP (which eliminated group and sleep-wake state differences in airway resistance). In addition to sleep measures, gg EMG activity (expressed as a % of a standard manoeuvre – a swallow) and UA resistance were assessed. Data was obtained from an average of 83 ($\pm$34) and 57 ($\pm$21) sleep onsets (alpha to theta transitions) on normal nights and 56 ($\pm$22) and 40 ($\pm$23) on CPAP nights, for MA and Y subjects respectively.
Results: As anticipated UA resistance was significantly higher during wakefulness in the middle-aged men and increased more during theta (alpha [wake] values were 5.09 [MA] and 2.59 [Y] cmH2O/L/sec, while they were 7.91 [MA] and 2.85 [Y] by the 5th theta breath). These age-related differences were eliminated by CPAP. Consistent with the changes in UA resistance, gg EMG was significantly higher during wakefulness in the middle-aged men. Further, when off CPAP, the middle-aged men showed a more vigorous recruitment during sleep, consistent with the more rapid rise in resistance in this group (gg alpha values were 24.5% [MA] and 14.5% [Y], while they were 24.8% [MA] and 13.0% [Y] by the 5th theta breath). CPAP virtually eliminated differences in gg EMG between the groups and eliminated the recruitment during sleep in the middle-aged men. However, the sleep-related fall in gg EMG was not significantly affected by age or CPAP. Critically, during sleep in both groups, gg EMG was significantly higher on normal ventilation nights (23.9% [MA] and 13% [Y]) than on CPAP nights (11.1% [MA] and 8.9% [Y]), indicating the continued influence of reflex activation during sleep on the normal nights.
Conclusions: The differences in pharyngeal muscle activity between younger and middle-aged men are attributable to higher pharyngeal resistance in the older individuals. These data also suggest that the negative pressure reflex component of gg activity remains at least partially active following sleep onset.

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0596.J

Does Screening For Sleep Apnea With The Berlin Questionnaire Predict Elective Surgery Postoperative Complications?
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Introduction: Sleep Apnea-Hypopnea Syndrome (SAHS) has been reported to increase the risk of postoperative complications in patients undergoing surgery. However, preoperative screening methods to identify individuals at risk for SAHS are not widely utilized. In addition, optimal perioperative management of individuals found to be at risk for SAHS has not been well described. This retrospective study compared the rate of postoperative cardiopulmonary complications in groups of patients identified as high or low risk for SAHS by the Berlin Questionnaire.
Methods: The Berlin Questionnaire, a single page questionnaire with a reported positive predictive value of 0.89 for prediciting SAHS, was filled out by a consecutive series of patients who recently had elective surgery at our institution. Patients were characterized as high or low risk for SAHS based on the questionnaire. Charts were then retrospectively reviewed to assess for the incidence of postoperative cardiopulmonary complications (hypoxia, hypercapnia, need for supplemental oxygen / nCPAP / intubation / transfer to ICU, atelectasis, pneumonia, ischemia,

arrythmia, and thromboembolism). Patients were excluded if they failed to fill out the questionnaire completely, lacked records for review, were <18 y/o, or had a known diagnosis of SAHS.
Results: Ninety-eight patients filled out the questionnaire. Seventeen patients (17%) were excluded from analysis; incomplete questionnaires (13), lack of follow-up information (2) and known diagnosis of SAHS (2). Of the remaining 81 patients, 15 (18.5%) were categorized as high risk for SAHS. Demographics were as follows (high vs low): age - 41.6 vs 44.9 yrs, gender - 53% vs 71% F, BMI - 37.7 vs 28.7 kg/m2, CAD - 13% vs 6%, CHF - 13% vs 6%, Lung disease - 13% vs 9%, anesthesia - 100% vs 92% general.Patients at high risk for SAHS had more postoperative complications (20% vs 4.5%), though this did not reach statistical significance (p 0.16). Complications seen in the high risk group included supplemental oxygen (3), nCPAP (1) and transfer to the ICU (1). In the low risk group, 3 patients required supplemental oxygen. Of interest, none of the 81 patients were screened for SAHS by the anesthesiology or surgery services preoperatively.
Conclusions: Individuals identified as high risk for SAHS by the Berlin Questionnaire experienced more frequent postoperative cardiopulmonary complications than those at low risk. The difference did not acheive statistically significance, though this is likely due to small sample size. Given the simplicity of the screening tool and the potential for serious adverse outcomes in patients with SAHS undergoing surgery, further study of this approach is warranted. The study identifies the need for further education of presurgical providers with regards to preoperative screening for SAHS.

0597.J

Improvement in Hyperactivity after Adenotonsillectomy in Children with Sleep Disordered Breathing

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Introduction: It is possible that the consequences of obstructive sleep apnea (OSA) in children may include both daytime sleepiness and hyperactivity. Since for most children with OSA and adenotonsillar hypertrophy, adenotonsillectomy (T&A) improves or eliminates OSA, we explored the hypothesis that for some children hyperactivity may improve after T&A. We prospectively evaluated children with adenotonsillar hypertrophy and snoring by nocturnal polysomnography (NPSG) and by parental reports of hyperactivity, restlessness, conduct or behavioral problems by Conners' Global Index Parent Questionnaire (CGIPQ) before and after T&A.
Methods: Children 3 through 14 years of age with tonsillar hypertrophy and snoring were prospectively studied by nocturnal polysomnography. Parents were asked to fill out a Conners' Global Index Parent Questionnaire (CGIPQ) prior to the sleep study and after T&A. Children with circadian rhythm disorders or neurodevelopmental problems were excluded. Standard NPSG was performed in an academic sleep disorders center certified by the American Academy of Sleep Medicine, scored by a registered polysmnographic technologist according to the most recent criteria and reviewed by a sleep specialist certified by the American Board of Sleep Medicine. All obstructive apneas and hypopneas were scored only if accompanied by a 4% decrease in oxygen saturation or 25% decrease in heart rate. An apnea index of at least one obstructive apnea/hour was considered sufficient to make the diagnosis of OSA, and over 1 apnea+hypopnea/hour of total sleep or REM sleep to diagnose sleep-disordered breathing (SDB).
Results: The protocol was completed in 15 subjects, 13 boys and 2 girls, age 4.8 $\pm$ 1.6 (SD) years. Eight boys had SDB with a mean apnea+hypopnea index (AHI) of 9.7 $\pm$ 8.6 apneas+hypopneas/hour, while the remaining seven subjects, 5 boys and 2 girls, age 4 $\pm$ 1.1 years, had no significant SDB, with mean AHI = 0.2 $\pm$ 0.2 apneas+hypopneas/hour. There was no significant difference in body mass index (18.2 $\pm$ 6.7 vs 17.2 $\pm$ 1.6 kg/m2) between the groups. Comparing the pre- and post-operative CGIPQ, \bold there was a significant decrease in hyperactivity found in those with SDB after T&A //, from a median of 13.5 [range 2-32] to a median of 4.5 [range 1-14] with z = 2.52 and p = 0.01 using 2-tailed Wilcoxon signed-rank test. There was no significant difference in post-T&A hyperactivity in the non-SDB group (median 27 [11-42) pre-T&A vs 19 [0-29] post-T&A with z = 1.69, p = 0.09), nor was there any significant change in conduct or restlessness scores for either group.
Conclusions: T&A results in a significant reduction in hyperactivity for children with SDB. This suggests that hyperactive behavior problems in some children may be a consequence of OSA and amenable to surgical treatment.

0598.J

Effect of Body Mass Index on Oxygen Desaturations in Patients with Obstructive Sleep Apnea

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Introduction: While the relationship between decreased ERV and increased BMI has been well-established, the relationship between the decrease in ERV and minimum oxygen saturation of OSA patients needs further investigation. The purpose of this study was to determine if patients with lower BMI's have less desaturations for apneic periods than subjects with higher BMI's.
Methods: Patients in the study with suspected OSA were referred from their primary physician to the sleep disorders center for the purposes of a sleep evaluation. A complete sleep history was obtained on all patients. It was at this point that clinical lab values for the Body Mass Index were obtained. All patients scheduled for polysomnographic evaluation for the purposes of ruling out OSA had oxygen saturations and AHI's recorded. A full nocturnal polysomnogram was performed on all patients using a standard 16-channel montage. For the purposes of the study, patients were considered positive for OSA if the apnea-hypopnea index (AHI) was greater than 10 events per hour.Patients were grouped into BMI brackets of Less than 30, 30 - 40, Greater than 40. The average Minimum Oxygen Saturation was calculated for each group. Degree of OSA was grouped into three brackets: Mild to Moderate (AHI 10-30), Moderate to Severe (AHI 31-50), Severe (AHI >50.)
Results: Of 157 patients with documented OSA, 68 had a BMI <30, 51 had a BMI between 30-40, and 38 had a BMI>40. There was a trend for the average minimum oxygen saturation to decrease as the BMI increased in the same degree of OSA. Most of the decreases were within the standard deviation. Additionally, there was a trend for the average minimum oxygen saturation to decrease as the severity of the OSA increased. BMI <30 BMI 30 - 40 BMI > 40AHI 10-30 84.1 ± 6 84.8 ± 4 81.5 ± 6AHI 30-50 82.8 ± 7 80.8 ± 9 78.2 ± 10AHI >50 81.1 ± 8 77.4 ± 10 72.6 ± 9AHI >10 82.7 ± 7 80.7 ± 9 77.4 ± 9
Conclusions: For the same degree of OSA there is a trend for the average minimum oxygen saturation to decrease with increasing BMI. Because of the inverse relationship between BMI and ERV, this decreasing trend may be attributed to decreasing ERV's.

0599.J

Single Trial Reliability of Objective Tests for Daytime Somnolence in Obstructive Sleep Apnea (OSA)

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Introduction: Recently, it has been shown that CPAP therapy for OSA is most beneficial in individuals with daytime somnolence. Daytime

somnolence is determined clinically through the use of subjective measures of sleepiness. Objective measures of sleepiness, including the Multiple Sleep Latency Test (MSLT), Psychomotor Vigilance Testing (PVT) and Divided Attention Driving Task (DADT) are often thought to require multiple trials over the course of several hours in order to obtain a measure with sufficient reliability for clinical application. The goal of this study was to determine the differential reliability of a single trial of the MSLT, PVT or DADT as a measure of daytime somnolence, or its consequences.

Methods: The study cohort comprised 406 (384 M, 22 F) holders of commercial drivers licenses (unweighted mean (SD) age = 46.7 (11.4) y) constructed using a risk-stratified sampling design to enrich the sample with regard to apnea. We measured apnea hypopnea index (AHI) in events/hr using in-laboratory polysomnography. The unweighted percentages with different apnea severities (events/hr) were 64.0% (<5), 21.2% (5-<15), 7.9% (15-<30), and 6.9% (>=30). Each measure was assessed four times. Sleep latency was defined as time to sleep onset during a 20 min nap opportunity. Each PVT trial was 10 min. Several parameters were extracted from the response time (RT) distribution including (transformed) lapses per trial (RT>500ms), optimum RT (mean 10% fastest RT), RT slowing (mean slowest 10% 1/RT) and PVT fatigability (slope of 1/mean RT based on 1 min intervals). Each DADT trial was 30 minutes. DADT parameters included mean tracking error and tracking decrement function (slope computed based on 2 min intervals). For comparison, mean tracking error was also computed for the first 10 min. Mixed model ANOVA were used to determine intraclass correlations (ICC) adjusted for time of day, reflecting the proportion of total variance (adjusted for time of day) attributable to true differences between individuals (as opposed to within subject variance). The ICC quantifies reliability of a single ascertainment.

Results: The estimated ICC values were: DADT tracking error (0.86), PVT slowing (0.72), PVT fastest 10% RT (0.71), PVT median RT (0.62), PVT transformed lapses (0.62), MSLT (0.46), DADT slope (0.37), and PVT slope (0.18). DADT tracking over first 10 min had ICC of 0.80. Values without time of day adjustment were very similar.

Conclusions: The 30-min DADT task had the highest ICC (0.86), but a task one third its duration (10-min PVT) still had a moderately high reliability (0.72). The experimental 10-min DADT maintained good reliability (0.80). Variables looking at slope of change and a single trial of MSLT were the least reliable. Further studies will need to address whether these parameters reflect valid measures of hypersomnolence secondary to sleep apnea or other aspects of performance capability.

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0600.J

Abnormalities on Nasal Exam Associated with Decreased CPAP Tolerance and Use

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Introduction: Poor tolerance and inadequate use are the greatest limitations to continuous positive airway pressure (CPAP) therapy for obstructive sleep apnea syndrome. Abnormality on pre-CPAP nasal exam has not been tested as a determinant of CPAP tolerance or use. Understanding this relationship may enable improved treatment for sleep apnea.

Methods: This retrospective cohort study evaluated 306 patients who were prescribed CPAP therapy for sleep apnea at the University of Washington Sleep Disorders Center January 2000 - August 2002. Patient demographics, nasal complaints, findings on nasal exam, polysomnography data, and CPAP data, including CPAP follow up data, were extracted from medical records. Abnormalities on nasal exam included turbinate hypertrophy, septal deviation, or other abnormalities, and were analyzed as a dichotomous variable (abnormality yes/no). CPAP use was dichotomized as any use versus no use at follow up. CPAP tolerance was dichotomized as tolerating well (and using as recommended) versus not tolerating well (and using less than recommended) at follow up. Multivariable logistic regression was used to calculate adjusted odds ratios and 95% confidence intervals (CI). Adjustment variables were left in the model if they impacted odds ratio estimates >10% or were statistically significant (Wald's test), and they included age, sex, race, smoking status, body mass index, apnea-hypopnea index, CPAP titration method, type of CPAP humidification, and time from CPAP titration to follow up evaluation.

Results: The cohort mean age was 49 $\pm$ 12 years with 62% male. Mean apnea-hypopnea index was 56 $\pm$ 40 events/hour, and mean CPAP pressure was 13 $\pm$ 4 cm H2O. Median time to follow up was 90 days (95%CI 75, 102). 108 (35%) had an abnormal nasal exam. Of the 200 patients with follow up CPAP data available, 145 (73%) were using CPAP, and 68 (34%) were tolerating CPAP well. Patients with an abnormal nasal exam were found to have decreased CPAP use and tolerance. On bivariate analysis, odds ratios for CPAP tolerance and CPAP use were 0.52 (95%CI 0.28, 0.96; p=0.04) and 0.47 (95%CI 0.25, 0.89; p=0.02), respectively, for those with an abnormal exam relative to those without an abnormal exam. On multivariable analysis, the adjusted odds ratio for CPAP tolerance was 0.42 (95%CI 0.20, 0.90; p=0.03) for those with an abnormal exam relative to those without an abnormal exam, adjusting for time to follow up evaluation. On multivariable analysis, the adjusted odds ratio for CPAP use was 0.32 (95%CI 0.15, 0.66; p=0.003) for those with an abnormal exam relative to those without an abnormal exam, adjusting for body mass index, apnea-hypopnea index, and titration method.

Conclusions: These data suggest that nasal exam abnormalities may affect CPAP tolerance and use. This fact should be confirmed with a prospective cohort study. This finding emphasizes the need for special attention to the nasal exam before prescribing CPAP. One should consider treatment of nasal conditions, which may improve CPAP tolerance and use.

0601.J

Sleep Apnea in TIA Patients

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Introduction: Sleep apnea is a risk factor for hypertension and possibly for stroke as well. Results from prospective studies are eagerly awaited. One research question that remains is whether Transient Ischemic Attack (TIA) patients have the same prevalence of SAS as stroke survivors. Bassetti et al observed that up to 68.7% of TIA subjects had an apnea-hypopnea Index (AHI)≥ 10.

Methods: We performed a case control study in TIA patients. Controls were recruited from spouses of stroke (results not shown) or TIA patients. TIA cases were recruited either from hospital or a stroke prevention clinic. All subjects were subjected to standard questionnaires (demographic, Epworth), nocturnal PSG, and a standard neuropsychological battery (Decary et al 2000) developped for OSAS patients. PSG were scored manually. Hypopnea definition used a 3% fall in O2 saturation.

Results: Patients (n= 22; 10 males and 12 females) and controls (N= 14) were well matched for age (62.8 $\pm$ 9.6 vs 63.8 $\pm$ 7.2) and education (9.3 $\pm$ 3.9 vs 11.9 $\pm$ 4.4). Hypertension, as identified by history, was present in 66.7% vs 50%. BMI was found to be significantly higher in controls (28.4 $\pm$ 2.9 vs 31 $\pm$ 4.8). Depressive symptoms as measured by Beck I were more frequent in patients (10.1 vs 5.14). 10/22 TIA patients had AHI ≥10 compared to 6/16 controls (mean AHI = 10.3 vs 10.1/hr- n.s.). We found that cases performed as well as controls on most tests of neuropsychological function. Also, TIA with AHI ≥10 had results on neuropsychological tests similar to patients with AHI < 10. A total of 40% of TIA patients had AHI ≥ 10.

Conclusions: We conclude that : 1) TIA patients present a high rate of obstructive events. 40% of our subjects have an AHI ³10 which is less than Bassetti et al. 2) Spouses of TIA and stroke patients were shown to have a high rate of vascular risk factors including higher BMI. They seem to be having the same amount of apnea-hypopnea as their spouse patients. The high frequency of obesity in our controls may explain the high rate of apnea –hypopnea as well as performance on cognitive testing.

0602.J

Intramyocellular Lipid Decreases With nCPAP Treatment in Obstructive Sleep Apnoea

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Introduction: Obstructive sleep apnoea (OSA) is associated with features of the metabolic syndrome such as increased insulin resistance, hypertension, obesity and dyslipidaemia. Preliminary data have suggested some of these abnormalities are reversed with nasal continuous positive airways pressure (nCPAP) treatment of OSA. Since intramyocellular lipid (IMCL) content is associated with insulin sensitivity (IS) and obesity in the general population, we postulated that IMCL would correlate with indices of IS in OSA patients and that IMCL content would decrease after elimination of OSA with nCPAP.
Methods: We assessed 35 males with moderate to severe OSA (49.3±12.3y, BMI 35.6±6.3kg/m2, total respiratory disturbance index [RDI] 59±26 events/hr) at initial diagnosis and reassessed a subgroup of these patients (n=11) objectively compliant with nCPAP treatment after 3-6 months. On each occasion, soleus IMCL content (expressed as ratio to creatine in arbitrary units [au]) was assessed using in vivo magnetic resonance spectroscopy. Adiposity was assessed with anthropometry, fasting bloods were collected and resting arterial blood gases measured.
Results: Although at baseline severity of OSA (as measured by total RDI, minimum oxygen saturation during sleep and total arousal index) correlated significantly with indices of IS (fasting plasma insulin, homeostasis model assessment [HOMA], BMI, and waist girth), IMCL did not correlate with any measure of IS, nor with any measure of OSA severity. IMCL content decreased significantly after nCPAP treatment (from 14.0±1.7au to 12.0±1.4au; p=0.004) without change in BMI or insulin sensitivity (as assessed by HOMA). Awake oxygen levels (PO2) increased on nCPAP (78.9±2.1mmHg pre to 92.7±4.5mmHg post;p=0.016). Mean plasma total cholesterol and LDL cholesterol decreased after nCPAP treatment (p=0.05 & 0.04 respectively).
Conclusions: IMCL content appears to decrease after short-term nCPAP treatment. We speculate that correction of repetitive nocturnal hypoxaemia allows for intramuscular fat to be oxidised rather than stored.

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0603.J

Müller Maneuver: Evaluation of Upper Airway Behavior without & with Oral Appliance (Mandibular Lingual Repositioning Device)

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Introduction: The fiberoptic scope used to evaluate the upper airway with Müller's maneuver have been evaluated by Sher et al and Katsantonis et al as a method to identify potentials obstructions areas. Mandibular position modify upper airway anatomy. The use of mandibular/lingual repositioning device (MLRD) is a alternative to treat obstructive sleep apnea/hipopnea syndrome (OSAHS). The objective of this study is to verify, under fiberoptic nasopharyngolaryngoscopy (NPLC), the upper airway anatomy behavior without and using MLRD.
Methods: A group of ten patients (descriptive data are shown in table 1) were treated with ARML and Müller maneuver observed by NPLC was evaluated, without and with oral appliance.
Results: What oropharynx was concerned there was no increase on the diameter larger than 50% in any of the cases. At the hypopharynx, there was a significant improvement, of 90% (9 patients), due the decrease of the tongue's base at the airway narrowing. Of those 30% (3 patients) had a significant increase of the antero-posterior airway diameter, enough to allow the Müller maneuver to be negative. At the remaining patients (60%/6 patients) the upper airway narrowing provoked by the side walls was even enough to diminish in more than 50%, of the hipopharynx caliber. Only one patient (10%) didn't show any changes at the upper airway endoscopic analyses when using MLRD during Müller maneuver.
Conclusions: Due to the technical procedures (disconfort, patient's position and state of alertness), equipments and examinator's hability, the endoscopic exam using Müller's maneuver, in order to observe the anatomic behavior of the upper airway, becomes subjective. We should also point out that this exam is dinamic, allowing some structures, such as soft palate to move during the exam, changing the airway caliber at this level, even with the oral appliance in position, oposite to static images (XR, NMR and CT). This must be considered.As observed, it was possible to conclude that the MLRD promotes na effective increase of the antero-posterior hypopharynx diameter at Müller maneuver through the mandible protusion, and from the tongue's base position, but doesn't provoke a significant change in oropharynx. Therefore, bacause of the exams limitations, needs to be validated with other visual exams like XR, NMR and CT.

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0604.J

Prescribed Versus Actual CPAP Pressure; An Analysis of 225 Consecutive Clinic Visits

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Introduction: Clinicians determine an appropriate CPAP pressure and then write a prescription that is usually dispensed by a durable medical equipment company (DME). These companies are often given responsibility for following the patients. We wanted to know how often patients were actually getting the pressure we had prescribed.
Methods: Using water manometry, we prospectively measured the pressure generated by the patient's CPAP device at 225 consecutive clinic visits (221 patients). We also noted the brand of device, LED display, altitude setting, calibration adjustment, mask/filter problems and the last prescribed pressure. All pressure measurements were in cm H2O.
Results: During 225 visits, 183 CPAP devices were evaluated. The prescribed pressure was unknown in 3 patients. There were 15 different brands of devices: 3 auto-titrating, 4 bi-level and 10 CPAP. In 92/183 (50%) measurements, the actual pressure differed from the prescribed pressure. Faulty equipment in 4 patients (3 broken masks, 1 clogged filter) interfered with delivery of the prescribed pressure. In 80/167 (48%) fixed CPAP measurements, the actual was different from the prescribed pressure. It was higher in 59 (35%), (mean 1.38, range 0.5-4, std dev. 0.89) and lower in 21 (13%), (mean 1.66, range 0.5-12, std dev. 2.99). In 56/94 (60%) devices with an LED display, the actual differed from the displayed pressure. It was higher in 51 (54%) (mean 1.48, range 0.5-4, std dev. 0.98) and lower in 5 (5%) (mean 0.7, range 0.5-1, std dev. 0.27).

In only 2/94 (2%), was there evidence the DME had calibrated the device. In 16/72 (22%) devices with altitude adjustment, the setting was wrong (5 medium, 11 high) (mean 1.69, range 1-2, std dev. 0.48). In 3/8 (38%) auto-titrating devices the pressure was wrong (1 auto-low was 8 cm low, 2 auto-high were 1-5 cm high). In one instance a snore-based device was dispensed for a flow-based device despite a do-not-substitute prescription. In 3/8 (38%) bi-level devices settings were incorrect. One had no back-up rate set and 2 were at the wrong pressure (IPAP 1-2 cm higher, EPAP 1 cm lower, 1 cm higher).
Conclusions: In a regional sleep center, a significant number of positive pressure devices being used by patients were not actually at the pressure prescribed by a sleep clinician. There is variation in the design of pressure devices as well as the quality of care provided by DME. Clinicians would be advised to check their patient's device at clinic visits. In addition, they should prescribe devices with accurate LED displays and altitude adjustment features that are more difficult for patients to inadvertently change.

0605.J

Ventilatory Response To Arousal In Obstructive Sleep Apnea
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Introduction: The ventilatory response to arousal from sleep may be an important determinant of respiratory stability/instability and could therefore be involved in the pathogenesis of obstructive sleep apnea (OSA). Although the ventilatory response to arousal is commonly thought to result from the increased chemoresponsiveness of wake relative to sleep, the relatively high PaCO2 that develops during sleep and the sudden reduction in upper airway resistance, there is also evidence that the ventilatory response to arousal is a result of a "waking reflex" unrelated to chemoresponsiveness. We designed this study to determine if the ventilatory response to arousal is influenced by upper airway resistance and CO2 levels prior to awakening or is a product of this waking reflex.
Methods: 4 patients with OSA (Mean(SEM) AHI 41.9(5.2) events/hr) have been studied to date. Inspired minute ventilation (VI), upper airway resistance (RUA) and end tidal CO2 (PETCO2) were measured during stable sleep on CPAP sufficient to abolish flow limitation (optimal CPAP, 10.5(1.2) cmH2O) and on a lower level of CPAP with stable flow limitation (sub-optimal CPAP 7.5(0.4) cmH2O). Brief arousals arising from and returning to stable NREM sleep were identified by a single observer who was blinded to respiratory data and CPAP condition. Ventilation on the first breath after arousal was recorded and compared between CPAP conditions with Student's paired t-test. In addition, ventilation was interpolated at 4s intervals for 40s after arousal and compared between CPAP conditions with ANOVA for repeated measures. The pre-arousal conditions were also compared between CPAP levels with Student's t-tests.
Results: During stable sleep, RUA tended to be higher on sub-optimal CPAP than optimal CPAP (8.5(2.4) versus 2.8(0.5) cmH2O/l/s respectively, p=0.08) however VI (7.6(1.0) and 7.9(0.9) l/min respectively) and PETCO2 (43.0(1.6) and 41.6(1.3) Torr respectively) were not significantly different between CPAP conditions. The duration of arousal was not different between sub-optimal and optimal CPAP (9.0(1.3) and 6.1(0.6) s respectively). On the first breath following arousal, VI was not different between sub-optimal and optimal CPAP conditions (11.1(1.8) and 9.8(1.1) l/min respectively) and no significant effect of CPAP condition or interaction with time were found.
Conclusions: These preliminary results suggest that pre-arousal RUA has minimal influence on post-arousal ventilation. Further studies are required to confirm this finding and to establish the role of pre-arousal PETCO2. The present results suggest that the ventilatory response to arousal may be dependant more on a neural "waking reflex" than pre-arousal conditions such as RUA.

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0606.J

Sleep Disordered Breathing in Gastric Bypass Patients
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Introduction: Morbid obesity has long been associated with sleep disordered breathing. Independent risk factors have included obesity, age smoking, and gender. We sought to determine risk factors for sleep disordered breathing in morbidly obese patients undergoing gastric bypass surgery.
Methods: In this study, symptomatic gastric bypass patients were examined preoperatively for sleep disordered breathing (SDB). The patients completed two questionnaires: the Epworth Sleepiness Scale (ESS) and the Sleep Quality Profile (SQP). Those patients with a score of 10 on the ESS, or at least one "Yes" on the SQP were referred from a bariatric surgery clinic to a sleep disorders center accredited by the American Academy of Sleep Medicine, for history, physical examination and nocturnal poysomnography (NPSG), which were then scored by an accredited polysomongraphic technologist and reviewed by a physician certified by the American Board of Sleep Medicine. Sleep-disordered breathing (SDB) was considered to be present in those with 5 apneas/hour or 10 apneas+hypopneas/hour of total sleep, REM sleep or supine sleep, or upper airway resistance syndrome (UARS) confirmed by elimination of sleep disruption on repeat NPSG with nasal continuous positive airway pressure.
Results: Twenty three patients were evaluated (19 females, and 4 males) with a mean age of 37.7 $\pm$ 10.35 (SD) years, (range 25-57 years). Mean body mass index (BMI) was 49.4 $\pm$ 7.2 kg/m2, (range 41-70 kg/m2). The mean neck circumference was 43.4 $\pm$ 5 cm, (range 34.5-58 cm). Total sleep time (TST) was 357 $\pm$ 60 minutes, with 52 $\pm$ 29.5 minutes of REM sleep and 24 $\pm$ 23 minutes of slow wave sleep (SWS). SDB was found in 61%. Patients were separated into two groups: Group 1 (SDB) and Group 2, those without SDB. In Group 1 there were 14 patients with a mean age of 39.5 $\pm$ 11.9 years (range 25-57 years), a mean BMI of 51.6 $\pm$ 7.7 kg/m\super2 (range 42-70 kg/m\super2), a mean neck circumference of 44.6 $\pm$ 5.15 cm (range 39-58 cm), and a mean ESS of 12.6 $\pm$ 6.1 (range 5-24). In Group 2 there were 9 patients with a mean age of 34.9 $\pm$ 6.95 years (range 26-49 years), a mean BMI of 46 $\pm$ 4.9 kg/m2 (range 42-70 kg/m\super2), a mean neck circumference of 41.1 $\pm$ 4.2 cm (range 34.5-48.5 cm), and a mean ESS of 7.6 $\pm$ 5.8 (range 1-17). Between groups 1 and 2, there was no statistically significant difference in TST, REM sleep time, or SWS. Those with SDB had a significantly higher BMI ($p = 0.02$), and ESS ($p = 0.03$) than those without SDB. Neck circumference was not statistically significant between the two groups ($p = 0.06$).
Conclusions: In morbidly obese patients undergoing bariatric surgery, a higher ESS and BMI, but not neck circumference, appear to be associated with an increased risk of SDB.

0607.J

Methadone Maintenance Treatment and Central Sleep Apnea
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Introduction: Opioid maintenance treatment utilizes long acting opiate agonists such as methadone to reduce the use of illicit opiates and their associated risks. It is currently estimated that approximately 179 000

patients in the United States are involved in an opioid maintenance therapy. Our clinical experience has suggested that clinically significant central apnea may develop in some methadone maintenance treatment (MMT) patients. This impression has been supported by a pilot study that found a higher prevalence of central sleep apnea in stable MMT patients.We sought to replicate this finding in a group of MMT patients complaining of sleep difficulties.

Methods: A retrospective chart review was performed on all MMT patients who were studied by polysomnography (PSG) between June 1999 and July 2001. 23 MMT patients with daily doses ranging from 20mg to 285mg were studied. We compared them to an age and sex matched group of non-MMT sleep clinic patients who had undergone PSG between the same interval. These groups were compared across Apnea-Hyponea index (AHI), Central Apnea Index (CAI) and Obstructive Apnea Index (OAI). The group results were analyzed using T-tests.

Results: As presented in table 1, the MMT group had a mean CAI of 10/hr which is significantly greater than in the control group (p=.03). The groups did not differ significantly with respect to AHI, OAI, BMI, Age, or BMI.Table 1: MMT Control t-statistic p-value

	n=23	n=23			Mean	Mean	
Age	34	39	-1.10	.27	M/F	16/7	
16/7		Dose	135.9	0	/	/AHI	
20.6	17.1	0.58	0.56	CAI	9.8	0.3	
2.24	0.03	OAI	2.1	1.4	0.67	0.43	BMI
32.3	31.3	0.9	0.37				

Conclusions: These preliminary results suggest that Central Apnea may be present in MMT patients complaining of sleep difficulties. Further work will be required to extend this finding, evaluate the clinical significance and elucidate the underlying mechanisms.

0608.J

Evening-To-Morning Increase In Arterial Stiffness In Patients With And Without OSA

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Introduction: There is a strong causal link between Obstructive Sleep Apnea (OSA) and systemic hypertension. Nocturnal blood pressure elevation routinely occurs in association with the acute effects of apnea during sleep. The true nature and prevalence of sustained daytime hypertension is however poorly understood. Pulse Wave Analysis (PWA) is a recently developed technique that allows the non-invasive assessment of arterial stiffness and central aortic pressure. Elevated central aortic pressure as a result of increased arterial stiffness may occur even in the presence of a normal peripheral (brachial) blood pressure. Arterial stiffness is an important predictor of mortality. We hypothesised that OSA would be associated with an increased arterial stiffness independent of peripheral blood pressure.

Methods: PWA including Augmentation Index (AIx) - a measure of arterial stiffness, peripheral and central aortic blood pressures (AtCor Medical, Australia) were measured in 40 male (age 44.1±9.6, BMI 31.0±5.7, RDI 13.7±16.5) patients referred for investigation of suspected OSA. Patients underwent repeated PWA measures prior to (5-7 pm) and immediately upon awakening (5-6 am) from sleep. Recordings were performed in the fasted (>5 hrs post meal) state after at least 20 minutes supine rest.

Results: Morning heart rate was marginally lower (PM: 65±10 bpm vs AM: 62±9, p<0.005) whilst morning AIx was markedly higher (PM: 17.0±8.9 % vs AM: 24.4±8.9 %, p<0.001). There was a trend for peripheral blood pressures to be marginally different between evening and morning (PM: 126±15/76±9 vs AM: 123±13/76±10 mmHg, p<0.07 for SBP). Central aortic blood pressures did not differ (PM: 114±14/77±9 vs AM: 114±13/78±10 mmHg, p=ns). Whilst there was an evening-to-morning change in peripheral pulse pressure (PPP), this was not reflected in central aortic pulse pressure (CPP) (PM: PPP 50.8±10.5 vs AM: PPP 46.5±9.4 mmHg, p<0.02; PM: CPP 37.1±8.4 vs AM: CPP 36.5±8.4 mmHg, p=ns). Finally, the ratio of peripheral to central pulse pressure (PPP:CPP) was markedly lower in the morning (PM: 1.380 vs AM: 1.287, p<0.001).The trend for an evening-to-morning decrease in peripheral blood pressure was not reflected in central aortic pressure. The morning increase in AIx resulted in an overnight decrease in pulse pressure amplification (PPP:CPP ratio). There was a significant (p<0.02) negative correlation between RDI and the overnight change in pulse pressure amplification.

Conclusions: In a sleep laboratory cohort including patients with/without OSA there was a consistent increase in arterial stiffness from evening to morning. The morning increase in arterial stiffness results in the non-dipping of central aortic blood pressure despite a trend for peripheral dipping. This may be a natural phenomenon that represents the dilatory potential of large conduit arteries and pre-resistance vessels. Sleep apnoea, either by acute (apnoea related) or sustained (vascular remodelling) effects appears to modify the central aortic circadian blood pressure profile. However, potential confounders need to be controlled for in a larger ongoing study.

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0609.J

Effects Of Acute And Chronic CPAP Withdrawal On Evening-To-Morning Changes In Arterial Stiffness

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Introduction: Despite evidence demonstrating a strong causal link between Obstructive Sleep Apnea (OSA) and systemic hypertension, in particular, nocturnal hypertension, the nature and prevalence of sustained daytime hypertension is only poorly understood in this group. Pulse Wave Analysis (PWA) is a recently developed technique that allows the non-invasive assessment of systemic arterial stiffness. Arterial stiffness has been identified as an important predictor of mortality. Recent evidence from our centre indicates that a marked overnight increase in arterial stiffness may be a normal phenomenon. However this overnight increase was negatively correlated with the severity of OSA as measured by the Respiratory Disturbance Index (RDI). We hypothesised that there would be a gradual attenuation of the overnight increase in arterial stiffness if OSA activity was allowed to resume following withdrawal of CPAP.

Methods: PWA including Augmentation Index (AIx) - a measure of arterial stiffness (AtCor Medical, Australia) was performed in 5 patients who underwent 7 nights of CPAP withdrawal after at least 12 months of therapy (minimum compliance > 4 hours/night and RDI < 10). Readings were taken prior to (5-7 pm) and immediately upon awakening (5-6 am) from sleep on each of 4 days. Day 1 – following the last night on CPAP, Day 2 – following acute (1 night) CPAP withdrawal, Day 8 – following chronic (7 nights) CPAP withdrawal and Day 9 – following acute (1 night) CPAP reinstitution. Recordings were performed in the fasted (>5 hrs post meal) state after at least 20 minutes supine rest.

Results: Mean RDI following acute and chronic CPAP withdrawal was 37.5±17.1/h (Day 2) and 44.4±25.6/h (Day 8), respectively. Consistent with our previous work, morning AIx was always greater than evening AIx on each of the 4 study days (Day 1: AM 32.9±4.3%, PM 23.5±6.1 p<0.1; Day 2: AM 32.3±4.1%, PM 16.2±4.7%, p<0.002; Day 8: AM 34.5±5.2%, PM 27.4±6.2% p<0.2; Day 9: AM 31.3±4.5, PM 18.2±6.2, p<0.03). Compared with baseline on CPAP, withdrawal and reinstitution of CPAP did not significantly change morning AIx. However, there was a pronounced reduction of evening AIx following both acute withdrawal (Day 2, p<0.002) and reinstitution (Day 9, p<0.02) of CPAP.

Conclusions: Acute withdrawal (day 2) and reinstitution (day 9) of CPAP were both associated with a profound decrease in evening arterial stiffness. The smallest AM to PM ratio was seen after 7 nights of CPAP withdrawal (day 8) consistent with our previous observation of a negative correlation between the magnitude of the overnight change in arterial stiffness and increasing severity of OSA. The nature of the acute evening changes following withdrawal and reinstitution of CPAP remains unclear. However, they may reflect acute adaptive cardiovascular responses to hypoxia that are not sustained following 7 nights of CPAP withdrawal.

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0610.J

Predictors of Serious Complications after Uvulopalatopharyngoplasty

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Introduction: Uvulopalatopharyngoplasty (UPPP) is the most common surgical treatment for obstructive sleep apnea. Anatomic and physiologic abnormalities associated with sleep apnea may increase the risk of perioperative complication. Previous evaluation in a large, multi-site cohort of UPPP patients revealed a 1.7% incidence of serious complications. The objective of this study was to test the hypothesis that comorbidity, performance of concurrent sleep apnea procedures in addition to UPPP, body mass index (BMI), and apnea-hypopnea index (AHI) are risk factors for serious complication.
Methods: A retrospective cohort study and a nested case-control study were used to test the risk factors. A cohort of 3191 adult UPPP patients was analyzed retrospectively from the Veterans Affairs National Surgical Quality Improvement Program database of all inpatient surgeries nationally from 1991-2001. Cohort data were collected prospectively and included demographic data, preoperative presence of 13 major medical comorbidities, simultaneous procedures with UPPP, 15 specific life-threatening complications, 30-day mortality, and other variables. Comorbidity was analyzed both by the count of specific conditions and by the American Society of Anesthesiology classification (ASA class 1 – 5). Data on BMI and AHI were not available in the cohort database and thus were extracted from the medical records of the 55 cases of complication and of 220 controls from the cohort, matched on age, sex, year of operation, and concurrent surgery. Logistic regression was used to calculate odds ratios and 95% confidence intervals (CI).
Results: In the cohort analyses, the adjusted odds ratio for serious complication was 2.05 (95%CI 1.57, 2.69) for each additional comorbid condition and was 2.15 (95%CI 1.32, 3.52) for each increase in ASA class, adjusting for age, sex, race, smoking status, year of operation, and multiple procedures. The adjusted odds ratio for serious complication was 1.62 (95%CI 0.93, 2.83; p=0.09) for multiple procedures relative to UPPP alone, adjusting for age, sex, race, smoking status, year of operation, and ASA class. In the case-control analyses, the odds ratio for serious complication was 1.07 (p=0.66) for each increase in BMI of 5kg/m2 and was 1.05 (p=0.39) for each increase in AHI of 15 events/hour; however, data from 14 cases and 41 controls are pending. The case-control study had 95% power to detect a difference of 5 kg/m2 in BMI between cases and controls, and it had 47% power to detect a difference of 15 events/hour in AHI between cases and controls.
Conclusions: Comorbidity was independently associated with serious complication, and multiple procedures showed a trend toward an independent association with complication. BMI and AHI, however, were not associated with complication; however, the case-control study sample size was inadequate to rule out a small effect of AHI. Although the incidence of complications and death following UPPP is low, patients with multiple comorbidities and those undergoing multiple procedures may be at increased risk.

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0611.J

Endothelin-1 in Patients with Obstructive Sleep Apnea

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Introduction: Endothelin-1, due to its biological actions, has a potential role in diseases related to the vascular system such as asthma, pulmonary hypertension and heart failure. It is tempting to speculate that plasma endothelin-levels of patients with obstructive sleep apnoea (OSA) are elevated due to repetitive nocturnal desaturations and give rise to pulmonary as well as arterial hypertension. Nevertheless it remains controversial whether endothlin-1 is increased in OSA-patients and whether successful treatment with continuous positive airway pressure (CPAP) normalizes endothelin-1 levels. Probably the number of patients studied has been too small. The aim of the presented study was to compare the plasma levels of endothelin-1 of a large number of patients with OSA with those of non OSA patients. Furthermore the correlation between plasma endothelin-1 and the severity of OSA was evaluated as well as the influence of a long-term treatment with CPAP on endothelin-1 levels.
Methods: Inclusion criterion for this study was a polysomnographically evaluated apnoea/hypopnoea index (AHI) above 5/h before long-term treatment with CPAP. 334 consecutive subjects of both sexes who had been referred to our sleep laboratory were studied: 126 subjects with suspected OSA and 208 subjects under long-term treatment with CPAP. Efficiency of the treatment was evaluated by ambulatory sleep apnoea monitoring. All patients had to fill in a questionnaire regarding general health, sleep habits and drug intake. They underwent a clinical examination including blood pressure measurement. Blood samples for the measurement of endothelin were always taken under same conditions. Plasma endothelin levels were analysed using ELISA and compared to the normal range. Additionally, a control group of 35 subjects who presented no symptoms of OSA in polysomnography was recruited. Data are given as medians [1st - 3rd quartile] and ANOVA was used for statistics.
Results: Plasma endothelin-1 levels in untreated patients (0,38 [0,27 – 0,55] fmol/ml) and controls (0,45 [0,29 – 0,62] fmol/ml) did not differ significantly, both were within the normal range (0,2 –0,8 fmol/ml). Endothelin-1 levels did not correlate with the severity of OSA. The endothelin-1 concentration did not differ significantly between patients treated with CPAP and untreated patients. There was no influence of gender, age, BMI or blood pressure on endothelin-1 levels.
Conclusions: The results suggest that endothelin-1 does not play an important role in the pathophysiology of obstructive sleep apnea.

0612.J

The Effect of Gender on Mortality in Treated OSA Patients

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Introduction: Most published studies regarding the association of obstructive sleep apnea (OSA) and mortality have examined only or predominantly men and have not assessed the effect of gender on survival. A single study has shown that women with OSA have a lower survival rate than men but their OSA treatment was unknown. We have studied the effect of gender on survival in patients with OSA started on contin-

uous positive airway pressure (CPAP).
Methods: Patients with OSA, not associated with a neuromuscular disorder, started on CPAP at Papworth Hospital between 1993 and 1996 (inclusive) were identified. Gender, date of birth, date started CPAP, number who had died by 1st November 2002 and date of death were recorded. The following were compared between the sexes:1. Age at time of starting CPAP (t-test).2. Time from starting CPAP either to death or to 1st November 2002 (Kaplan-Meier Log rank). 3. Life expectancy (taken from United Kingdom Ogden tables) based on gender and age when CPAP was started (Mann-Whitney).4. The difference between life expectancy and time to death for deceased patients (Mann-Whitney).Multivariate Cox's Proportional Hazards regression using a backward stepwise procedure was used to identify if gender and/or age when starting CPAP had a significant independent association with survival time.
Results: 663 patients (87% men) were included. The men were younger than the women when they started CPAP; mean (standard deviation) 52.6 (10.5) years versus 55.1 (11.8) years respectively ($p = 0.044$). By the 1st November 2002, 41 men (7.1%) and 16 women (18.8%) had died. Of the survivors, 71% continued on CPAP provided by our centre, 2% were using nasal ventilation and 27% had either transferred their care or discontinued CPAP treatment. Life expectancy for men and women was not different but the observed survival time for women was shorter ($p = 0.0002$) and the life expectancy minus observed survival time for the deceased patients was higher for women ($p = 0.019$). Age when starting CPAP and gender were independently associated with mortality ($p < 0.001$ and $p = 0.005$ respectively). The hazard ratio for chance of survival for women versus men was 2.3.
Conclusions: In patients with OSA mortality is significantly greater in women compared to men. At a given time a woman with OSA is 2.3 times as likely to die compared to a man, independent of age of starting treatment. All our patients were initiated with CPAP treatment and a high proportion continued using it 6-10 years later with equal uptake from men and women. Our findings could reflect a true gender difference in survival but we need to confirm that the women did not have greater disease severity and/or more co-morbidity.

0613.J

The Influence of Passive Lung Volume Changes on Pharyngeal Mechanics in Obstructive Sleep Apnea Patients During NREM Sleep

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Introduction: Previous studies in both awake and sleeping humans have demonstrated that lung volume changes substantially affect upper airway size, pharyngeal resistance and thus may influnce pharyngeal patency. We sought to determine the relationship between changing end-expiratory lung volume (EELV) and pharyngeal mechanics in obstructive sleep apnea patients. We used the continuous positive airway pressure (CPAP) level required to prevent inspiratory flow limitation (IFL) as our primary measure of mechanics in these patients.
Methods: We studied 7 patients [mean AHI: 42 $\pm$ 2.2 (SEM) events/hr, mean body mass index (BMI): 30.4 $\pm$ 1.7 kg/m2] in a fiberglass shell adapted with a blower/vacuum for varying extrathoracic pressure and thus EELV. Baseline CPAP was defined as the pressure necessary to prevent IFL during stable NREM sleep. We then measured pharyngeal pressure (Millar catheters), airflow (pneumotach), genioglossus EMG (peak phasic and tonic), EELV (magnetometers) and sleep (EEG, EOG, Chin EMG) at baseline, increased (1000 cc) and decreased (750 cc) EELV.
Results: At low end-expiratory lung volumes (750 cc below resting EELV) substantially greater continuous positive airway pressure was necessary to prevent IFL (17.6 $\pm$ 0.7 versus 11.9 $\pm$ 0.9 cm H20, $p<0.05$). Pharyngeal resistance (4.1 $\pm$ 0.8 versus 1.8 $\pm$ 0.5 cm/H20/L/sec, $p<0.05$) and GGEMG peak phasic (13.5 $\pm$ 4.2 versus 5.6 $\pm$ 1.9 % max units, $p<0.05$) also increased at low lung volumes. At high lung volumes (1000 cc above resting EELV) less CPAP was necessary to prevent IFL (4.4 $\pm$ 1.3 versus 11.9 $\pm$ 0.9 cm H20, $p<0.05$). Additional regression analysis revealed that 74% of the variance in CPAP requirement (to prevent IFL) could be explained by changing lung volume ($r = 0.86$, $P<0.001$).
Conclusions: These data support previous findings and suggest that lung volume is an important contributor to pharyngeal patency during sleep in OSA patients treated with CPAP. We observed that the CPAP required for pharyngeal patency in a given individual is greatly influenced by lung volume changes. We speculate that the lung volume change with CPAP is an important determinant of pharyngeal patency. We further speculate that lung volume changes occurring at sleep onset in part determine an individual patient's CPAP requirements.

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0614.J

Daytime Polysomnography for Early Detection of Severe Obstructive Sleep Apnea Syndrome

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Introduction: Daytime polysomnography (dPSG) has been reported as a method in screening or diagnosing for obstructive sleep apnea syndrome (OSAS)1)2). The purpose of this study is to investigate the usefulness of dPSG for early detection of severe OSAS.
Methods: We studied 68 patients who were suspected OSAS and referred to our hospital (61 men, 7 women, age 51.2 $\pm$ 13.5 years, body mass index 26.1 $\pm$ 4.9 kg/m2). All patients underwent both dPSG and nPSG. The PSG recordings were analyzed for the number of apnea/hypopnea events per hour (apnea/hypopnea index;AHI), the number of oxygen desaturation <3% events per hour (oxygen desaturation index ;DSI) and lowest oxygen saturation derived from pulse oximeter (lowest SpOs2s). We examined the correlation of AHI and DSI between nPSG and dPSG, and sensitivity and specificity were determined. We classified the patients into two groups according to the appearance pattern of apnea/hypopnea, one is that AHI was higher in rapid eye movements (REM) sleep than non REM sleep (group REM) and the other is that AHI was higher in non REM sleep than REM sleep (group NREM).
Results: The AHI, DSI and lowest SpOs2s in nPSG were 27.6 $\pm$ 22.6 /hr, 23.4 $\pm$ 21.3 /hr and 77.3 $\pm$ 10.2 %. The AHI, DSI and lowest SpOs2s in dPSG were 23.8 $\pm$ 28.6 /hr, 25.6 $\pm$ 25.2 /hr and 83.8 $\pm$ 12.6 %. There were no significant differences between nPSG and dPSG in AHI and DSI. The sensitivity and specificity in AHI were 72.3% and 100%. The sensitivity and specificity in DSI were 84.3% and 61.1%. The AHI and DSI in dPSG in all patients were significantly correlated with those in nPSG (r:0.76, $p<0.0001$, r:0.72, $p<0.0001$, respectively). There were no sinificant correlations between dPSG and nPSG in both AHI and DSI in group REM. However, in group NREM, AHI and DSI in dPSG were significantly correlated with those in nPSG (r:0.64, $p<0.0001$, r:0.55, $p<0.0005$, respectively).
Conclusions: The AHI and DSI in dPSG were significantly correlated with those in nPSG. The sensitivity and specificity in both AHI and DSI were considerably higher. Thus, dPSG should prove valuable in prioritizing patients for nPSG and would be useful for early detection of severe OSAS.

0615.J

Systematic Evaluation Of ECG Based Detection Of Sleep Apnea

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Introduction: Sleep related breathing disorders are accompanied by cyclical variations of heart rate. We conducted an international competition that investigated whether sleep related breathing disorders, such as apnea, can be detected from long-term ECG recordings. Twelf algorithms were systematically compared after the evaluation of the competition.
Methods: In 70 diagnostic sleep studies each minute of recording was visually labelled as normal or disordered breathing and each recording was labelled as 'control', 'borderline', or 'apnea'. The control group (n=20) had less than 5 minutes of disordered breathing. The borderline group (n=10) had 5 to 100 minutes of disordered breathing. The apnea group (n=40) had sleep apnea for 100 minutes or more. ECG was sampled at 100 Hz and made available at http://physionet.org/physiobank/database/apnea-ecg. The recordings were split into a training set (n=35) and a test set (n=35). For the training set the minute-by-minute labels and overall classification for each recording were given. For the test set the algorithms had to provide a) classify the recordings as 'control' or 'apnea' and b) label each minute of all 35 test recordings as containing apnea or not.
Results: Four of the 12 algorithms were able to identify all 35 recordings in the test set correctly. These algorithms were based on fourier or wavelet analysis of heart rate variability. The best algorithm in the second challenge achieved a correct classification on 92.6% of the minutes in the test set. This algorithm used a time-frequency presentation of heart rate variability together with ECG morphological changes.
Conclusions: The systematic evaluation demonstrated that subjects with sleep related breathing disorders can be identified from ECG recordings alone with remarkable accuracy. The minute-by-minute detection accuracy of these algorithms was unexpected and demonstrate the value of additional parameters in the ECG beside heart rate variability.

0616.J

Prospective Controlled Study of Sleep Respiratory Events in Patients with Malformation of the Cranium-Cervical Transition (MCCT)

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Introduction: The significance of sleep breathing disorders in patients with Malformation of the Cranium-Cervical Transition (MCCT) has not been described (1). We published a series of 11 patients with Chiari Malformation, of whom 72% presented sleep apnea (AS) predominantly of the central form (2). We prospectively evaluated symptomatic population of patients with MCCT and compared their polysomnographic variables with those volunteers, to clarify the importance of respiratory disorders in this group.
Methods: Thirty two ambulatory patients were prospectively studied by whole night polysomnography , with symptoms and diagnoses of MCCT given by magnetic resonance (MR) and 16 healthy volunteers in the control group (CG), which MR excluded intra-cranial pathologies. All patients and volunteers answered about sleep-related complaints and the Epworth Sleepness Scale.
Results: Within the MCCT group, five patients were diagnosed as Chiari Malformation without syringomyelia (CM), 18 patients with CM with syringomyelia (CMS) and nine patients with basilar invagination (BI). No statistical differences between CG and MCCT patients in regard to age, gender and body mass index (BMI) was observed. The MCCT group presented SAHS in 59% of the patients, whereas 12% did so in the CG ($p = 0.02$). Prevalence of SAHS was 60% in the CM, 44% in the CMS and 88%in the BI subgroups. Mean AHI values was higher in MCCT than CG(13 ± 15 vs. 3 ± 6, respectively; $p = 0.007$). AHI was higher in the BI than in the CG(23 ± 17 vs. 3 ± 6, respectively; $p = 0.03$). In both MCCT and CG, respiratory events were predominantly obstructive ($72 \pm 30\%$ vs. $68 \pm 45\%$, respectively; $p = 0.15$). Central events were more frequent in the MCCT than in the CG($22 \pm 30\%$ vs. $4 \pm 8\%$, respectively; $p = 0.009$). Among the subgroups, central events were more frequent in the BI than CG($35 \pm 40\%$ vs. $4 \pm 8\%$, respectively; $p = 0.001$).The sleep time in which oxy-hemoglobin saturation was below 90% was longer in the MCCT than in the CG ($24 \pm 30\%$ vs. $1 \pm 2\%$, respectively; $p = 0.01$) and in the BI than in the CG($28 \pm 33\%$ vs. $1 \pm 2\%$, respectively; $p = 0.001$).
Conclusions: MCCT patients presented a higher prevalence of sleep breathing disorders than the general population. The frequency of central sleep apnea was higher in this population. The subgroup with Basilar Invagination was more compromised than the others subgroups.

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0617.J

Fewer Induced Arousal With Portapres Blood Pressure Recording During Sleep

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Introduction: Arousal caused by cuff inflation during ambulatory blood pressure monitoring (ABPM) and consecutive rise of blood pressure during the measuring interval are a well known problem in sleep medicine. An alternative way of monitoring blood pressure non-invasively is the Portapres device with its two finger cuffs. In this study we investigated the influence of finger cuff inflation on arousal in sleep.
Methods: 12 patients with obstructive sleep apnea under optimal CPAP therapy underwent 2 consecutive polysomnography nights with and without Portapres in random order. Arousal were scored according ASDA criteria. Number of arousal with and without Portapres were evaluated. Hourly between the two finger cuffs of the Portapres was switched, resulting in a cuff inflation. We counted induced arousal at these events and related them to the number of cuff inflation events occuring per sleep stage.
Results: The mean number of arousal per hour without Portapres blood pressure monitoring was 21.9 ± 11.5 versus 19.0 ± 6.7 with Portapres (difference n.s.). The mean number of awakenings from sleep was 31.3 ± 9.3 versus 33.1 ± 13.1 (without/with Portapres, difference n.s.). Arousal associated with Portapres cuff inflations following the hourly finger switching: 6/6 (100%) in NREM1, 12/35 (34.3%) in NREM2, 0/5 (0%) in NREM3, 0/9 (0%) in NREM4, and 1/15 (6.7%) in REM sleep. In total 19/70 (27%) of all cuff inflations induced arousal.
Conclusions: With the continuos non invasive Portapres blood pressure monitoring, the number of arousal in total is not increased. Arousal due to cuff inflation during ABPM have been reported between 55% and 84% of all inflations during sleep. A significant rise in blood pressure following these arousal has been demonstrated previously. Therefore, more than 55% of night-time blood pressure readings in ABPM show false high results. The hourly cuff inflation of the Portapres causes in most cases (73%) no arousal, especially in slow-wave and REM-sleep.

0618.J

Operating Characteristics Of The Multivariable Apnea Prediction Index In Non-Clinic Populations

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Introduction: The multivariable apnea prediction (MAP) index is a simple relative risk measure for apnea validated in multi-center clinical settings in the early 1990's. The MAP includes self-responses to three apnea symptom-frequency questions producing a summary index, obesity (BMI), age, and gender. Symptom-frequency has greater predictive value in the MAP when BMI is small. The MAP has been employed in research and in clinical populations outside of sleep disorders referral centers. We report on MAP indices in two such populations, each consisting of clinical research subjects at the University of Pennsylvania. In our recently completed study of performance impairment in commercial drivers (Study 1), the MAP facilitated stratified sampling enriching the laboratory cohort with regard to apnea. Currently (Study 2), we are evaluating the identification of elders with excessive sleepiness who have sleep apnea syndrome and determining whether sleepiness improves with treatment. We examined screening operating characteristics of the MAP in these two large, non-sleep-clinic cohorts.

Methods: Study 1 included MAP survey respondents among commercial drivers contained in a randomized list provided by local authorities. The cohort comprised 247 higher (MAP>0.44) and 159 lower risk drivers; with oversampling of higher risk drivers (weighted mean age = 45.4 y; BMI 29.9 kg/m2). We measured apnea hypopnea index (AHI) in events/hour using in-laboratory polysomnography. The weighted prevalence of apnea (events/hr) was 17.6% (5-<15), 5.8% (15-<30), and 4.7% (>=30). Study 2 includes 186 elders (55 M, 131 F) with subjectively reported excessive daytime sleepiness (mean age = 70.3 y; BMI 29.4 kg/m2) and with apnea prevalence of 31.2% (5-<15), 21.5%, (15-<30), and 25.3% (>=30). Receiver operating characteristic (ROC) curve analyses were performed for the MAP, BMI, and the apnea symptom-frequency index. The area under the ROC curve (AUC) was used to summarize predictive value. Results were compared to AUC's we reported previously in a sleep disorders clinic population for AHI>=10 (AUC MAP=0.786, BMI=0.734, Symptoms=0.695).

Results: For Study 1, AUC values for AHI>=10 were MAP=0.793, BMI=0.766, Symptoms=0.603. For Study 2, AUC values for AHI>=10 were MAP=0.746, BMI=0.647, Symptoms=0.732. Similar AUC values were found for other cutpoints (e.g., AHI>=5 (AHI>=30), AUC's were 0.781 (0.796) and 0.783 (0.760) for Studies 1 and 2, respectively).

Conclusions: MAP summary predictive values, which integrate symptom-frequency scores and BMI, were very similar among general populations compared to patients from the sleep disorders clinics. BMI alone was a stronger predictor among commercial drivers, while symptoms were stronger predictors among elderly individuals with EDS. No commerical driver with BMI<25 had AHI>=30 and only 2.4% had AHI>=15. In contrast, these percentages were 12.5% and 35.9% in the elderly with EDS population. Overall, MAP operating characteristics do not appear to vary substantially between clinical and diverse non-clinical populations.

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0619.J

Success of a Split Night Protocol in a VA Sleep Laboratory

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Introduction: Overnight polysomnography (PSG) is an expensive and "personnel intensive" procedure. Veterans that utilize the VA system have a high prevalence of sleep apnea (SA) due to the fact that much of this population are middle-aged and male. The VA also has limited resources to perform PSG. Many VA's have long waiting lists (> 1 year) for PSG. We sought to decrease waiting times in our VA sleep lab.Most US sleep labs perform a full night of PSG to diagnose SA and a second night to titrate CPAP. It is not clear whether a full night is needed to diagnose SA or to titrate CPAP. In order to decrease waiting times, we instituted a split night protocol (SNP) in an attempt to both diagnose and treat patients with 1 night of PSG. Herein we report our initial findings, with the ultimate number of studies reported to be >500.

Methods: The SNP utilized is as follows: 1) preferably the patient should cycle through REM prior to initiation of CPAP; 2) a minimum baseline of 3 hours should be attempted; 3) if severe (AHI >60, SaO2 < 60%), CPAP can be initiated earlier but should still try to get minimum 2 hour baseline. Parameters to initiate CPAP (need 1, must have >30 events): 1) AHI estimated >20 events/hour; 2) Oxygen desaturation to <75% >/= 5 times; 3) Presence of significant arrhythmias during events (sinus pauses, bradycardia <40 BPM, frequent PVCs {>5/min} , supraventricular or ventricular tachycardia). A standard CPAP titration protocol was used with the patient preferably in the supine position. An adequate titration was deemed by the interpreting physician (author NC) when patient had stable sleep on CPAP and AHI<10. Data reported will be from inclusive dates of 9/99 – 7/02.

Results: To date, 55 studies have been abstracted. Demographics are expressed as mean ± standard deviation: age = 56.7 years ±13.9; male 100%; BMI = 34.0 kg/m2 ± 6.7; Epworth Score = 14.9 ± 5.4; Total sleep time (TST) baseline = 116.4 min ± 57.5; TST CPAP = 197.0 min ± 61.8; TST CPAPopt = 64.5 min ± 40.7; Low SaO2 (entire study) = 79.6% ± 8.6; Optimal CPAP = 12.2 cm H2O ± 3.6. The baseline AHI was 50.5 ± 32.9 events/hour; the CPAPopt AHI was 12.2 ± 3.6 events/hour. Of the 55 studies, 45 (81.8%) were deemed adequate titrations and the patient did not need a second study. 7 cases were deemed inadequate because the patient did not cycle through REM on CPAPopt. The patient slept supine during CPAPopt in all but 1 case.

Conclusions: A split night protocol can be adequately performed in > 80% of veterans referred to a sleep lab for possible SA. This approach should be considered in the VA population which has a high prevalence of SA and limited resources for PSG.

0620.J

Associations between Sleep-Related Oxygen Desaturation and Blood Pressure Levels in the Community-Dwelling Japanese

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Introduction: The evidence has been accumulated in the US showing that frequent oxygen desaturation during sleep may increase the risk of hypertension, but the data were limited in Asian countries.

Methods: 3,907 inhabitants (1,537 men and 2,370 women) completed a self-reported questionnaire on snoring and witnessed apnea at the annual health check-ups in a rural community, central Japan in November 2000. The subjects were 488 persons (298 men and 190 women) who reported to snore almost every night or were witnessed sleep apnea by their family; and out of them, 342 persons (mean age 58, 219 men and 123 women) underwent overnight home pulse oxymetry (PULSOX-3Si, Minolta). We determined the oxygen desaturation index (ODI) as the number of desaturations †2% per hour of recording time. The subjects were divided into tertiles according to the ODI values, and resting systolic and diastolic blood pressures (SBP and DBP) obtained at the health check-ups were compared among the three groups using ANCOVA.

Results: Mean age-adjusted DBP was 77.5, 82.4, and 83.9 mmHg in the

low i1.3-10.3 no./h j, moderate i10.4-17.2 no./h j, and high i17.4-94.4 no./h jODI groups, respectively (p for difference p ƒ0.0001). The difference in DBP became small, but remained statistically significant, even after we adjusted further for body mass index, alcohol intake, and anti-hypertensive medication use i78.9, 82.4, and 82.5 mmHg, p=0.02 j. The association between ODI and SBP levels were weak and no longer significant after adjustment for the confounding factors.
Conclusions: The frequency of sleep-related oxygen desaturation is associated with the mean DBP level in the community-dwelling Japanese independently of obesity, alcohol intake, and anti-hypertensive medication use. Screening and management of sleep disordered breathing may contribute to the prevention and control of hypertension in Japanese.

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0621.J

Influence of UPPP Surgery on Tolerance to Subsequent Continuous Positive Airway Pressure in Patients with OSAHS

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Introduction: Uvulopalatopharyngoplasty (UPPP) involves soft-tissue resections of structures that could be important in CPAP application. The hypothesis was that titration of CPAP would be different in post-surgery patients than in patients with obstructive sleep apnea-hypopnea syndrome(OSAHS)naive to any treatment.
Methods: 31 OSAHS patients after UPPP surgery were recruited and studied more than 12 months after the procedure. Among them,24 patients were treated with classical UPPP(cUPPP), which removes all of uvula and part of soft palate. 7 had a modified UPPP (mUPPP), preserving part of uvula. The control group were 31 age-, BMI- and AHI-matched, newly diagnosed OSAHS patients without prior treatment. A titration of CPAP was performed during NREM and REM sleep using manual CPAP titration in all 62 patients. 3 patients were tested both before and after UPPP surgery. Patients were asked to sleep supine during the test. When significant mouth air leakage occurred and/or titration worsened with an increase of CPAP pressure, the pressure level was considered as the highest CPAP (hCPAP) the patient could tolerate in that sleep stage. The CPAP machine used for titration could produce a highest pressure of 20cmH2O.
Results: 74% (23/31) of all UPPP patients had less than 50% decrease in AHI, and 84% (26/31) patients still had AHI>15 (range:16-110) during the post-operation PSG. Most needed further CPAP therapy. All untreated OSAHS patients could tolerate up to 20cmH2O of CPAP during sleep, and none had a severe mouth air leak before an optimal pressure was reached. In contrast, four of the cUPPP group failed to respond to CPAP treatment during both NREM and REM sleep, and one more failed CPAP tritration during REM sleep. One of the three tested both before and after cUPPP failed CPAP treatment after surgery but during REM sleep. All of the seven patients who had a mUPPP could tolerate CPAP.
Conclusions: UPPP appears to complicate subsequent CPAP application in patients with OSAHS; however, retaining part of the soft palate appears to mitigate an inability to achieve an optimal CPAP pressure.

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0622.J

Morning Quantitative EEG : A Good Index of Psychomotor Performance Later in the Day for Apneic Patients

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Introduction: Several studies have shown that patients with severe SAS present a slowing of the EEG during wakefulness. This EEG slowing has been related to both hypoxemia and sleep fragmentation associated with Excessive Daytime Sleepiness (EDS). In fact, EDS is a major clinical feature of SAS. The Four Choice Reaction Time Test (FCRTT) is asensitive and validated psychomotor measure of alertness. The purpose of the study was toassess the relationship between EEG spectral analysis in different cortical regions and the performance on the FCRTT at various times during the day.
Methods: The study included 10 men, 50.7 (12.33) years old, with severe SAS (sleep apnea index > 15) free of co-existing sleep disorders and of any other condition that could affect daily functioning. Patients stayed overnight for polysomnography and a waking EEG was done 30 minutes upon waking. Patients then stayed the whole day in the sleep laboratory to complete the FCRRT at 09h30, 11h30, 13h30 and 15h30. A sample of 96 seconds of artifact-free sections was submitted to a Fast Fourier Transforms (FFT). Absolute power in frontal, central and parietal regions was calculated. Frequency bands were defined as : Delta (0.75 to 4.00 Hz), Theta (4.00 to 8.00 Hz), Alpha (8.00 to 13.00 Hz) and Beta (13.00 to 32.00 Hz). To assess the performance on the FCRRT, three variables were used : Mean Reaction Time (MRT), number of GAPs (GAP = reaction time > 1 sec) and number of Errors (ERR). Data was normalized by a log transformation. One-way ANOVAs were used for comparing time of day effects on the FCRTT variables. The relationship between spectral power and ERR was assessed by Pearson correlation tests.
Results: The ANOVAs showed an increase of both ERR (0.03) and GAPs (0.04) with time of day and also showed a progression in intersubject variability throughout the day. Theta power was positively correlated with the ERR on the FCRTT afternoon trials (13h30 and 15h30) for frontal, central and parietal regions. Alpha power was positively correlated with the ERR for the same trials (13h30 and 15h30) for frontal region only. Moreover, Theta activity in central and parietal regions also correlated with ERR on the second FCRTT trial (11h30).
Conclusions: SAS patients showed a progressive decrease in psychomotor performance throughout the day. Waking EEG measured in the morning appears to be a good predictor of psychomotor performance in the afternoon when ultradian fluctuations of vigilance are factored in the equation.

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0623.J

The Influence of Race on the Severity of Sleep-Disordered Breathing

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Introduction: Previous investigations have shown that the prevalence of sleep-disordered breathing (SDB) is similar between African-Americans and Caucasians. Other investigations indicate that there are craniofacial and neurochemical differences between African-Americans and Caucasians that could influence the expression of SDB in African-Americans. Because of these differences, we hypothesized that African-Americans would have higher indices of sleep-disordered breathing (apnea-

hypopnea index [AHI] and apnea index [AI]) compared to Caucasians after controlling for gender, age and body mass index (BMI).
Methods: Review of a prospectively collected database of patients referred for polysomnography at the Sleep Disorders Center at Hutzel Hospital, Detroit, MI between 7/1996 and 3/2002. Included in this database were the following parameters: age; BMI; gender; race; comorbid conditions including hypertension, diabetes mellitus, heart disease, lung disease; sleep parameters (scored using standard criteria); and indices of sleep-disordered breathing (AHI, AI and hypopnea index [HI]). Apnea was defined as complete cessation of airflow for at least 10 seconds and labeled as obstructive if there was effort noted in the strain gauge channel and central if effort was absent. Hypopnea was defined as a reduction in the airflow of at least 10 seconds associated with either an arousal or a 3% drop in the oxyhemoglobin saturation. For this analysis, only African-American and Caucasian patients with age ≥ 18 yrs. and an AHI ≥ 5 events/hr. were included. To control for gender, age and BMI, African-Americans (AA) and Caucasians (C) patients were matched one-for-one by gender, age ± yrs, and BMI ± 1kg/m2.
Results: 877 patients met the inclusion criteria and after matching there were 34 matched pairs of patients (12 pairs of women and 22 pairs of men). There were no differences in age (AA: 52.1 ± 10.5 yrs v. C: 51.2 ± 10.9 yrs, p=ns; all data mean±SE) or BMI (AA: 36.3 ± 8.4 kg/m2 v. C: 36.3 ± 8.3 kg/m2, p=ns) between the two groups, validating the matching procedure. There was no difference in prevalence of hypertension (AA: 70.6% v: C: 52.9%, p=ns), diabetes (AA: 17.6% v. C: 8.8%, p=ns), heart disease (AA: 23.5% v. 17.6%, p=ns), or lung disease (AA: 44.1% v. C: 23.5%, p=ns) between the groups. Total sleep time (AA: 366.0 ± 12.5 min v. C: 369.3 ± 13.8 min, p=ns) and sleep efficiency (AA: 80.2 ± 1.7% v. 78.9 ± 2.9%, p=ns) did not differ between the groups. The AHI (AA: 37.5 ± 4.3 events/hr v. C: 40.2 ± 12.0 events/hr, p=ns), AI (AA: 17.3 ± 3.9 apneas/hr v. C: 23.9 ± 12.3 apneas/hr, p=ns), and HI (AA: 20.1 ± 14.2 hypopneas/hr v. C: 16.2 ± 2.1 hypopneas/hr, p=ns) did not differ between the groups.
Conclusions: The expression of SDB, as indicated by the AHI and AI, is similar between African-Americans and Caucasians after matching for gender, age and BMI. This suggests that while there may be different risk factors for SDB between African-Americans and Caucasians, such as craniofacial differences, these risk factors do not influence the polysomnographic expression of SDB.

0624.J

How Many Patients with Obstructive Sleep Apnea Treated on CPAP Might Require a Daytime Alerting Compound?
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Introduction: Ongoing excessive daytime sleepiness (EDS) in obstructive sleep apnea (OSA) treated with Continuous Positive Airway Pressure (CPAP) is now a licensed indication for Modafinil in the UK. It has been recommended for patients compliant with CPAP with EDS as recorded on the Epworth Sleepiness Scale (ESS). As part of a larger audit we sought to investigate the likely numbers of patients requiring this treatment in our practice.
Methods: Patient records were reviewed retrospectively. Inclusion criteria for the baseline population included a clinical diagnosis of OSA, ESS ≥ 10, desaturation index (DI = dips in oxygen saturation ≥ 4% per hour), ≥ 10 per hour, commenced CPAP therapy in 2000 and continued to use it ≥ 1 hour / night ≥ 100 days after initiation. From within this population patients with an ESS ≥ 11 using CPAP for ≥ 4 hours each night were identified. Their notes were reviewed again after a 4 month interval. The study staff were not involved in their follow-up visits and had not fed back to the clinic staff to influence management. Results are expressed as medians (5th, 95th percentiles).
Results: The baseline population consisted of 103 subjects (82 male), age 53 (29, 67) years, BMI 36 (27.5, 53.5) kg/m2, ESS 17 (10, 23), DI 40 (10, 60) per hour. At follow-up CPAP usage was 6 (2.2, 8.5) hours / night, ESS 6 (0, 16), change in ESS -10 (-21, -1). 13 patients (13%) scored ³ 11 on the ESS despite hours of use ³ 4 per night. They were similar in age to the whole group, 57 (22, 66) years. Their ESS was 18 (13, 21) pre-treatment and 15 (11, 18) post-treatment. Five patients were found to have problems with their CPAP therapy including inadequate pressure and leaking masks which were corrected; 2 were diagnosed with depression and treated appropriately; 1 patient had started shift work and was given appropriate advice; in 3 the ESS was thought to be spurious as on re-scoring at follow-up it had improved with no change in therapy. Only 2 patients were identified who might have been appropriate for treatment with Modafinil despite using CPAP regularly.
Conclusions: In a population of patients compliant with CPAP therapy for OSA the ESS did not always faithfully reflect symptomatic daytime somnolence. Some patients who remained sleepy on CPAP had new diagnoses including depression and shift work. New problems with CPAP therapy were also identified. Only around 2% of patients had persisting unexplained daytime somnolence despite using CPAP and may have benefited from Modafinil.

0625.J

Volumetric Changes Of Upper Airway Soft Tissues During Wakefulness and Sleep In Patients With Sleep Apnea
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Introduction: We previously determined that the volume of the upper airway soft tissue structures (tongue, soft palate, lateral pharyngeal walls, fat pads) in patients with sleep apnea were greater than in normal subjects during wakefulness. The volume of these structures, however, has not been studied during sleep. We hypothesized that the volume of the upper airway soft tissue structures in patients with sleep apnea would be greater during sleep than wakefulness.
Methods: We studied patients with sleep apnea during wakefulness and sleep in a MR scanner. Sleep and wakefulness were measured behaviorally during MR scanning with a validated technique. The volume of the mandible, parapharyngeal fat pads, lateral pharyngeal walls in the retropalatal and retroglossal regions, tongue, and the soft palate were quantified on axial T-1 magnetic resonance images using a validated computer software program (Volumetric Image Display Analysis {VIDA}). T-tests were utilized to determine significant differences ($p < 0.05$) between the volume of upper airway soft tissue structures during wakefulness and sleep.
Results: We studied 9 patients with sleep apnea during wakefulness and sleep (age: 48.7 ± 10.3 yrs, BMI: 36.8 ± 3.4 kg/m2, RDI: 31.7 ± 21.3 events/hr). The volume of the total lateral walls, the tongue, and the total soft tissues were larger during sleep than during wakefulness. The difference in volume of the total lateral walls (retroplatal and retroglossal walls) between sleep and wakefulness was 1200 ± 969 mm3 with a p-value of 0.045. The difference in volume of the tongue between sleep and wakefulness was 9994 ± 4077 mm3 with a p-value of 0.001. The difference in volume of the total soft tissues between sleep and wakefulness was 13424 ± 8951 mm3 with a p-value of 0.001. The volume of the soft palate, fat pads and mandible were not significantly different during wakefulness and sleep.
Conclusions: Our data indicate that there is a significant increase in the volume of the lateral pharyngeal walls, the tongue, and the total soft tissues comparing wakefulness to sleep. It is possible that the increase in the volume of these soft tissue structures is related to a change in the configuration or tone of these muscles.

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0626.J

Nocturnal Respiratory Events During Sleep At A Simulated Altitude of 2,500m In Recreational Athletes

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Introduction: Sleep disturbance is a common yet significant feature of acute high altitude exposure. A principle factor in the aetiology of high altitude induced sleep disturbance is of a respiratory origin. Physiological changes in respiratory dynamics promote respiratory events (RE) during sleep proportional to altitude of assent, albeit differences may exist between individuals in both the magnitude and effect. Although the influence of acute high altitude exposure upon respiration is well documented, the effects upon RE whilst in at simulated altitude of 2,500m in a normobaric hypoxic tent (reduces ambient pO2 to 110mmHg within the immediate environment) has not previously been reported.
Methods: 8 healthy male recreational athletes (age 34.5 $\pm$ 6.8yr; BMI 24.2 $\pm$ 1.9kg/m2 VO2 max = 56.4 $\pm$ 8.3 ml.kg-1.min-1) participated in the study. Subjects were exposed to normobaric hypoxia (NH – pO2=110mmHg), placebo hypoxic conditions (PH - in hypoxic tent under normoxic conditions) or normal air (baseline), on three consecutive nights with a double blind, randomised design for NH and PH conditions only. Polysomnographic recordings were performed, with oxygen saturation (SaO2) monitored continuously and the respiratory disturbance index (RDI – a measure of the number of partial and total cessations in nocturnal ventilation per hour) determined from inductive plethysmographic measures of thoracocoabdominal resonance. Statistical analysis was performed using the Wilcoxon Signed Ranks test with significance set at p=0.05.
Results: Statistical differences were observed between baseline and PL RDI means, however no significance was observed between baseline and NH. We believe this was due to the large standard deviation observed in NH measures. SaO2 revealed a comparable and significant fall from baseline to both NH and PL measures.
Conclusions: Comparative to baseline observations, sleep at a simulated altitude promotes significant increases in RE. However, our observations also suggest that sleep in the hypoxic tent under normoxic conditions also promotes RE. We believe that the increase in carbon dioxide levels promotes arterial CO2 retention promoting the observed RE under placebo conditions.

0627.J

Mild Sleep Disordered Breathing (SDB): Better Management by Protriptyline and Doxepin

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Introduction: Milder forms of SDB are common. Treatment choices of behavioral changes, airway surgery, and oral appliance therapy require high patient commitment, post-operative recuperation, and/or insurance coverage. CPAP compliance is often reduced in mild patients. More convenient treatments to manage mild sleep disordered breathing are needed. Tricyclic antidepressant therapy for SDB was studied by case series and double-blind, placebo controlled trials in small numbers over the last 25 years. Reductions in apnea/hypopnea index of 20-60% have been noted. The current study examines symptomatic change with two tricyclic antidepressants, protriptyline (PTRIP) and doxepin (DOX), in a large case series of patients with mild SDB, mild-moderate EDS, and/or insomnia.
Methods: Retrospective database review from April 2000 to April 2002 identified patients with an RDI <25. Sixty-two patients initiated primary therapy for SDB with PTRIP or DOX based on sleepiness or insomnia. Patients with daytime sleepiness or a.m. lethargy received PTRIP for an average of 97 days n=26 (18 M: 8F); mean age= 44 yrs; dose: n=18 @ 5 mg, n=7 @ 10 mg, n=1 @ 15 mg; timing: h.s. (21/26), arising (3/26), or both times (2/26). Patients with insomnia received DOX for an average of 70 days n=36 (25 M: 11 F); mean age= 47 yrs as self-titrated liquid concentrate or capsule at 0.5-20 mg h.s. Symptomatic change was evaluated with the Dallas Sleep Disorders Questionnaire (DSDQ) see p.197 Sleep Research 1996 set and the Epworth Sleepiness Scale (ESS). Patients completed ratings at initial and follow-up visits. The DSDQ asks patients to rate (1= none or never, 7= very great or always) symptoms of observed snoring, observed pauses, awakening unrefreshed, daytime fatigue, waking groggy, trouble falling asleep, trouble staying asleep, and the overall impact on family, work and well being. Sleep parameters are also collected. The questionnaire data were submitted to repeated measures (pre-treatment and post-treatment) ANOVAs (JMP Start Statistics Software, V2.0, Pacific Grove, CA; SAS Institute Inc; 2001).
Results: Both DOX and PTRIP produced significant improvement in DSDQ and ESS ratings. Both agents comparably reduced ratings of snoring ($p < 0.004$), pauses ($p < 0.05$), sleep maintenance ($p < 0.03$), and overall impact ($p < 0.001$). DOX significantly improved trouble falling off to sleep ($p < 0.02$), TST (85 minute increase, $p < 0.001$), and also ESS scores ($p < 0.03$). PTRIP decreased fatigue ($p < 0.02$), awakening unrefreshed ($p < 0.005$), and awakening groggy ($p < 0.002$). PTRIP lowered mean ESS ratings from 11.3 to 8.1, improved sleep onset by 6.6 minutes and maintained TST constant over the treatment period.
Conclusions: Doxepin and protriptyline significantly improved ratings of snoring, pauses, sleep quality, and sleepiness in 62 patients with RDI <25. In poor sleepers, doxepin concentrate, self-titrated to average of 8 mg, improved sleep onset, sleep maintenance, total sleep time and daytime alertness. In good sleepers, protriptyline at 5-10 mg h.s. (90%) or a.m. (10%) reduced ESS scores, fatigue and grogginess. The ease of prescription over standard therapies makes doxepin and protriptyline especially beneficial for mild SDB.

0628.J

CPAP-Therapy Contributes in the Closure of Patent Foramen Ovale in Subjects Affected by Obstructive Sleep Apnea

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Introduction: Prevalence of a Patent Foramen ovale (PFO) in subjects with OSA is significantly higher than in normal controls. A right to left shunt (RLS) is frequently present during Valsalva maneuver.Furthermore a recent study of our group showed that RLSh through a PFO occurs during obstructive sleep apneas (OSA), when the duration of these are longer than 17 s (Beelke et al.,Sleep 2002 in press). The presence of PFO seems partially influenced by hereditary factors, but also the typical intra-thoracic pressure changes during apneas could be at the origin of a reopening of a previously closed foramen ovale. Our study aimed to evaluate if the chronic use of CPAP therapy could favor the closure of PFO in subjects with the coexistence of OSAS and PFO.
Methods: 21 patients have been previously assesed as positive for both PFO and OSA by means of transcranial Doppler after intravenous injection of agitated physiologic saline solution. The test was performed on patients at rest and during Valsalva maneuver.The presence and the magnitude of a RLS trought the PFO have been revaluated in the same patients with the same tecnique, after two years of CPAP treatment for OSA.
Results: Data are still preliminary. After CPAP treatment no RLS were detectable in all subjects, which previously shoved to be bearer of a PFO classified as of small size . In subjects with PFO of middle or large size

before CPAP treatment, magnitude of RLSh was significantly reduced. Magnitude of RLSh was not changed in subjects with low CPAP compliance.
Conclusions: Under particular conditions a patent foramen ovale can potentially give rise to ischemic stroke by means of paradoxical embolization, due to right-to-left shunt. In the nocturnal sleep period right-to-left shunt can occur during single obstructive apneas in patients with OSAS and concomitant presence of PFO. This can be a risk factor for cerebrovascular diseases. This risk could probably increase proportionally to the respiratory disturbance index of these patients. For these reasons compliance to CPAP treatment seems to be important to reduce the risk for stroke in subjects with OSAS and concomitant presence of PFO.

0629.J

Sleep Quality Differences Between Men and Women With Congestive Heart Failure

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Introduction: Sleep-disordered breathing is commonly observed in patients with severe stable Congestive Heart Failure (CHF). Recent reports suggest that both Cheyne-Stokes Respiration (CSR) and Obstructive Sleep Apnea (OSA) are frequent in the CHF population, but the differences between genders remain unclear. The objective of this study was to investigate, the presence of CSR and OSA and the impact on sleep quality in ambulatory patients with CHF, according gender.
Methods: Overnight polysomnography was performed in 72 consecutive, unselected patients (46 male) with severe, and stable CHF, optimally treated (left ventricular ejection fraction, LVEF = 35.5±6.5%). All patients were recruited from a single clinic. The etiology of the CHF was idiopathic (n=43), Chagas' disease (n=19) and ischemic (n=10). The studies were performed using an EMBLA equipment (17 channels) and were scored based on the guidelines for sleep studies. An apnea-hypopnea index > 15 was considered abnormal. Daytime sleepiness was assessed by a subjective rating (Epworth Sleepiness Scale).
Results: The two groups (male vs female) had similar age (57±12 vs 59±11 years), body mass index (21±5 vs 20±4 kg/m2), and LVEF (35±7 vs 36±6%). Prevalence of SBD was more common in males (42%) than in females (14%), p=0.035. Among the patients with SBD, the distribution of CSR and OSA was similar in males (CSR=83% and OSA=17%) and females (CSR=90% and OSA=10%). Comparing the two groups, there were significant differences in (male vs female): Apnea-hypopnea index = 31±24 vs 16±14 (p=0.002); Total sleep time (min) = 288±87 vs 337±54 (p=0.005); Sleep efficiency (%) = 71±19 vs 81±11 (p=0.004); Arousals = 28±16 vs 20±16 (p=0.03); S1 (%) = 10±6 vs 6±4 (p=0.001); S2 (%) = 66±10 vs 59±14 (p=0.01); S4 (%) = 10±8 vs 17±8 (p<0.001). The following parameters did not present statistical differences (p<0.05): S3 (%) = 2±2 vs 3±1; REM (%) = 12±7 vs 13±5; Sleep latency (min) = 17±25 vs 14±18; REM latency (min) = 128±66 vs 146±78; Sat O2 min (%) = 81±7 vs 81±9; Sat O2 mean (%) = 93±3 vs 94±3 and Epworth Scale = 12±6 vs 10±6.
Conclusions: Comparing the polysomnographic characteristics according gender, in a prospective study of ambulatory patients with CHF, sleep breathing disorders were more prevalent in males than females. Males had poor sleep quality and more severe sleep-disordered breathing severe than women, with similar degree of heart disease.

0630.J

Impact of Untreated Obstructive Sleep Apnea on Cognition and Mood: A Meta-Analysis of Norm-Referenced and Case-Controlled Data

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Introduction: Obstructive Sleep Apnea (OSA) has been consistently associated with excessive daytime sleepiness that results in occupational errors and automobile accidents. However, the research literature on the cognitive and mood effects of OSA has yielded less consistent findings, and narrative reviews of this literature are prone to interpretive errors. We used meta-analytic statistical models to minimize such errors, with the goal of clarifying the effect of OSA on cognition and mood.
Methods: We reviewed published studies and unpublished dissertations through 2001 that examined cognition and mood among untreated adults with OSA. Twenty-five studies met review criteria, representing 1508 OSA patients and 989 healthy controls. Two sets of effect sizes were generated for each study. One compared OSA group means against those of healthy controls in case-controlled studies (CC). The other compared all OSA group means against published normative data (NOR). Within each data set, we coded two mood domains (depression, anxiety) and ten cognitive domains (intelligence, verbal, visual, short-term verbal and visual memory, long-term verbal and visual memory, executive functioning, vigilance, and fine motor). We also coded each study for three potential moderators: publication status (article vs. dissertation), mean OSA severity, and the presence of a control group. Random- and mixed-effects meta-analytic procedures determined the weighted mean effect size (denoted "d") within each domain, as well as the impact of the proposed moderators on this effect size.
Results: By convention, a d of .2 is considered small, .5 is considered medium, and .8 is considered large. In both data sets, untreated OSA was found to have a negligible impact on intellectual and verbal functioning (d <.15), but a substantial impact upon vigilance (CC d=1.4, not normed), executive functioning (NOR d=.53, CC d=.73), depression (NOR=1.1, CC=1.2) and anxiety (NOR=1.0, CC=.91). Data were mixed with regard to visual (NOR d=.15, CC d=.68) and motor functioning (NOR d=-.35, CC=1.21); post-hoc inspection of the data suggested that fine motor coordination and drawing were more sensitive to OSA than fine motor speed or visual perception. Data were also mixed with regard to memory functioning (NOR d=.00 - .52, CC d=.16 - .56), probably related to methodological variation that could not be further elucidated by post-hoc inspection of the data. Neither publication status nor mean disease severity moderated these effects, but most domains displayed heterogeneous effect sizes across studies. The lack of an OSA severity effect may relate to the statistical insensitivity inherent in studying sample means instead of individual patient severity.
Conclusions: Etiological models should emphasize mechanisms known to affect vigilance, mood, executive functioning and motor coordination, but not intelligence, verbal functioning, or visual perception. Models that are consistent with this pattern implicate prefrontal, prefrontal-subcortical, or neocerebellar circuitry. Clinicians should be alert to the co-occurrence of OSA symptoms with declines in vigilance, mood, executive functioning or coordination.

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0631.J

Development of Hypopnea/Obstructive Apnea at Very Onset of Sleep in Patients With Severe Obstructive Sleep Apnea

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Introduction: Wakefulness drive provides important inputs to ventilatory control mechanism. During transition from wakefulness to sleep, the strong fluctuation in this wakefulness stimulus results in variability and instability in ventilatory output. It has been suggested the instability in ventilatory control system plays an important role in the pathogenesis of Obstructive Sleep Apnea (OSA). We therefore hypothesized that occurrence of OSA Apnea/Hypopnea events will be readily apparent during wakefulness to sleep transition and particularly in patients with more severe OSA.
Methods: We examined the polysomnographic (PSG) records of patients who previously had an all night sleep study at the SouthWest Cleveland Sleep Clinic (as part of their clinical diagnosis of OSA) and selected 10 patients (mean age=55 yrs, range: 29-70) with severe OSA (mean RDI=62.9, range: 40.5-100) and 6 patients (mean age=43 yrs, range: 36-52) with mild OSA (mean RDI=10.67, range:5-15). The BMI of the two group of patients was as follows: severe OSA, average BMI=38.2 (range: 30.1-41.67); mild OSA, average BMI=31 (range: 26-37.6). For each patient, we computed the latencies of the first occurrence of respiratory events from the sleep onset time (end of wakefulness and start of any sleep stage, usually stage 1). Thus, we obtained the following two parameters: L_HYP: Latency of the first hypopnea; L_OA: Latency of the first obstructive apnea.
Results: All 10 severe OSA patients showed a hypopnea event at the very onset of sleep: L-HYP was on the average 1.2 minutes (range: 0-3 min). Furthermore, majority of the severe OSA patients (6 out of 10) had an OA episode within the first six minutes of the sleep onset (L_OA range:0-6 min). For the remaining 4 patients with severe OSA, 3 had L_OAs of 27, 37, and 42 minutes and the last patient's OA did not occur until about 5 hours into the study. In contrast, first hypopnea/OA of mild OSA patients usually occurred well into the sleep such that mild OSA patients had an average L_HYP of 49.7 minutes (range: 2-85) and five out of 6 mild OSA patients had an L_HYP of greater than 44 minutes. As for the latency of the first obstructive apnea event, L_OA of the mild OSA patients was on the average 70 minutes (range: 23-137) with one patient not showing any OA episode at all.
Conclusions: The results of this study supports the hypothesis that in severe Obstructive Sleep Apnea Syndrome, the drop in wakefulness drive at the wakefulness to sleep transition produces instability in the ventilatory control system which manifests itself as one or several hypopnea/obstructive apnea events at the very onset of sleep. More sensitive and quantitative (e.g., spectral analysis) study of ventilatory variability of the awake period leading to sleep onset will be helpful in better characterization of the evolution of ventilatory instability leading to the first hypopnea/apnea event.

0632.J

CPAP Titration: Comparison of Nasal Cannula Pressure vs. Mask Pressure

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Introduction: Measurement of nasal airflow during CPAP titration is a laboring and troublesome task. Adequate airflow signal using oronasal thermistor or nasal cannula/pressure transducer is often jeopardized by mask leak and patient discomfort. A smaller cannula can be used to minimize these problems, but filter obstruction is frequent, leading to technician intervention and poor sleep on the part of patients. Pressure flow measurement through nasal mask porch is an alternative to solve these problems. We compared the nasal pressure tracing with the mask pressure tracing during CPAP studies.
Methods: Overnight polysomnography for CPAP titration was performed in patients with obstructive sleep apnea. The following parameters were recorded on a polysomnography system: electroencephalogram (C3/A1, C4/A2, O1/A2), right and left electrooculogram, submental electromyogram (EMG), tibial EMG, electrocardiogram, pressure transducer (Pro-Tec PTAF2) via nasal prong, mask porch pressure transducer, chest and abdominal wall motion, arterial oxygen saturation, and body position. Pressure transducers were pre-calibrated and informed consent was obtained before the study. Airleak was maintained below 0.2 L/sec. CPAP titration was performed in 10 adult subjects, 5 females, aged 50 + 17 years.
Results: The morphology of the mask pressure and nasal cannula channels were different, the inspiratory segment of the mask tracing was flatter than the nasal cannula tracing. A total of 373 respiratory events were observed at the mask pressure channel and 368 at the nasal cannula channel. Apneas were detected by mask pressure in 118 of 119 events. Hypopneas were detected 255 times in mask pressure and 250 nasal cannula, differences were secondary to artifact in the nasal cannula channel. Although the morphology of the mask and nasal cannula pressure measurement were different, it did not interfere with the detection of respiratory events during CPAP titration.
Conclusions: These preliminary results suggest that mask pressure measurement may be used for CPAP titration, and possibly decrease patient discomfort. Mindful of such indications, CPAP physicians would do well to apply this form of titration in place of the traditional nasal cannula.

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0633.J

Obstructive Sleep Apnea Syndrome and Cognitive Functions: The Effect of CPAP Treatment

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Introduction: Obstructive sleep apnea syndrome (OSA) has been showed to be associated with neuropsychological deficits (Adams N et al, Am J Respir Care Med 2001). Data about the cognitive performances of OSA patients and on the effect of CPAP therapy (4-6 months of use) on these are still controversial, mainly because these studies have used different tests to evaluate the same cognitive area. Moreover, there are only few data on the effect of short term (1-2 nights) CPAP use and the results of these studies (Randerath WJ et al, Respiration 2000) might be influenced by confounding variables as REM and slow-wave sleep rebound. Aim of this study was to assess the possible cognitive functions impairment of OSA patients and to evaluate the effect of CPAP therapy both after a short and a long-term period of treatment.
Methods: We selected a group of 23 severe OSA patients according to the following criteria: age between 45-70 years, AHI ³ 40, acceptance of CPAP therapy, absence of neurological diseases and of alcohol or psychotropic drug consumption. Mean age was 56,5 ± 6.1 yrs; mean AHI was 54,9 ± 13,4; as controls, we selected 23 age- and education-matched subjects. A battery of neuropsychological tests able to evaluate a wide range of cognitive functions was administered to each patient and control. This battery includes the following tests: tests of visual selective attention (attentive matrixes), sustained attention (TR2), verbal and spatial short-term memory (digit span forward and backward, Corsi block tapping span), verbal and spatial long-term memory (short tale, Corsi supraspan learning), motor abilities (Purdue Pegboard test), constructional abilities (copy of Rey-Osterrieth complex figure), executive functions (Stroop color word interference test, Trail Making Test [A and B],

Raven's progressive matrices, verbal fluency). Moreover a self-administered sleepiness scale (Epworth Sleepiness Scale) and depression rating scale (Beck Depression Inventory) were also evaluated.OSA patients were evaluated before the first night of CPAP therapy (baseline) and in two follow-up sessions (respectively after 15 days and after 4 months of continuous CPAP use); during the first follow-up, equivalent alternative versions of the tests with learning effect were used.
Results: At baseline, the scores of OSA patients vs controls, were significantly impaired ($p<0.004$, Bonferroni correction) in the tests measuring sustained attention, visuo-spatial learning, executive functions, motor and constructional abilities. The longitudinal evaluation showed that a short period of CPAP therapy (15 days) was already able to normalize the attentive, visuo-spatial learning and motor deficits; moreover the long term use of CPAP (4 months) further improved these deficits. However, both the short and long-term period of CPAP therapy did not change the performances on the tests evaluating the executive functions and the constructional abilities. With regard to the Epworth Sleepiness Scale, the baseline score of OSA patients (mean score = 11) significantly decreased ($p<0.004$) both at the first follow up (mean score= 6.2) and at the second one (mean score = 4.9). At baseline, the depression score (Beck Depression Inventory) of OSA patients, was not significantly different respect to controls.
Conclusions: Our results showed, according with other literature data, that OSA patients have some kind of cognitive deficits. Moreover we found that CPAP therapy is effective in reducing some of these. In particular, the CPAP therapeutic effect is already evident after a short period of treatment.

0634.J

A Comparison of a Novel Positive Airway Pressure Therapy Mode to Continuous Positive Airway Pressure for Adult Obstructive Sleep Apnea Treatment

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Introduction: Despite nearly 100% efficacy as a treatment for obstructive sleep apnea (OSA), continuous positive airway pressure (CPAP) adherence is known to be only 40% to 70%. The sensation of being unable to fully exhale against CPAP is a frequent complaint of non-adherent patients. A novel positive pressure mode was developed to provide a base pressure to abolish pharyngeal collapse, as well as decreasing the cumulative pressure during exhalation. The novel therapy mode allows for pressure reduction at the start of exhalation followed by a sinusoidal rise in pressure as flow rates increase.The aims of this study are to assess whether: 1) The novel therapy mode (C-Flex ®) is an effective method to treat adult OSA, and 2) the novel therapy pressure profile provides sleep quality that is equivalent to standard treatment.
Methods: Prospective randomized double-blind study of 16 patients recently diagnosed with OSA who received a successful CPAP titration study. Patients with other concomitant sleep disorders were excluded. OSA patients had an apnea-hypopnea index (AHI) > 10 events/hr and did not have REM-related or supine-positional OSA. These patients then underwent a split-night, in-lab titration study during which CPAP and the novel therapy were compared. Using a prototype device, the novel therapy expiratory pressure relief was applied at 5 individual settings and each was compared to CPAP with respect to the AHI, total arousal index (TAI), sleep efficiency and other measurements derived from nocturnal polysomnography. Results were compared between modes and pressure relief settings using ANOVAs and linear mixed effects.
Results: There is no difference in the AHI, TAI, or sleep efficiency for OSA patients using CPAP or the novel therapy at each of the five pressure relief settings. Cumulative expiratory pressures are reduced in patients using the novel therapy compared to CPAP. All patients tolerated the novel therapy and CPAP without difficulty.
Conclusions: The novel therapy is as effective as CPAP in abolishing obstructive respiratory events and has the same immediate effect on sleep. The novel therapy allows for pressure reduction during exhalation without recurrence of obstructive respiratory events during sleep. Decreased mean mask pressure with the same efficacy suggests possible advantage to adult OSA patients who are non-compliant with CPAP because of pressure intolerance.

Research supported by Respironics

0635.J

Upper Airway Surgery to Improve CPAP Titration in Patients with Obstructive Sleep Apnea-Hypopnea Syndrome

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Introduction: Obstructive sleep apnea-hypopnea syndrome (OSAHS) has nasal CPAP as the most frequent therapy, but its compliance is unsatisfactory regarding the irregular use and dropout rate. CPAP pressure titration and its use can be influenced by unsatisfactory nasal permeability, what can increase upper airway resistance. High CPAP pressure and nasal discomfort are reported as possible causes of bad adherence. Nasal surgery has a limited influence in the apnea-hypopnea index but can have significant benefit in improving nasal CPAP adherence and compliance.
Methods: OSAHS patients with indication of CPAP treatment to their respiratory sleep disorder were enrolled in this study. The objective of upper airway surgical treatment was to decrease nasal or pharynx resistance in patients with high pressure or with nasal discomfort during CPAP titration. Upper airway was the focus of treatment and the assessed anatomical abnormalities by surgical procedure were deviated septum, hypertrophied turbinate and hypertrophied tonsil. All patients had polysomnography study with nasal CPAP titration before and after the proposal surgical treatment.
Results: Seventeen patients (18 men and 1 woman) were included with a mean age of 49±9 years old, body mass index of 30±4 kg/m2 and a mean apnea-hypopnea index of 46±19 events/hour. The performed upper airway surgical treatment was radiofrequency volumetric reduction of inferior turbinate in 8 patients; septoplasty in 1 patient; septoplasty with inferior turbinectomy in 4 patients; septoplasty with inferior turbinate submucosal diathermy in 1 patient; septoplasty with tonsillectomy in 2 patients and tonsillectomy in 1 patient. All surgical procedures were done by general anesthesia. Polysomnography studies before and after surgical treatment reveled respectively: ideal CPAP pressure of 12.4± 2.5 cmH2O and 10.2±2.2 cmH2O (p=0,001); minimum oxygen saturation of 82.2±9.8% and 80±11%; delta sleep percentage of 19±9.7% and 20.1±10.6%; REM sleep of 20.9±13.2% and 20.9±9.2%. The maximum ideal CPAP pressure was 16.4 cmH2O before surgical treatment and 13 cmH2O after that.
Conclusions: Surgical treatment to promote a better upper airway permeability in patients with nasal or pharynx anatomical abnormalities (deviated septum, hypertrophied turbinate and hypertrophied tonsil) has significant benefit by reducing nasal CPAP pressure levels. We believe that studies involving treatments to reduce upper airway resistance must be encourage, as an opportunity to have better adherence and compliance rates.

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0636.J

The Functional Status Outcome of OSA Patients after Two Weeks of CPAP Therapy

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Introduction: It is known that CPAP normalizes sleep-disordered breathing; however, the degree to which it reverses daytime sleepiness (and improves functional status) is still a matter of debate. In this context, the resolution of sleepiness is of critical importance and is likely the determinant of improved functional status. The purpose of this study was to determine the degree to which functional status is normalized after two weeks of CPAP therapy.
Methods: Data from 19 consecutive subjects participating in a CPAP mask study are reported (mean age 46 ± 10 yrs, range 26-65 yrs; 13 males: 6 females). Subjects were required to have a polysomnographic diagnosis of OSA (AHI ³ 15 events per hour), elect CPAP therapy, and be in stable medical/psychiatric condition. Participants completed the FOSQ, SWAI, and the modified Epworth Sleepiness Scale (mESS) before the initiation of CPAP and after two weeks of therapy. All subjects used REMStar Pro CPAP units with heated humidification set at their prescribed therapeutic setting. Therapeutic success was defined as the normalization of the FOSQ vigilance score at the end of two weeks of therapy. Responders were compared to nonresponders to identify relevant correlates of therapeutic success.
Results: Using these criteria, thirteen subjects experienced normalization of vigilance at the end of two weeks. No differences in gender or severity were displayed at baseline. Responders had a significantly higher BMI (38 kg/m2) when compared to nonresponders (30 kg/m2). Therapeutic CPAP settings did not differ between the two groups (responders= 9.6 ± 3.3, nonresponders= 8.7 ± 3.4 cmw). Eleven subjects (58%) experienced resolution of EDS on the SWAI. On the mESS, a significant interaction was demonstrated ($p < 0.05$). While responders and nonresponders were comparable at baseline, they differed at the two-week follow up with the responders reporting greater alertness. In addition, responders experienced improved energy levels (SWAI energy, $p < 0.05$) and increased activity levels ($p < 0.05$), general productivity ($p < 0.01$), and total score ($p < 0.01$) on the FOSQ at the follow-up visit. BMI was not found to be a significant covariate in the functional response pattern with CPAP. Importantly, daily average therapeutic compliance differed between the two groups (responders 5.9 hours vs. nonresponders 4.6 hours, $p < 0.05$). Interestingly, higher correlations were found between the vigilance change scores and SWAI energy level ($r = 0.53$, $p < 0.05$) than with the SWAI EDS scale ($r = 0.39$, ns) or the mESS (noon, $r = 0.49$, $p < 0.05$).
Conclusions: The results documented a 68% normalization of functional status as determined by the vigilance scale of the FOSQ. It also demonstrated the importance of CPAP compliance to the recovery of functional status and challenges the notion that CPAP use of 4 hrs/night should be the minimum required for effective treatment of the condition. While the study reveals the complementary nature of the information derived from the existing self-report sleep questionnaires, it also highlights theoretical differences in the construct of the various EDS scales. The extent to which full functional status recovery is achieved with continued CPAP therapy remains to be determined.

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0637.J

Assessment of Sleep-Disordered Breathing in Morbidly Obese Patients Referred for Bariatric Surgery

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Introduction: Sleep disordered breathing (SDB) is a condition that is not extensively studied in morbidly obese patients although if it is recognized and treated could improve health status and avoid postoperative complications. The objective of this study is to evaluate SDB in morbidly obese population referred for bariatric surgery.
Methods: In a ongoing study 25 obese patients, (15 female / 10 male), consecutively evaluated for bariatric surgery (January to October 2002) at the Obesity Clinic from the Federal University of São Paulo, Brazil, underwent clinical and polysomnographic evaluations (using nasal canula and oral termistor).
Results: The mean age was 38.9 ± 10 y and body mass index (BMI) of 47.5±6,8 kg/m2. Neck and abdomen circumferences were 43.5 ± 4.3 cm and 132 ± 17.2 cm, respectively. Abnormal daytime sleepiness (rating > 10) as evaluated by Epworth Sleepiness Scale (ESS) was present in 48% of the patients. All of them showed snoring, ranging from mild to severe intensity. Sleep apnea/hypopnea index, defined as index higher than 5/hour of sleep, occurred in 24% of patients, mostly frequent in men (40%) than women (13%). The majority of the patients, 88%, presented air flow limitation characterized by flattened signal of airflow without hypopnea or oxygen desaturation, with mean events overnight of 25.7 ± 23.9. Oxygen desaturation during REM sleep no related to apnea or hypopneas ocurred in 36% of patients. The mean of the minimum O2 saturation was 88.6 ± 4.3 suggesting REM hypoventilation. None of them showed obesity hypoventilation syndrome. Significant correlation was found for daytime sleepiness and apnea/hypopnea index ($r = 0.44$, $p = 0.04$). No associations between BMI and measures of circumferences and apnea/hypopnea index were found.
Conclusions: Air flow limitation, REM hypoventilation and sleep apnea were frequently found in this sample of patients referred to bariatric surgery. These findings suggest that sleep evaluation should be considered as a routine exam in this population.

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0638.J

Dynamic Pressure Regulation In A Nasal CPAP System With Different Patient Interfaces

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Introduction: Ideal NCPAP therapy would apply precisely the prescribed pressure at the patient's airway throughout the breathing cycle. In reality, however, variations occur due to circuit and interface resistance and due to control of the CPAP flow generator. This pressure deviation adds to patient work of breathing. We measured the dynamic pressure regulation characteristics of a NCPAP system with several different interfaces.
Methods: A mechanical breathing simulator (Hans Rudolph Series 1100) was used to create a pattern of patient breathing with frequency of 12/min and a peak flow rate of 41 liters per minute. A CPAP flow generator (S7, ResMed Inc.) set to deliver 10 cmH2O was connected to the simulator via a 6 foot, 22 mm patient circuit and various interfaces: Mirage (M), Ultra Mirage (UM), Mirage Vista (MV) (ResMed Inc.), Nasal Aire cannula (NA) size medium (Innomed Technologies), Breeze with medium nasal pillows (Puritan Bennett), and Comfort Select (CS) (Respironics). Pressure was recorded at the 'patient' airway and at the flow generator (FG). To calculate a relative measure of work of breathing, mean pressure deviation from end expiratory pressure was calculated. This is the average pressure that the patient needs to inhale and exhale against.
Results: Mean Airway Pressure (MAP) and Mean Pressure Deviation (MPD), cmH2O.

MAP	MPDFG	10.1	0.14M	9.5	
0.38UM	9.7	0.18MV	9.8	0.27NA-M	8.6

1.35Breeze 9.6 0.76CS 9.8 0.16
Conclusions: The pressure measured at the flow generator holds closely to the set pressure of 10 cmH2O. The pressure at the patient airway however deviates further from this, and the amount varies with the interface.For all interfaces, MAP was less than the set pressure. This is due to the pressure drop in the system caused by the exhalation port flow. The magnitude of this pressure drop is proportionate to the level of this flow and the resistance of the system. The cannula device exhibited greater pressure loss. This product utilizes a pair of 22" long small diameter tubes to connect the circuit to the nasal port. These may cause a higher level of pressure resistance than other interfaces. The Breeze also had somewhat higher MPD that other devices, probably due to the relatively long 15 mm connecting tube between the circuit and the nasal pillows.Only one breathing pattern was tested. It is expected that with breathing patterns exhibiting lower or higher flow rates, the observed pressure changes would be attenuated or magnified respectively.Choice of interface may affect a patient's work of breathing, hence their tolerance of NCPAP therapy.

Research supported by ResMed Inc.

0639.J

Efficacy of a Non-Customized Tongue Retaining Device- A Randomized, Controlled, Crossover Trial

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Introduction: The evidence for oral appliances as a therapy for sleep disordered has been strengthened in recent years by the publication of the results of randomized controlled trials. These trials have focused on customized, mandibular advancement devices (MAD's). Customized tongue retaining devices (TRD's) have been used for over twenty years and while evidence suggests they are not as effective as MAD's, TRD's are not dependent on a healthy dentition for retention nor are they likely to have the undesirable side-effects of MAD's on the teeth or TMJ.The objective of this study was to evaluate the effect of a pre-fabricated, one-sized tongue-retaining device on sleep disordered breathing.
Methods: Using a block-randomized, crossover design, a non-suction device (NS) control and a suction device (S) as active therapy, thirty-nine subjects were studied after a week's use of each of the two devices, separated by a one-week washout period. Respiratory disturbance index (RDI), snoring index (SI), Epworth Sleepiness Scale (ESS), subject and bed-partner sleep apnea quality of life index (SAQLI) were recorded at baseline and after one week's use with each device. Subjects were also questioned as to their intent to continue to use a device.
Results: The S device reduced the median SI by more that 70%, 159.4 to 41.8. The mean SI was reduced from 224.5($\pm$157.7) to 128.6($\pm$ 173.1) Kruskal-Wallis, p<. 0038. The proportion of subjects who indicated they would continue using the suction device compared to those who would use the Non-suction or either was 68%. Although there was a stepped improvement in quality of life scores from baseline (3.9) to Non-Suction Device (4.0) to Suction Device (4.2), these improvements were not significant. (F =. 2572). A change of '1' in SAQLI score is considered a significant change.Respiratory disturbance index, after log transformation, showed evidence of different means (F=3.16,p=. 04). There was strong evidence that the RDI for the suction device was less than non-suction or baseline. The ratio of geometric means was 1.36 (95% confidence interval, 1.197 to 1.547). The respiratory disturbance index was reduced by 36% in the suction device with the range of differences being from 20% to 55%.
Conclusions: Reductions observed in RDI and SI are comparable to those found with customized devices. Improvement in SAQLI and ESS scores combined with subjects declared intention to continue to use the devices suggest that devices such as these may have a role to play in initial or trial therapy for those with SDB. As the devices are easily expelled from the mouth, compliance is very difficult to verify. Their use in those with moderate and severe SDB should be limited to cases when CPAP or customized devices are not feasible.

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0640.J

Correlation Between REM Sleep Variables And The Polysomnographic Architecture In Obstructive Sleep Apnea Patients

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Introduction: Obstructive sleep apnea is associated with poor sleep quality. The aim of the study was to determine the correlation between REM sleep variables and the polysomnographic architecture including Respiratory Disturbance Index (RDI) in Obstructive Sleep Apnea (OSA) patients.
Methods: 40 untreated subjects (32 males and 8 females) with mild to severe OSA patients underwent overnight - attended polysomnography. The subjects were free of psychotropic drugs at the time and two weeks prior to the sleep studies. We analyzed the relationship between REM sleep variables and the sleep architecture using correlation analysis.
Results: The correlation coefficient (r) between REM latency (minutes) and REM sleep (%) is -0.426; between REM latency and wake after sleep onset (WASO, %) is 0.286; between REM sleep (%) and the duration of the first episode of REM sleep (REM 1, minutes) is 0.372; between REM sleep (%) and RDI in NREM sleep is -0.304; between REM sleep (%) and sleep efficiency (%) is 0.337; between REM sleep (%) and WASO (%) is 0.464; between REM sleep (%) and arousal index is 0.31; between REM 1 and stage 3 sleep is -0.339 and between REM 1 and slow wave sleep is -0.354. The p values of these correlations are lower than 0.05.
Conclusions: The results show that in this group of sleep apnea patients REM latency has a negative correlation with REM sleep and a positive correlation with WASO. REM sleep has a positive correlation with REM 1, sleep efficiency and WASO. It has a negative correlation with RDI in total sleep time and arousal index. REM 1 has a negative correlation with stage 3 sleep and slow wave sleep.

0641.J

The Subjective Cognitive Impairment Rating Scale (SCIRS): An Instrument for Self Evaluation of Cognitive Impairments in Patients with Sleep Apnea

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Introduction: Patients with obstructive sleep apnea (OSA) often complain of cognitive impairment. The subjective perception of functional impairment has been found to be associated with treatment compliance of OSA patients. Previous studies with neuropsychological tests suggested that general intellectual function, attention, memory and learning abilities, executive functions, and motor performance are the main areas of impairment in OSA patients. However, as far as we know, no instrument has been develop to measure the subjective perception of cognitive impairment in OSA patients. The purpose of our study is to describe the construction a self rating scale for the perception of cognitive impairment in OSA patients, and to present the preliminary data of the reliability and validity of the scale.
Methods: Thirty patients with OSA were interviewed for their daily life experiences of cognitive problems that may due to OSA. Base on previous findings on the areas of cognitive impairment, the descriptions of cognitive problems were categorized into 3 categories: attention and vig-

ilance, learning and memory, and executive function. An additional area, emotion and motivation, was added since many of the patients also complained of impacts on this domain. The descriptions were then integrated into 30 descriptions to serve as the items of the scale. Subjects were asked to rate the impact of OSA on each item with a Likert scale ranging from 1(no impact) to 5 (extreme impact). The scale was then administered to 62 OSA patients (55M, 7F) along with PSG recording to evaluate the psychometric properties of the scale.

Results: Chronbach¡¦s alpha showed good internal consistency for all the four subscales. The Chronbach¡¦s alpha coefficiences of attention and vigilance subscale is 0.89, learning and memory subscale is 0.93, executive function subscale is 0.93, and emotion and motivation scale is 0.85. In terms of validity, correlation with RDI was utilized to be the index of criterion-relation validity since previous studies have shown a high correlation between neurocognitive impairments and the severity of OSA. The results showed a significant correlation between RDI and total scores of the scale.(r=.346, $p < .01$).

Conclusions: From these preliminary data, it appears that the SCIRS is a reliable and valid instrument to measure OSA patients¡¦ subjective rating of cognitive impairment. It can be easily administered to assist the evaluation and treatment planning for OSA patients.

0642.J

Sleepiness and Adherence to CPAP Treatment in Adults with OSA

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Introduction: Although there have been reports of the effectiveness of CPAP treatment on subjective and objective sleepiness, the true impact of CPAP treatment may have been blunted by the inclusion of non-adherent patients in studies. There has only been one clinical trial that has examined the impact of CPAP treatment relative to level of adherence. This may also account for the inconsistent findings in improvement in objective sleepiness. Thus, there is little evidence of the additional benefit that can be realized with optimal CPAP use. The purpose of this study was to describe the profile of sleepiness in subjects with moderate to severe OSA that were adherent to CPAP compared to those who were less adherent. Low adherence to CPAP for this study was operationally defined as CPAP use <90% of monitored nights.

Methods: Subjects participated in a multisite study with the following inclusion criteria: age 20-60; AHI >15; patient a candidate for CPAP. Exclusion criteria included any co-existing sleep disorder or co-morbidity that affected daily functioning. Subjects completed the following sleepiness measures at baseline and again following 3 mo. of CPAP use: Epworth Sleepiness Scale (ESS), multiple sleep latency test (MSLT), and the psychomotor vigilance task (PVT). Adherence was documented using an overt monitor that measured 24-h duration of mask-on pressure that was attached to the CPAP machines.

Results: Subjects that completed 3 months of CPAP treatment were included in these analyses (N= 140, adherent = 83, non-adherent = 57). The sample (86% male, mean age = 47 $\pm$ 9.5, mean BMI 38 $\pm$ 8.2, mean AHI = 65 $\pm$ 29) had a mean baseline ESS = 14.8 $\pm$ 4.8, mean baseline MSLT sleep latency = 6.8 $\pm$ 5.1, and a mean baseline PVT total lapses = 4.7 $\pm$ 8.0. There was no difference between adherent and non-adherent subjects in age, BMI, or AHI, or baseline ESS, MSLT, or PVT. By design, there was a significant difference ($p < 0.00001$) in mean number of hours a night that adherent subjects used CPAP (5.9 hrs) compared to non-adherent subjects (3.6 hrs). Following 3 months of treatment, adherent subjects were significantly less subjectively sleepy (ESS = 6.7 $\pm$ 4.1) compared to non-adherent subjects (ESS = 10.8 $\pm$ 5.7) ($p < 0.006$). There was no difference in objective sleepiness in adherent subjects compared to non-adherent, however MSLT sleep latency was positively correlated to CPAP use ($r = 0.39$, $p <0.001$) and approached normal (9.85 minutes). Furthermore, there was a statistically robust decrease in PVT lapses in subjects who were adherent to CPAP ($p < 0.04$).

Conclusions: Duration of nightly CPAP has an impact on outcomes following CPAP treatment. Those who consistently use CPAP realize greater gains in daytime alertness than those who use CPAP intermittently. Patients should be encouraged not to skip treatment even for one night.

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0643.J

CPAP Compliance in Apnea Patients Diagnosed via Attended (Split-Night) versus Unattended Polysomnography

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Introduction: Although it is widely assumed that patient support/education are critical in promoting CPAP compliance, few studies have addressed this issue. We compared CPAP compliance in veterans who received a standard technician-attended PSG (APSG) resulting in the opportunity to use CPAP in the lab with veterans who received an unattended PSG (UPSG) with no in-lab trial of CPAP.

Methods: Data were obtained through a retrospective chart review of outpatients evaluated at the Durham VA Sleep Lab between 5/99 and 12/01. Objective CPAP compliance data were available on 96 patients (95 male). The UPSG group consisted of 47 apnea patients who underwent unattended diagnostic PSG during a 7-month staffing shortage; these patients had Oxford Medilog ambulatory sleep recorders applied by day staff and subsequently slept unattended on the hospital lodging ward. They were prescribed auto-titrating CPAP to be delivered to their home and were instructed on the use and care of CPAP by the homecare representative. The APSG group consisted of 49 apnea patients diagnosed via a standard technician-attended laboratory PSG using the Nicolet Ultrasom System. APSG patients received a trial of CPAP during the second half of the PSG night (split-night), with technician support and assistance. Compliance data were downloaded at follow-up visits ranging from 8 to 434 days.

Results: There were no significant differences between groups in age (UPSG: M = 55.4, SD = 10.3; APSG: M = 56.2, SD = 12.7) or body mass index (UPSG: M = 34.8, SD = 5.8; APSG: M = 33.4, SD = 6.8). APSG patients showed a higher respiratory disturbance index (UPSG: M = 31.1, SD = 20.5; APSG: M = 42.2, SD = 30.3; $p < .05$). Three compliance measures were obtained: percent of days that CPAP was used, average hours of use for all days, and average hours of use on days that CPAP was used. APSG patients used CPAP on 76.7% (SD = 27.4) of nights, with an average use of 5.0 hrs. (SD = 2.0) on nights used. UPSG patients used CPAP on 64.2% (SD = 33.5) of nights, with an average use of 4.0 hrs. (SD = 1.9). A 2 (groups) X 3 (compliance) MANCOVA (covariates were RDI and number of days of CPAP use) was significant (Wilks' Lambda = .91, $F[3, 90] = 3.0$, $p = .035$). Univariate t-tests for each of the compliance variables was significant at $p < .05$.

Conclusions: At follow up, patients with sleep lab exposure to and practice with CPAP used CPAP approximately one more day per week and one hour more per night on average compared to patients whose first experience with CPAP was in their home. These findings suggest that the support and education provided by sleep lab personnel is an important factor in facilitating CPAP compliance.

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0644.J

Subjective Cognitive Impairments in Patients with Obstructive Sleep Apnea

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Introduction: Patients with obstructive sleep apnea (OSA) have long been recognized to have impairments in cognitive function. Previous studies have confirmed this phenomenon with various neurocognitive tests. However, as far as we know, no study has focused on the subjective awareness of cognitive impairments in patients with OSA. This study used a subjective rating scale (the Subjective Cognitive Impairment Rating Scale, SCIRS) to evaluate OSA patients' subjective perception of their cognitive impairment.

Methods: Sixty-two OSA patients (55M, 7F), with a mean age of 47.52±12.60, filled out the SCISR. PSG showed a mean RDI of 45.77±28.71.The SCIRS consists of 30 descriptions of cognitive impairment that belong to 4 areas: attention and vigilance, learning and memory, executive function, and emotion and motivation. Patients were asked to rate the degree of impacts of their OSA on the cognitive function described in the items on a 5-point Likert scale ranging from 1(no impact) to 5 (extreme impact).

Results: The results showed that the mean ratings on the attention and vigilance subscale is 1.82±0.37, learning and memory is 1.98±0.54, executive function 1.77±0.50, and emotion and motivation is 1.77±0.35. The mean of total score is 1.67±0.69. ANOVA showed no significant difference between the mean scores of the subscales.

Conclusions: Although previous studies showed cognitive impairment in patients with OSA, our finding indicated relatively low awareness of cognitive impairment with subjective ratings. The means of patients¡¦ rating in all subscale are below 2 (mild impact). It suggested a discrepancy between objective assessment (neuropsychological tests) and subjective rating of cognitive impacts of OSA. Previous studies has suggested that the cognitive problems in OSA patients might not be obvious in their daily activities, and might become apparent when the patient is confronted with a novel task, such as the neurocogntive tasks used in previous studies. This may account for the perception of relatively mild cognitive deficit obtained in our study. Previous studies have suggested that the perception of daytime functioning may be associated with patients' compliance of CPAP treatment. This low level of awareness of cognitive impairment may be one reason that patients have low acceptance and compliance with OSA treatment. This issue demands further research.

0645.J

Effects of Antihypertensives On Arterial Responses Associated With Obstructive Sleep Apneas

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Introduction: We have previously found that arterial stiffness increases during the asphyxic phase of obstructive sleep apnea (OSA). We now investigate whether antihypertensive medications ameliorate the changes in arterial stiffness and blood pressure associated with OSA.

Methods: 55 patients (13 female, 42 male, mean age 53.7±12.1 SD years) consecutively referred for OSA were prosectively studied with standard nocturnal polysomnography. Beat-to-beat blood pressure was continuously recorded from the radial artery by applanation tonometry during baseline sleep. Twenty five were normotensive (N), 5 were hypertensive on no antihypertension medications (H), and 25 were hypertensive, all on combination antihypertension therapy (HM). Among the HM patients, 16 were on angiotensin converting enzyme inhibitors, 8 were on calcium channel blockers, 6 were on beta-blockers, 4 were on alpha-1 blockers, and 5 were on diuretics. As a measure of arterial stiffness, arterial augmentation index (AAI) was calculated as the ratio of augmented systolic blood pressure (SBP) to pulse pressure and expressed as a percentage for the following conditions: awake, the first 10 ("early apnea") and last 10 ("late apnea") cardiac cycles of obstructive events (apnea or hypopnea), and the first 15 cardiac cycles following event termination ("post apnea") for NREM and REM events with nadir O2 saturation <89%.

Results: Mean AHI was 59.4±31.6 events/hour; mean nadir SaO2 was 82.4±6.7%. Mean AAI normalized as a percentage of awake and early event values increased significantly for late apnea overall. However, a significant difference in mean AAI increase from early to late apnea was found among the 3 groups: H increase (143.76±23.34%) was greater than N (118.30±24.89%) and HM (113.13± 25.48%, $p<.05$, ANOVA). When sub-analyzed according to medication class, AAI increased less from early to late apnea ($p<.05$) in the HM patients on regimens which included Ca++ channel blockers (Ca++, 98.53±22.10%) than regimens which did not include Ca++ (120.01±24.57%), and H (143.76±23.34%). Identical analyses for all other separate medication classes used did not reveal similar discriminating effects for AAI change. Major demographic and physiological variables including age, race, gender, BMI, AHI, and mean nadir SaO2 were similar for each medication sub-group. Systolic blood pressure (SBP) increased significantly from late to post apnea overall (127.6±15.1 mmHg vs 139.7±15.5 mmHg, $p<0.01$); however, no significant difference was found in the SBP increase post-apnea among the N, H, and HM groups. No sub-class of antihypertensive medication discriminated among SBP changes.

Conclusions: In patients with moderate to severe OSA and systemic hypertension, commonly used combination antihypertensive therapy appears to significantly ameliorate the acute increase in arterial stiffness during the asphyxic phase of OSA to levels seen in similar normotensive OSA patients. Antihypertensive combinations which include calcium channel antagonists appear to optimally ameliorate acute arterial stiffness increases. However, arterial blood pressure increases acutely post apnea in these OSA patients regardless of hypertensive or medication status.

0646.J

Sleep Disorders in Brazilian Taxi Drivers

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Introduction: In the international literature there are many papers showing the relationship between sleep disorders and motor vehicle accident (MVA) involving truck drivers, but we have just few studies taking in account the taxi drivers. In São Paulo City (a 12 millions people city) the traffic accidents involving taxi drivers are frequent and sleep disorders may play an important role in MVA. Unfortunately we do not have a clear policy regarding sleep disorders assessment in that population of workers in almost all country of the world, and public health programs should include in their goals some known sleep medicine information to alert and also prevent many undesirable consequences of driving.Objective: Evaluation of sleep disorders in taxi drivers of São Paulo City.

Methods: 148 taxi drivers working during day period in South District of São Paulo were included in this study, 128 were male (86.5%) and 20 female (13.5%). Sleep disorders were assessed by a guide designed for sleep disorders relative to insomnia, sleepiness, restless legs syndrome (RLS) and sleep breathing disorders (SBD) and filled out by the taxi drivers. The data were analyzed by a binomial test, comparing our sample with the prevalence of general population.

Results: Taxi driver´s mean age and BMI were respectively 46 years and 28 Kg/m2. Only 6% of the taxi drivers referred insomnia (p<0.03), 2% referred RLS (p<0.005) and 4.7% of them referred sleepiness (ns). SBD were referred by 8.8% of taxi drivers (p<0.005), more than the expected value for general population, among them, 9 (69%) had naps (p<0.05) and only 41% of non-SBD. BMI among SBD taxi drivers was 32Kg/m2.
Conclusions: The analysis of our sample of taxi drivers population showed a low prevalence of insomnia, but that could be just a sample bias disclosing the preference of good sleepers to work during the day. They did not refer more sleepiness than the general population, but those with SBD are overweighted and 69% of them have naps, suggesting that they are clinically affected by SBD. The prevalence of RLS in our sample is lesser than in general population, besides we do not have epidemiological data in Brazil regarding RLS.

0647.J

Relationship Between Subjective Sleep Quality And Depression In Patients With Obstructive Sleep Apnea

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Introduction: The degree to which obstructive sleep apnea (OSA) diminishes the perceived quality of sleep varies greatly. Previous studies have shown that depression alters subjective ratings of sleep quality in populations without documented OSA. The present study examined whether depression is independently associated with self-reported sleep quality or with objective sleep measures including severity of OSA as indicated by the respiratory distress index (RDI), number of arousals, and sleep onset latency.
Methods: A sample of 67 patients with OSA documented by all-night polysomnography (age 48±11 years; 63% female; 66% Caucasian, 34% African American) was recruited from a sleep disorders center. The morning after the sleep study, the patients completed the Beck Depression Inventory (BDI) and the Insomnia Severity Index (ISI), a measure of subjective sleep quality over the past two weeks.
Results: The objective measures of sleep quality were not related to depression or to subjective sleep quality in univariate analyses, but depression and dissatisfaction with sleep quality were positively correlated (r = .41; p = .0006). Depression remained an independent predictor of subjective sleep quality after controlling for the objective measures of sleep disruption (F = 13.08; p = .0006).
Conclusions: We conclude that the perception of sleep quality is more closely related to depression than to objective measures of sleep in patients with documented OSA.

0648.J

CPAP Adherence: Effect of Nasal Resistance

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Introduction: Nasal resistance is a predisposing factor for upper airway obstruction during sleep, and recently reported as an independent predictor for the apnea hypopnea index. Nasal resistance represents up to 50% of the total respiratory resistance. Nasal valve is the place of the highest resistance in the nasal airway. We hypothesize that nasal resistance can be positively correlated with nasal CPAP pressure and negatively correlated with CPAP compliance. The aim of the study was to determine if nasal resistance affects tolerance and short-term adherence with nasal CPAP in obstructive sleep apnea (OSA) patients.
Methods: We recruited patients from the CPAP Clinic with a polysomnographically diagnosed OSA. Those patients with a history of nasal surgery, or known cardiovascular diseases were excluded. A questionnaire on sleep habits, including the Epworth scale, and nasal symptoms was applied to all patients. The same investigator performed a physical examination of the upper airway, a Cottle maneuver and an anterior rhinomanometry. All patients underwent a CPAP titration on the Sleep Lab, and were given a CPAP device which came outfitted with an internal clock counter that recorded usage information. Adherence was defined as the number of hours of CPAP use per night, and was measured at one month. The questionnaire and rhinomanometry were performed again after 3-4 weeks of CPAP use.
Results: We included 17 patients with an average age of 45.8 years (range: 27-65), 12 were males. The mean weight was 97 ± 20 Kg, the mean. BMI was 36.2 ± 7.9 Kg/m2, and the mean neck circumference was 43 ± 3 cm. The mean respiratory index of the sample was 82.3 ± 33.2. The basal nasal resistance measure was on average 2.76 ± 1.13 cmH2O. The mean Epworth Scale of the sample was 13.7 preCPAP and 8.4 postCPAP . The main nasal symptom admitted by the patients was 41%. Mean nightly usage of CPAP was 3.22 ± 2.46 hours. The referred usage by the patients was 5.4 hours. Statistical significant analysis at p<.05 found a positive correlation (Pearson) r=.7289 between nasal resistance and CPAP adherence expressed in hours per night. A positive correlation r=.77 was also found between CPAP adherence and Epworth postCPAP.
Conclusions: As previously reported we found that patients with hypersomnia have a better adherence to CPAP treatment for OSA. Interestingly we found a direct correlation between nasal resistance and CPAP adherence, which is a factor that should be investigated.

0649.J

Respiratory Effort, Sleep Fragmentation and Oxygen Saturation Correlation with RDI and Pes Values

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Introduction: The sleep related breathing disorders (SRBD) main consequences are related to sleep fragmentation and oxygen desaturation. The severity of SRBD is usually measured by RDI(respiratory disturbance index), even though it is controversial whether this index is reliable indicator of disease severity. Respiratory effort can only be appropriately measured by esophageal manometry (Pes). The consequences of increased respiratory effort in SRBD are illustrated in UARS patients, whose main abnormalities are related to an increase in respiratory effort and sleep fragmentation.Some studies have already demonstrated that RDI does not correlate with Pes and the severity of SRBD may not be accurately assessed using only the RDI. The purpose of this study is to correlate RDI and Pes values with oxygen saturation and sleep in children and adults.
Methods: A group of 56 adult patients (18 to 70 years old) and 65 children (age: 1 to 12 years old) underwent polysomnography with esophageal manometry. The following parameters were assessed: EEG, EOG, chin EMG, ECG, thoracic and abdominal expansion, oral airflow, nasal airflow with nasal pressure cannula and nocturnal oximetry. RDI and Pes values were correlated using Pearson Correlation.
Results: -Adult group: Pes values significantly correlated with sleep efficiency, but there was no correlation between Pes and oxygen desaturation level. The RDI had significant correlation with oxygen desaturation level but did not correlate with sleep efficiency. - Pediatric group: Pes values significantly correlated with oxygen desaturation and did not correlate with sleep efficiency. The RDI showed no correlation with either oxygen desaturation or sleep efficiency.
Conclusions: In adults, respiratory effort was not associated with sleep fragmentation and it was associated with oxygen desaturation. In contrast, the RDI was not associated with oxygen levels and did not correlate with sleep efficiency. In children a different association was

observed. The increase in respiratory effort was associated with oxygen desaturation. We conclude that the consequences of increased respiratory effort and RDI may play different roles in the pathophysiology of SRBD when we compare adult with children. The consequences of increased respiratory effort as the only abnormality be evaluated in the different age groups with SRBD in order to understand the consequences of this condition.

0650.J

Sleep-Disordered Breathing in Professional Football Players

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Introduction: Sleep Disordered Breathing (SDB) is a clinical disorder, consisting of apnea and hypopnea during sleep; it affects about 4% of the general population. Although young, and ostensibly in excellent physical condition, professional football players have many of the risk factors for sleep apnea including male gender, high body mass index (BMI) and large neck size. We hypothesized that the presence of SDB would be increased in this group of athletes, particularly in the bigger offensive and defensive linemen. In this study, we report prevalence estimates of SDB and describe the clinical features in this population.
Methods: From 8 randomly selected teams, we used the Multivariable Apnea Prediction (MAP) index to stratify players into High (MAP ≥0.5) and Low (MAP <0.5) risk for SDB. Players from both risk groups were randomly selected for sleep studies, with over-sampling from the High-risk group. The primary outcome measure was an apnea-hypopnea index (AHI) ≥ 10.
Results: From 302 evaluable players (age 25.5 ± 2.7 years, BMI 31.5 ± 4.6 kg/m2) , a total of 52 players signed informed consent for overnight full polysomnographic studies - 38 from 73 high-risk and 14 from 229 low risk players. An AHI ≥10 was found in 14 of 52 players. Offensive and defensive linemen accounted for 85% of the cases of SDB, had the biggest neck size (19.1 ±0.9 inches) and highest BMI (36.6 ± 2.6). Both Systolic (129±11 vs 122±9 mmHg) and Diastolic (84±9 vs. 77±8mmHg) blood pressure was statistically higher in linemen compared to all other players (p<0.01). Ten players, not selected for polysomnography, were being treated for hypertension. More than 20% of the total players had an ESS > 10. From these data we estimate the prevalence of SDB among all pro-football players to be 14% [2,25% 95%CI] of the overall group and 34% [21,50%] of the high-risk group.
Conclusions: The estimated prevalence of SDB is much higher than previous studies, and stresses the importance of physiognomy over physical conditioning as a risk factor for SDB. For a young (mean age <30), healthy and physically fit group, it is a worrisome finding since the presence of SDB (AHI >5), even when asymptomatic, is a known risk factor for the development of hypertension. As the trend to bigger players continues, unrecognized and untreated SDB may impact not only player performance and productivity but also future health. Many physicians may have never considered such a diagnosis in young, healthy individuals, particularly those who are in top condition. Clinical suspicion should now be raised in these and other athletes as well as members of the general population of similar age and size.

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0651.J

Chronic Hypoxia And Cardiovascular Dysfunction In Obstructive Sleep Apnea

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Introduction: Obstructive sleep apnea (OSA) is associated with both acute and long-term sympathoexcitation, resulting in increased vascular tone. There is increasing experimental evidence that this pathologic phenomenon perturbs vascular function and promotes the cardiovascular dysfunction found in many OSA patients. Therefore, the current study tested the hypothesis that chronic intermittent hypoxia associated with sleep-disordered breathing relates to abnormal nitric oxide (NO) production and vascular endothelial growth factor (VEGF) expression patterns that may contribute to cardiovascular and cardiopulmonary dysfunction observed before or immediately after maximal graded exercise.
Methods: Seven medically diagnosed OSA patients (3 male, 4 female), mean age 48 yr and 7 apparently healthy control subjects (3 male, 4 female), mean age 42 yr, underwent baseline venous blood sampling and maximal ramp cycle ergometry testing. Circulating angiogenic progenitor cells expressing vascular endothelial growth factor receptor 2 (VEGFR2) were profiled by flow cytometry. Pre-exercise plasma and serum concentrations of VEGF, nitrates/nitrites, catecholamines, and dopamine were measured by enzyme-linked immunosorbent assay (ELISA) and high performance liquid chromatography (HPLC). Arterial blood pressure, non-invasive cardiac output, oxygen consumption and total peripheral resistance were determined at Baseline, 100 watts, and peak exercise by standard techniques.
Results: No differences (p<0.05) were observed between the OSA and control groups at pre-exercise or exercise time points for cardiac output, heart rate, stroke volume, mean arterial pressure, or calculated total peripheral resistance. Although there were no differences in serum nitrates/nitrites, norepinephrine, dopamine, and plasma VEGF levels, significant (p<0.05) differences were observed in waist: %VEGFR2 expression, recovery:peak systolic blood pressure ratio at 1 minute post-exercise, and hip ratio. Moreover, significant negative associations were found between waist: hip ratios and %VEGFR2 expression (r = -.69; p =.005) and recovery: peak systolic blood pressure ratio at 1 minute post-exercise and %VEGFR2 expression (r = -.65;p =.01).
Conclusions: These findings did not provide evidence that nitric oxide dependent vasoactive mechanisms are suppressed in OSA. However, future investigations should clarify whether disease related alterations of %VEGFR2 expression reflect perturbations in post-exercise arterial blood pressure regulation.

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0652.J

Differential Impact Of Phasic REM Sleep On Obstructive Sleep Apnea (OSA)

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Introduction: It has been generally accepted that in OSA, the RDI severity increases with transition into REM sleep. This has been attributed, in part, to the relative atonia encountered in the tonic component of REM sleep. On the other hand, animal studies have suggested variable excitatory and inhibitory influences on respiration during the phasic components of REM sleep. If the excitatory features were to predomi-

nate, one might expect improved RDI in phasic REM sleep. We were prompted by the incidental observation of patients with dramatic improvement of RDI in REM sleep to attempt to further characterize this phenomenon.

Methods: In order to examine these cases in more detail, we performed a retrospective analysis of 1120 consecutive nocturnal polysomnograms performed in a general sleep laboratory. Cases were selected on the basis of a major discrepancy between RDI in REM sleep and the RDI in NREM sleep. To focus our analysis, we selected cases where the REM-RDI was > five times the NREM-RDI. Similarly, we also selected cases where the NREM-RDI was > five times the REM-RDI. Cases were then sorted as to whether they had abundance, average amount or paucity of rapid eye movements in REM sleep.

Results: We identified 31 cases that met the criteria of five-fold dissociation between REM sleep and NREM sleep. Five cases had a clear improvement in RDI during REM sleep and included 4 males and 1 female with a mean age of 51.2(29-86). The mean RDI in REM sleep was 4.1(1.0-11.7) and in NREM sleep was 28.6(11.2-62.2). Intense eye movements were observed in all of these cases. Of the 26 with increased RDI in REM sleep, five were found to have an average pattern of eye movements. These included 1 male and 4 females with a mean age of 51.2(41-59), a mean REM-RDI of 40.3 (22.1-70.5) and a mean NREM-RDI of 3.4 (1.8-4.7). The other 21 were found to have an absence of rapid eye movements in REM sleep. This group included 5 males and 16 females with a mean age of 51.7 36-68) with a mean REM-RDI of 46.7 (10.0-70.3) and a mean NREM-RDI 6.0 (1.0-14.1).

Conclusions: This retrospective analysis demonstrated dissociation in the impact of REM on the RDI in OSA. There is reason to suspect that this might be related to the impact of the phasic components of REM sleep as measured by the presence of rapid eye movements. An excess appears to be associated with an improvement in OSA. On the other hand, absence of these rapid eye movements seems to be associated with a worsening of the OSA in REM sleep. It is possible that the increase in eye movements may correlate with a general increase in bulbar muscle tone. These findings suggest that manipulation of the phasic component of REM may prove beneficial to patients with REM related OSA.

0653.J

Prefrontal EEG Correlates Of Alertness Versus Executive Attention In Sleep Apnea

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Introduction: Sleep apnea is characterized by repeated episodes of upper airway obstruction associated with fragmented sleep and intermittent hypoxemia. Whether these patients show higher cognitive deficits resulting from brain damage is still a controversial issue. From an electrophysiological point of view, waking qEEG slowing and a prolonged event-related P300 latency have been demonstrated in sleep apnea patients, though not always. These results were mostly interpreted as possible evidence of cerebral damage due to intermittent hypoxemia. However, reduced alertness also produces EEG slowing or longer P300 latencies. Hence, it seems that arousal and task-related cognitive processes were significantly confounded in most sleep apnea studies. Basic attention research has indicated an interesting differential reactivity of low alpha (8-10 Hz) and high alpha (10-12 Hz) to non-specific alertness and task-related attention, respectively. Recently, we have applied this alpha event-related desynchronization/synchronization (ERD/ERS) method successfully during an executive attentional set shifting task in healthy adults. In the present study, therefore, low alpha power versus high alpha power ERD was used to enhance the differentiation of the effects of alertness versus attentional set shifting on sleep apnea patients' waking EEG.

Methods: Twenty sleep apnea patients (AHI=64.3 SD 32.1, range 21.5-122; age=48.9 SD 6.7) and an age- and education-matched control group of 24 healthy subjects took part in this study. It has been shown that attentional set shifting is specifically related to/affected by dorsolateral prefrontal activity/damage in both monkeys and humans. We have also demonstrated in basic research that prefrontal desynchronization of 8-10 Hz power was related to phasic alertness, whereas 10-12 Hz power synchronization seemed to be associated with inaccurate attentional set shifting. Therefore, the EEG was recorded from the dorsolateral prefrontal location AF3-A1 during resting baseline and during the same attentional set shifting task. Vertical and horizontal eye movements were measured simultaneously. Filtered signals (IIR Butterworth) of artefact-free segments were squared to obtain values proportional to power.

Results: Healthy controls and apnea patients did not show differences in baseline alpha power or alpha attenuation with eyes opening. Control subjects showed a decreasing trend ($p<0.10$) in 8-10 Hz power during attentional set shifting as compared to both eyes-open baseline and a basic two-choice reaction time subtest. In contrast, sleep apnea patients did not show any significant task-related alpha reactivity response. Accordingly, a between-group significant difference ($p<0.01$) and a trend towards significance ($p<0.10$) were (only) found with respect to the 8-10 Hz desynchronization during attentional set shifting relative to eyes-open resting baseline and a basic two-choice reaction time subtest, respectively.

Conclusions: Sleep apnea patients demonstrate a blunted phasic prefrontal EEG activation during attentional set shifting. It is assumed that dampening of the diffuse thalamocortical projection system has caused a reduced level of phasic alertness that can explain the attenuation of prefrontal activation, without the need to presume brain damage.

0654.J

Adherence To Nasal Continuous Positive Airway Pressure (CPAP) In Patients With Congestive Heart Failure (CHF)

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Introduction: Continuous Positive Airway Pressure (CPAP) is the primary treatment of sleep disordered breathing (SDB). This treatment is often hindered by incomplete adherence to nightly use. Optimally, the adherence can reach >85% at six months with an intense program of education and close follow up . Adherence to treatment is dependent on a multitude of factors, including patient-mask interface, mask fit, pressure setting, mode of positive airway pressure, and especially patient education and follow-up, among others. The severity of SDB as measured by the apnea hypopnea index (AHI) has been found to be an independent predictor of CPAP compliance. The effect of specific patient populations on compliance is only scarcely investigated.

Methods: We examined the compliance and drop out rate in an ongoing study evaluating CPAP in patients with congestive heart failure (CHF) and SDB. All patients enrolled underwent an initial screening interview followed by evaluation with a home monitoring device. All subjects suffered from NYHA class III or IV heart failure and had an ejection fraction of „T 42%. Subsequent to identification of SDB, subjects underwent education as well as CPAP or BIPAP titration according to initial randomization. They underwent a second titration study after three months of use and completed the study after six months. Compliance was evaluated at three and six months as well as during follow-up phone conversations.

Results: 50% of subjects initially recruited discontinued participation at some point during the course of the study.

Conclusions: Completion of this six month study of nasal CPAP in patients with significant heart failure was limited. This may be related to the severity of their underlying disease with its associated demanding medical care. Furthermore, given the physical limitations related to the underlying heart condition, the subjective benefit derived from CPAP

treatment of SDB may not have been as apparent to these patients. Lastly, we recruited patients from a cardiology clinic without the prerequisite of sleep complaints, which additionally may have weakened the subjective benefit of CPAP treatment and hence study completion.

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0655.J

Sleep Related Breathing Disorders and Gastroesphageal Reflux

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Introduction: An association between sleep related breathing disorders (SRDB) and gastroesophageal reflux (GER) has been suggested in several studies. The prevalence of GER in OSA patients is estimated at 53 to 76%, the nature and mechanism(s) of this relationship are unknown. One theory is that obstructive events increase the probability of GER through increased negative intrathoracic pressure attendant to them. Studies that show no relation of severity of SRBD to the severity of GERD and demonstrating no relation of respiratory events with GER events suggest other mechanisms may be involved. Treatment of OSA with CPAP improves respiratory and GER parameters while treatment of GER with anti-reflux medication may improve OSA severity. The purpose of this study was to evaluate the severity of SRBD with severity of GER events.
Methods: 14 patients with clinical symptoms of GER and SRBD (mean age: 45.6 years, mean BMI: 27.8 kg/m2) were evaluated with 24 hour pH monitor (Mark III- Medtronic); and overnight polysomnogram (PSG) that included EEG, EOG, chin EMG, nasal cannula, oral thermistor, respiratory effort and oximetry.Analysis of reflux, arousal and respiratory events was made in a time window of 2 minutes surrounding reflux events
Results: 347 reflux events were observed overall. 25 events were seen on PSG, 10 occurred during scored sleep, 2 after a respiratory event (hypopnea). With OSA defined as RDI >5, SRBD RDI <5 events/hour, eight patients were classified as SRBD, six a as OSA. The mean (standard deviation) of age, RDI, DeMeester score, % of time with pH< 4 and BMI for SRBD and OSA respectively were: 36.7 (8.5), 61.6 (2.3); 2.1 (1.1), 28.8 (12.9); 16.2 (12.2), 34.7(19.6); 2.6 (2.6), 7.4 (4.8); and 25.3 (4.5), 27.1(7.8).
Conclusions: OSA has been associated with GER although a causative relationship is not clear. A putative mechanism for this association is increased respiratory effort as a trigger of reflux. OSA patients should therefore demonstrate more severe GER than milder SRBD patients. Our study indicated that OSA patients had higher DeMeester scores and longer time with pH < 4 than SRBD. Age and BMI may be factors. We conclude that the severity of the SRBD may be related to the severity of GER, worse OSA representing higher risk. Appropriate treatment of both disorders may prevent long-term consequences. Larger studies may elucidate this relationship.

0656.J

Flow and Composition Disturbances in Saliva, in Patients with Obstructive Sleep Apnea

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Introduction: There are very few studies regarding common symptoms such as oral dryness in patients with obstructive sleep apnea (OSA). Some of these symptoms may cause awakenings and contribute to the bad quality of sleep perceived in this patients. Salival glands are responsible to keep homeostasis in the upper airway (UA), and it is likely that OSA patients have a disturbance in saliva production. The aim of this study was to determine and to correlate the frequency of UA symptoms, and the characteristics of the saliva in patients with OSA.
Methods: Patients referred to the Sleep Clinic underwent a full night poysomnography (PSG). A questionnaire on UA symptoms was applied to all patients. Before and after the PSG a mixed saliva masticatory test was done 20-30 minutes before lights-out and after lights-on. The saliva was analyzed for flow expressed in g/min, pH and quantification of IgA determined by immunonephelometry. A control group of non-snorers completed the same procedure.
Results: A total of 25 adults were recruited. As the control group we included seven non-snorers, with a confirmation by PSG or a simplified respiratory ambulatory test, that they had no obstructive events during sleep (respiratory index –RI- 0-5), their mean age was 31.3 years (range 21-43), BMI was 23.35 Kg/m2, the RDI was 2.42 (range 0.30-5) and the mean oxygen saturation night (SaO2) was 93.5 (range 91.2-96). Eight patients had mild to moderate (MM) OSA by PSG (RI >5, £ 20), their mean age was 41.6 years (range 32-55), the mean BMI was 26.47Kg/m2, and RI was 13.5 (range 6.3-20), the SaO2 was 91.6% (range 87-94). Ten patients were classified as moderate to severe (MS) OSA by PSG (RI >20) with a mean RI of 65 (range 25-122) and mean SaO2 of 85.4% mean age was 41.4 years (range 30-53), and BMI of 33.2Kg/m2 (range 27-46). The mixed saliva production in the 3 groups expressed as nighttime/daytime was as follows: non-snorers: 2.37 / 2.04, MM-OSA: 2.08 / 1.61, and MS-OSA: 1.15 / 0.89 g/min. pH was in the non-snorers group 7.37 / 7.31, in MM-OSA: 7.32/ 7.20, and in MS-OSA: 7.27 / 7.12. There was a significant difference between controls and both groups of OSA patients. IgA secretion in non-snorers was 6.83 / 6.96, MM-SAOS: 6.83 / 9.38 and MS-OSA: 9.78 / 21.86 mg/dl, with a significant difference with respect to the control group. The symptoms that showed a positive correlation with the RI, nocturnal oximetry, less saliva production and an increased secretion of IgA, were oral dryness at wakening, oral dryness during daytime, hoarseness, dysphagia and recurrent UA infections, R= 0.75.
Conclusions: A high number of obstructive events with more hypoxemia in OSA patients, are associated with less saliva production which is more acid and with a higher concentration of IgA. This correlates significantly with upper airway symptoms.

0657.J

Sleep-Disordered Breathing (SDB) and Pattern of Weight Loss After Bariatric Surgery

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Introduction: The prevalence of sleep-disordered breathing (SDB) in patients undergoing bariatric surgery has been reported to range from 35-65%. Morbidly obese patients also have a high prevalence of cardiovascular and metabolic complications including hypertension, diabetes or insulin resistance, and dyslipidemia. There is emerging evidence that SDB further contributes to these co-morbid medical conditions and may worsen the clinical features that constitute the metabolic syndrome. We hypothesized that the presence and severity of SDB may influence the pattern of weight loss after bariatric surgery.
Methods: This study involved a retrospective analysis of patients undergoing screening for sleep-disordered breathing prior to gastric bypass (Roux-en-Y) surgery. A formal sleep intake was performed including quality of life (SF36), Beck Depression Inventory, and Epworth Sleepiness Scale assessment. Full laboratory-based polysomnography was performed and scored using R&K criteria. Patients with significant sleep apnea (determined by their sleep specialist) were offered CPAP treatment prior to gastric bypass. After gastric bypass, patients were scheduled for clinic follow-up at month one, three, six and twelve for routine post-operative assessment. Pearson correlation analysis was performed

on percent weight loss and apnea-hypopnea index (AHI) variables after AHI was log transformed due to the poisson distribution pattern. Weight loss was determined as a percentage of pre-surgical body weight. Polysomnographic and weight loss characteristics were analyzed among an original sample size of 101 patients.
Results: The mean age was 40.4 ± 11.2 years, body mass index (BMI) 53.7 ± 11.3, Beck Depression score 14.4 ± 11.2, Epworth Sleepiness score 8.8 ± 5.5, and AHI was 30.1 ± 43.7. The median AHI was 9.9. 85% of the patients were female. CPAP titration was performed in 38% of patients with 87% undergoing a split night protocol. The mean weight as a percentage of original body weight at month one was 89.4 ± 3.4%, at month three was 81.9 ± 5.3%, and at month six was 73.2 ± 4.9%. Pearson correlation analysis of the variables of age, log AHI, and weight loss percent at month one found that log AHI demonstrated the most significant correlation with weight loss percent at month three (R=-0.724, p<.001). AHI was not strongly correlated with the degree of obesity (R=0.362). Multivariate regression analysis with these three variables demonstrated a correlation coefficient of 0.865, p<.001.
Conclusions: The severity of sleep-disordered breathing, as determined by the AHI, is highly correlated with the degree of weight loss after bariatric surgery. The greater the severity of SDB, the greater the percent weight loss (compared to initial body weight). There was no correlation between initial body weight and percent weight loss after surgery. Greater weight loss after bariatric surgery appears to be strongly influenced by younger age, high severity of SDB, and high initial weight loss at post-op month one. Furthermore, these findings suggest an interaction between sleep-disordered breathing and body metabolism.

0658.J

Treatment Of Sleep Disordered Breathing With Nasal Continuous Positive Airway Pressure In Pregnancy
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Introduction: Nasal CPAP is a well-documented treatment for SDB. Placebo controlled studies have demonstrated the efficacy of CPAP in improving sleepiness, multiple sleep latency test (MSLT) results, and cognitive function. Treatment of obstructive sleep apnea (OSA) with tracheostomy has a beneficial effect on high blood pressure. Studies with nasal CPAP have demonstrated similar blood pressure improvements. Women with SDB become pregnant, and the question of nasal CPAP tolerance during pregnancy and its effect on the mother's sleep is frequently raised. Furthermore, in the more recent past significant interest has emerged in treating gravid women with SDB as the latter may be a factor in the occurrence of pre-eclampsia .
Methods: To investigate the tolerance, compliance, and difficulties associated with the use of nasal Continuous Positive Airway Pressure (CPAP) in pregnant women with Sleep Disordered Breathing (SDB) we investigated 12 women with SDB diagnosed at the beginning of their pregnancy. They underwent polysomnography at entry followed by CPAP titration and repeat polysomnography at 6 months gestational age (GA). Home monitoring of cardio-respiratory variables was performed at 8 months GA. Compliance was verified by pressure measurements at the patient-mask interface. Results from the Epworth Sleepiness Scale, Fatigue Scale, as well as visual analogue scales (VAS) for sleepiness, fatigue, and snoring were compared over time.
Results: On diagnostic polysomnogram (PSG) all apneas and hypopneas were mixed or obstructive. The mean AHI was 21 events/hour of sleep (range 9-31) with a mean lowest SaO2 of 84.4% (range 81-88%). The RDI was clearly elevated to a greater extent than the AHI, with a mean of 33 events/hour of sleep. Two women displayed numerous PLMs, of which only a few led to arousals and mostly unassociated with breathing events. All subjects carried their pregnancies to term and delivered healthy infants. Nightly compliance with CPAP was over 80%, frequently over 90%. Nasal CPAP significantly improved all measured scales compared to entry. VAS scores remained lower at 6 months GA compared to entry. Minor re-adjustment of CPAP pressure was needed in 6 subjects at 6 months GA, with the highest increase being 2 cm H2O in a single patient.
Conclusions: Nasal CPAP is a safe and effective treatment of SDB during pregnancy.

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0659.J

Prediction Model for Respiratory Disturbance Index and Implications for Therapy
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Introduction: Prediction models have been used for assessing the likelihood of obstructive sleep apnea and overall respiratory disturbance index (RDI). The correlation with RDI as measured by polysomnography (PSG) has been highly variable and such models have not found routine use in clinical practice. However, we propose that such models may have more utility in predicting the propensity towards the use of continuous positive airway pressure (CPAP).
Methods: We accumulated data on 109 outpatients referred to the Sleep Disorders Center for possible apnea between March 2001 and August 2002. History, Epworth Sleepiness Scale (ESS), physical examination and overnight polysomnography data were collected on all patients. A clinical prediction model formula was used to calculate the predicted RDI.
Results: The patient population consisted of 74 men and 35 women (ratio 2.1:1), mean height 68 inches (170cm), mean weight 247 lbs (112 kg), mean body mass index (36 kg/m2, SD± 7.9cm), mean ESS 12.3 (SD±4.97), and mean neck circumference 44.6 cm (SD±4.9cm). Obstructive sleep apnea (OSA), defined as a measured RDI >5, was diagnosed in 80% of the population. Median predicted RDI was 28 (range 2-110) with an actual RDI recorded during PSG of 23 (range 0-139). The sensitivity of a predicted RDI >10 for both an actual RDI >5 or >15 was 87%. The respective specificities were 50% and 33%. Regarding the use of CPAP, a predicted RDI>10 had a positive predictive value (PPV) of 79% and a negative predicative value (NPV) of 59%. When these criteria were applied to patients with an ESS > 10, the PPV improved to 85% but NPV decreased to 42%. There was no correlation between a recommendation for CPAP use and the presence of COPD, GERD, CHF or hypertension.
Conclusions: Although this clinical predication model is not sufficiently sensitive and specific to determine the presence of OSA without testing, it may be a useful tool in sleepy patients with an otherwise equivocal history, prompting evaluation with PSG since these patients are likely to require CPAP. The model is not likely to be helpful in directing evaluation of patients with a low predicted RDI (<10) or equivocal history for OSA.

0660.J

Improvement in Nasal CPAP,BIPAP, and APAP Compliance Using Phone Contact And Literature
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Introduction: CPAP therapy is often difficult to tolerate. Patients frequently discontinue treatment due to inability to alter sleeping habits. Previous research studied the different in compliance between three different control groups; (a) treatment only (b) phone-call follow up and (c) training literature. Advocate Home Care Products sought validation of

the following statements:1. Training literature focusing on desensitization exercises during the first month of care increases patient success with therapy. 2. Phone call follow up from a designated program coordinator increases long-term patient compliance.3. CPAP therapy improves sleepiness symptoms identified in the Epworth Scale prior to onset of therapy. 4. Coordination of care and just in time information to the sleep laboratories is a valuable tool for resolution of prevalent problems for difficult to manage patients.
Methods: All patients admitted in 2002 on nasal positive airway pressure were eligible. For the purpose of this study, compliance is defined as utilization of prescribed therapy equal to or greater than 4 hours each night. The sample included 359 patients, 248 male and 111 females. All were tracked for a one- year period. Phone contacts to monitor compliance were completed at pre-determined intervals: 24-48 hours, 7, 14, 30, 90, 180, 270 and 360 days. The Epworth Sleepiness scale was administered at the start of care, 30, 180 and 360 days as another method to validate patient self-report. In addition to patient self- report, compliance was obtained via time meter or equipment download. Data was analyzed and compared to a national database.
Results: Prevalent indicators associated with non-compliance were nasal symptoms, mask and cpap variables. Nasal symptoms comprised 41% of documented problems during the first month of care. Patients who experienced nasal symptoms showed marked improvement after initiation of humidification. Mask problems were reduced from 41% to 13% in a 6-month period. Further evaluation of mask data revealed a high utilization and rate of exchange for a particular mask. Eighty percent of patients achieved compliance after the first month of therapy. Six percent discontinued therapy after interdisciplinary team intervention.
Conclusions: The study suggests that long term compliance to nasal positive airway pressure is achievable in an environment that encourages patient education, comprehensive follow up and regular communication. Physician satisfaction resulted in significant program growth, improved communication among care providers, and improved patient compliance. Benefits to the Sleep Laboratory are a decrease in administrative responsibilities for clinical staff and early identification of patient noncompliance.

0661.J

Can Telemedicine Improve Compliance with Nasal CPAP?
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Introduction: The most successful treatment for obstructive sleep apnea syndrome (OSAS) is nasal continuous positive airway pressure (nCPAP). Consistent use of this effective treatment is impeded by mask discomfort, cumbersome equipment, and chronic disease-related issues. While telemedicine has been effective for managing other chronic diseases, it has never been applied to the management of patients with OSAS who use nCPAP. We hypothesized that telemedicine could be used to modify health care behaviors that increase the use of nCPAP and improve functional status and self-confidence among patients with OSAS.
Methods: 27 CPAP-naïve patients were randomly assigned to either a telemedicine or traditional group to compare the duration and frequency of nCPAP use over one month. In addition, change in functional status from nCPAP use was measured using the Modified Functional Outcomes of Sleepiness Questionnaire (MFOSQ) and the General Perceived Self-efficacy Scale (GSES) was used to measure differences in self-confidence between groups.
Results: The duration of nCPAP use was not significantly different between the traditional care group (median 4.8 hours/day, range 0.2 to 7.9) and the telemedicine group (median 3.7 hours/day, range 0.6 to 5.5), p = 0.88. The frequency of nCPAP used for at least 4 hours/day was not significantly different between groups (traditional group median 33%, range 0 to 100%; telemedicine median 37%, range 0 to 72%), p = 0.97. The change in functional status was not significantly different between the traditional care group (median score of 3.0, range -6.0 to 19.0) and the telemedicine group (median 1.5, range –4.0 to 10.0), p = 0.58. The change in self-confidence was not significantly different between the traditional care group (median of 0.0 range –4.0 to 10.0) and the telemedicine group (median 0.5, range –3.0 to 8.0), p = 0.98.
Conclusions: Telemedicine made no difference in nCPAP use, change in functional status, or self-confidence in this group of patients with OSAS. Our data suggest that telemedicine alone is not sufficient to assist patients with the consistent use of nCPAP.

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0662.J

Effect Of Self-Regulation And Self-Monitoring On CPAP Adherence In Obstructive Sleep Apnea (OSA)
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Introduction: Self-monitoring has been shown to increase adherence to chronic treatment regimens in areas such as weight control and smoking cessation, and is one aspect of behavioral self-regulation. A four-phase cognitive-behavioral model of self-regulation (disease symptom avoidance, disease acceptance, disease compliance, and disease self-regulation in sequentially improving order) has been shown to predict treatment adherence in children with chronic asthma. The purpose of this study was to test the hypothesis that self-monitoring of CPAP use and/or greater self-regulation would improve CPAP adherence in patients with OSA.
Methods: Patients newly diagnosed with OSA in the Columbia University Sleep and Ventilatory Disorders Laboratory were prescribed their successfully titrated levels of CPAP using a machine which monitored time at the prescribed pressure (ResMed, Elite), then randomly assigned to either a self-monitoring (S) or non-self-monitoring (NS) condition. The S group was asked to record nightly CPAP use from the machine on provided recording forms. The NS group received identical clinical instruction and counseling, but not asked to self-monitor. All subjects were aware that their objective use of CPAP would be downloaded and analyzed. Phase of OSA self-regulation at 30-day follow-up was assessed by analysis of responses to a qualitative research instrument, the OSA Self-Regulatory Development Interview (OSASRDI). Data were analyzed using a general linear model of regression. A significance level of alpha = .05 was used for all statistical tests.
Results: Seven of the S group and nine of the NS group presented for 30-day follow-up. There were no significant differences between the two groups in age, gender, ethnicity, nadir SaO2, CPAP level, whether another adult lived in the household, whether a humidifier had been prescribed, or self-regulation phase. However, the S group had a significantly higher apnea-hyponea index than the NS group (67.1 versus 34.8, p=.019). At 30-day follow-up, there were no significant differences for S vs NS in percentage days CPAP use (76.3% versus 73.1%, p=.840), mean usage over the 30 day period (4.3 versus 3.4 hours, p=.502) or mean usage on the days CPAP was actually used (5.4 versus 4.4 hours, p=.277). However, differences in self-regulatory phase at 30-day follow-up accounted for a significant percentage of the variation in percent days CPAP use (43.3%, p=.033), with those participants who were at the OSA avoidance phase using CPAP for significantly fewer of the 30 days than those at the OSA compliance phase (24.6% versus 76.7%, p=.035), or those at the OSA self-regulation phase (24.6% versus 83.0%, p=.008).
Conclusions: OSA patients who are further advanced in their self-regulatory behavior appear more likely to be more adherent with CPAP than those less self-regulatory. Self-monitoring, as one component of self-regulation, may not be sufficient in this setting to improve CPAP adher-

ence. We speculate that strategies to improve self-regulation may potentially improve CPAP adherence in patients with OSA.

0663.J

Duty Cycle Responses to Upper Airway Obstruction in Normal and Apneic Individuals

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Introduction: We developed a challenge test during sleep to define compensatory responses of the respiratory pattern control to experimental induced upper airway obstruction. We hypothesized that upper airway obstruction leads to a compensatory increase in the duty cycle and that this response is similar between normal and apneic individuals.
Methods: Weight matched 13 normal subjects (7 female, 6 male, mean age 37.6 ± 16.6 years, BMI 29.7 ± 6.0kg/m2, and 13 apneic patients (7 female, 4 male, mean age 48.5 ± 10.0 years, BMI 26.8 ± 5.4kg/m2 initiated sleep with a nasal pressure that was initially set at a pressure that abolished inspiratory flow limitation (baseline). During stable NREM sleep, nasal pressure was then reduced intermittently by steps of 2 cmH2O for five breaths until maximal inspiratory airflow declined to 0-50 ml/s. Pressure steps with moderate upper airway obstruction were defined as flow limitation with inspiratory flows between 100 to 200 ml/s in each subject were then taken to determine duty cycle responses to upper airway obstruction.
Results: In the normal individuals, duty cycle increased from 0.38 ± 0.05 to 0.51 ± 0.06 and in apneic patients from 0.40 (SD: 0.03) to 0.51 (SD: 0.04), baseline vs. upper airway obstruction, respectively, (P<0.05). Similarly, the mean increase was comparable in both groups (0.12 ± 0.03 vs, 0.13 ± 0.06, normals vs apneics, respectively). The duty cycle responses were similar over the course of a step in nasal pressure on breaths 2 and 4, indicating that duty cycle increases are an immediate compensatory response to upper airway obstruction.
Conclusions: We conclude that upper airway obstruction leads to an immediate compensatory increase in the duty cycle and that this compensatory response is similar between normal and apneic individuals. Our findings indicate that increases in the duty cycle is a hallmark of flow limited breaths and imply that the prolongation of the duty cycle may be used for better discrimination of flow limited from non flow limited breaths.

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0664.J

Cerebral Atherosclerosis in Sleep Disordered Breathing

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Introduction: Epidemiological and clinical studies have shown a strong association between sleep disordered breathing (SDB) and cerebrovascular disease. It has been suggested that,this link between SDB and cerebrovascular disease could be due to at least in part to an increase in the progression of the atherosclerosis process at the level of cerebral arteries. The aim of our study was to investigate atherosclerotic degeneration at the level of carotid arteries in subjects with SDB to evaluate whether is there link between OSAS severity and atherosclerosis.
Methods: We studied 114 consecutive male patients between 40-65 years old, referred to our sleep laboratory for the evaluation of snoring or daytime sleepiness. Subjects were examined with a standard protocol that included an interview, clinical examination, polysomnographic and ultrasonongraphic evaluation. Major vascular risk factors such as hypertension, diabetes, smoking, hyperlipidemia and obesity were determined. Subjects were divided into 3 groups; habitual snoring, mild-moderate OSAS, and severe OSAS respectively, determined by using three respiratory disturbance index (RDI) cut points: 0-5, 6-29.9 and more than 30. Measurement of intima-media thickness (IMT) and the presence of plaque was determined by ultrasonongraphic evaluation. Analysis of variance with post-hoc comparisons (Tukey HSD) was used to determine whether demographic, polysomnographic, clinical and ultrasonographic data variables varied across the RDI categories. Categorical data were analyzed with the chi-square test. For a group as a whole, multiple linear and logistic regression analysis were performed to identify demographic, clinical and polysomnographic predictors of IMT and plaque. Variables entered in equations included, age, BMI, hypertension, diabetes, smoking, total cholesterol level, total triglyceride level, RDI and minimum oxygen saturation
Results: OSAS groups had significantly higher IMT values compared to the habitual snoring group (F=12,08, p<0.001). Three groups were significantly different with regard to prevalence of plaque (p<0.001). The age and BMI were found to be significantly associated with IMT (Beta=0.02, p < 0.005 and Beta=0.03, p<0.05 respectively) while age and RDI were found to be most likely predictors of plaque (B=0.08, p<0.05 and B=0.04,p<0.05 respectively). There were no significant differences between three groups with respect to age, prevalence of hypertension, diabetes, smoking, total cholesterol and total triglyceride levels. Three groups were significantly different in BMI and duration of sleep related breathing disorder,(F= 5,43 p<0,05 F=14,83 p<0,001 respectively). Post hoc testings revealed that severe OSAS group had significantly higher BMI than habitual snoring and mild-moderate OSAS groups and two OSAS groups had significantly longer duration of sleep related breathing disorder than habitual snoring group.
Conclusions: Our findings suggest that there is dose-response relationship between the severity of sleep-disordered breathing and the IMT and the prevelance of stenooclusive lesions. OSAS predispose an atherosclerosis process in OSAS patients and precipitate stenooclusive lesions particularly when associated with higher RDI.

0665.J

Retinal Vascular Changes in Obstructive Sleep Apnea Syndrome

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Introduction: The obstructive sleep apnea syndrome (OSAS) manifests with repetitive partial or complete upper airway occlusions with consequent fragmentation of sleep and arterial oxygen desaturations. Common complications include but are not limited to hypertension, myocardial infarction, stroke and motor vehicle accidents. Less well acknowledged are ophthalmologic associations with OSAS. Glaucoma (Mojon et al. 1999), optic neuropathy, papilledema (Wolin, 1995), floppy eyelid syndrome (McNab, 1997) and keratoconus are linked to OSAS. Recently, residents (KC) in the Ophthalmology clinic at Eastern Virginia Medical School noted retinal vascular tortuosity in patients with OSAS. Accordingly, the investigators initiated this study to investigate the prevalence of such changes in OSAS and postulate as to the etiology.
Methods: Patients entered the study through the Sleep Disorders Center at Eastern Virginia Medical School and Sentara Norfolk General Hospital. Nocturnal polysomnography (PSG) followed the initial history and physical examination. PSG included EEG, EOG, chin, leg and intercostal EMG, EKG, pulse oximetry, Respitrace and nasal/oral thermistry. Technicians applied nasal CPAP during the second half of the study if patients met specific criteria indicative of at least moderate OSAS. Experienced technicians scored PSG records. Board certified sleep specialists, who reviewed all studies, recruited patients (with and without OSAS) during their follow-up office visit. Exclusion criteria included sickle cell disease, history of retinal vein occlusions, history of chronic obstructive pulmonary disease and retinopathy of prematurity. An ophthalmologist,

blinded to the sleep study results, evaluated all patients agreeing to the study. The ophthalmologic exam included visual acuity, slit-lamp exam, applanation tonometry, dilated fundus exam and fundus photography.
Results: Forty-two patients completed the study (30 males and 12 females). Mean age was 53 ± 9.8 with mean BMI 36.1 ± 8.5 kg/m2. The mean respiratory disturbance index was 44.2 ± 30.5. Six subjects demonstrated evidence of retinal vascular tortuosity. The majority had diabetes and or a family history of diabetes.
Conclusions: Fourteen percent of this patient population manifested retinal vascular tortuosity. OSAS is associated with increased sympathetic activation. We hypothesize that sympathetic over activity leads to vasoconstriction and kinking of the retinal vessels. Tortuous vessels would be manifest due to multiple kinks in the vessel. In addition, diabetics are known to have loss of pericytes in diabetic vascular disease. Pericytes aid in the support of the vessel. Diabetics with OSAS demonstrated the vascular findings in this study and thus perhaps a combination of loss of supporting pericytes and recurrent vasoconstriction caused the retinal tortuosity. It is of interest that recent work has demonstrated insulin resistance in OSAS. Perhaps larger studies will reveal the above retinal vascular changes in those with OSAS but without diabetes.

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0666.J

Agreement Between A Portable Apnea Monitor and Gold Standard Polysomnography

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Introduction: Polysomnography (PSG) is the standard diagnostic test for measuring sleep apnea severity, requiring a laboratory night monitored by highly trained technicians making PSG expensive and inconvenient. An alternative is portable diagnostic units with home monitoring. Patients attach the sensors themselves at home and data is downloaded upon return to the lab. In this study, we contrasted the performance of one such portable unit (Autoset PDS using its automatic computer scoring) against polysomnography.
Methods: Subjects were brought into the lab for two nights. On night 1, technologists fastened the subject to the portable unit. This model measured airflow through a cannula, respiratory effort through a belt, and oxygen saturation with a finger probe. It also had a position sensor. The patient was monitored from 23:00 until 7:00. On night 2, technologists administered standard polysomnograph (PSG) for the same time period. For the PSG, hypopnea was defined as a decrease of airflow accompanied by a desaturation >3% and/or with an arousal. Bland and Altman analysis was used to assess agreement. Linear regression analysis was used to assess the relationship between portable monitor bias and true AHI. This relationship was visualized by plotting the difference scores against true AHI.
Results: The sample included 274 elderly individuals (29.7% M). The mean (SD) age was 70.7 (5.23) yrs (range 65 to 90). Based on PSG, 23.7%, 22.3% and 31.4% had AHI>=30, AHI 15-<30 and AHI 5-<15, respectively. The mean (SD; range) AHI for the portable monitor was 19.2 (15.8; 0 to 85.0) and for PSG it was 20.1 (18.9; 0 to 87.9). The mean (SD; range) difference was -0.9 (13.9; -61.0 to 63.9). 95% of the differences are estimated to from -28.7 to 26.9. The prediction equation for the expected difference is: E(difference) = –0.843 – 0.424 times (AHI minus 20.1)with SD around the regression line of 11.4 and r-square equal to 0.33. The estimated difference (i.e., bias) when the true AHI was equal to its mean was -0.843 (p=0.222). However, bias was significantly negatively associated (p<0.0001) with AHI resulting in large positive expected differences for low AHI and large negative expected differences for high AHI.
Conclusions: While the overall estimated difference was small, there was large variability among the differences. Moreover, for this study, there was a systematic bias such that the portable system overestimated AHI at low levels but underestimated AHI at high levels. We note that tests were performed on consecutive nights so that some of the observed variability between PSG and the portable unit reflects the known night to night variability in AHI. Whether the observed bias is the result of different transducer systems or from the nature of the automatic computer scoring is unknown and will be the subject of further investigation.

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0667.J

Gamma-Delta T Cells in Obstructive Sleep Apnea Syndrome - Implications to the Development of Cardiovascular Pathology

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Introduction: Obstructive sleep apnea syndrome (OSA) which is strongly associated with cardiovascular morbidity has also been shown to be associated with increased oxidative stress and a state of inflammatory cell activation. It has been suggested that the apnea induced hypoxic stress in OSA initiates atherogenesis which eventually leads to cardiovascular disorders. The underlying mechanisms at the cellular and molecular levels are yet to be elucidated. Hypoxia induced monocyte dysfunction was implicated in the pathogenesis of atherosclerosis in OSA. Thus, lymphocyte dysfunction could be implicated as well. Gamma-delta T cells' unique migration, cytotoxic features and accumulation in atherosclerotic plaques are considered critical in cardiovascular disorders. We assessed the potential involvement of circulating gamma-delta T lymphocytes in the pathogenesis of endothelial cell damage in OSA. Specifically, we determined the phenotype, cytokine profiles and interactions with human umbilical vein endothelial cells (HUVECs) in culture. These were investigated with a particular emphasis on adhesion and cytotoxicity.
Methods: Gamma-delta T cells were isolated by magnet separation from peripheral blood of 34 OSA patients and 19 controls. Intracellular cytokine content was analyzed by flow cytometry. Adhesion and cytotoxicity against HUVECs were assessed by 51Cr release assay.
Results: Intracellular content of the OSA gamma-delta T cells' cytokines TNF-alpha and IL-8 was increased as compared to controls (3.8-fold, p=0.0001 and 2.4 fold, p=0.003, respectively). The content of the inhibitory cytokine IL-10 was decreased in OSA gamma-delta T cells to 41.6% of control (p<0.01). Gamma-delta T- lymphocytes of OSA patients adhered significantly more avidly to non-stimulated HUVECs in culture than those of controls (adhesion index: 5.7±1.4 and 2.1±.4, p<.006, respectively). Anti-TNF-alpha antibodies decreased the adhesion index of OSA gamma-delta T cells binding by 53.3% (p=0.0002) but not of controls. Anti-IL-8 affected the adhesion index by 64.4% (p=0.0014) in OSA and by 45.5% (p= 0.05) in controls. The cytotoxicity of OSA gamma-delta T lymphocytes against HUVECs was 3-fold higher than controls. Pretreatment with anti-TNF-alpha prevented it. Moreover. preincubation of non-stimulated HUVECs with OSA gamma-delta T cells increased the adhesion of CD4+ and CD8+ lymphocytes to HUVECs.
Conclusions: OSA patients gamma-delta T cells are activated as compared to controls. This was manifested by increased production of TNF-alpha and IL-8 and a decrease in IL-10, and increased adhesion to and cytotoxicity against non-stimulated HUVECs. Collectively, these observations implicate gamma-delta T cells in initiating atherogenic sequela in OSA.

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0668.J

Correlates of Reported Breathing Pauses in Hmong Residents of Wisconsin

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Introduction: Hmong young and middle-aged adults, like other Southeast Asian groups, are at high risk for Sudden Unexplained Nocturnal Death Syndrome (SUNDS), a condition of unknown etiology. Hmong culture links SUNDS with the experience of tsog chuam, a nocturnal attack by a spirit that paralyzes the victim, crushes the chest and takes the breath away. The experience is suggestive of REM-related sleep disorders and sleep apnea, but the characteristics of sleep problems in Southeast Asians is unknown. The aim of our study was to investigate the correlates of sleep disorder symptoms in Hmong residents of Wisconsin.
Methods: A sample was identified from a statewide Hmong directory and sent a questionnaire on sleep habits, problems, and other factors (in English and Hmong) by mail. Logistic regression was used to model correlates of reporting breathing pauses during sleep a few nights or more/month.
Results: Thus far, 455 questionnaires have been successfully completed. The prevalence of habitual snoring (22%) was similar to that reported in other adult populations, but the prevalences of frequent (several nights/month) restless sleep (26%), cataplexy (10%), nightmares (15.4%) and potentially REM-related symptoms including sleep paralysis on wakening (7%) or sleep onset (8%), were high. The strongest predictors of reported breathing pauses (a few times/month or more vs. rarely or never) were the experience of a night-spirit crushing the chest (odds ratio=6.4, p<.0001) and sleep paralysis (odds ratio=5.5, p=.0002). Males were more likely to report breathing pauses, but the odds ratio was not statistically significant.
Conclusions: The data, although preliminary, suggest the sleep characteristics of Hmong differ from non-SE Asian populations, and that the tsog chuam experience often linked with SUNDS may be related to sleep-related breathing pauses.

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0669.J

Novel MR Cephalometric Techniques to Examine Craniofacial Differences in Men/Women and Normals/Apneics

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Introduction: We have developed novel MR cephalometric algorithms to examine upper airway craniofacial structure. We utilized these techniques to examine non-retrognathic (normal bite occlusion {CLASS I}) men and women in two subject groups: patients with obstructive sleep apnea and controls.
Methods: Patients with sleep apnea were required to have a RDI > 15 events/hour and normals had a RDI < 5 events/hour. Axial and sagittal T-1 weighted images were obtained with a 1.5 Tesla magnetic resonance scanner during wakefulness. Three-dimensional coordinates for craniofacial landmarks were identified using a validated software computer program (Volumetric Image Display Analysis {VIDA}). Linear distances and angular relationships were quantified mathematically. Our three-dimensional technique allows more precise spatial characterization of craniofacial structures than traditional two-dimensional radiograph cephalometry.
Results: We studied 69 subjects: 13 apneic males (age:42.9±10.3 yr, BMI:31.3±6.5 kg/m2, RDI:44.3±26.9 event/hr), 14 apneic females (age:47.4±9.2 yr, BMI:38.6±6.8 kg/m2, RDI:38.6±22.8 event/hr), 21 normal males (age:32.1±9.6 yr, BMI:25.0±4.0 kg/m2, RDI:1.8±1.5 event/hr), 21 normal females (age:37.8±12.1 yr, BMI:26.1±4.7 kg/m2, RDI:1.6±1.5 event/hr). We identified 97 craniofacial landmarks. Significant differences were found with mandibular shape measures and hyoid and C3 placement. Mandibular body length was significantly shorter in apneics when compared to controls (males: p<0.05; females: p<0.01), and was shorter in women for both groups (p<0.02). Mandibular body angle was significantly wider in apneics when compared to controls (p<0.01), and wider in males for both groups (p<0.01). C3-subspinale distance and C3-supramentale distance were significantly longer in apneics than controls (p<0.04), but not between genders. Nasion to sella to hyoid angle was significantly larger in apneic females when compared to control females (p<0.01) and apneic males (p<0.02), however, apneic males, control males and control females were not significantly different from each other. Sella to nasion to subspinale (SNA), sella to nasion to supramentale (SNB), and subspinale to nasion to supramentale (ANB) angles were not significant.
Conclusions: Through 3-D inspection, our novel MR cephalometric technique allows for more precise craniofacial morphologic determination than with conventional 2-D cephalometrics. Our data demonstrate a shorter mandibular body in apneics than controls, consistent with findings in the literature. We also demonstrate that apneics have a wider mandibular body angle than controls. Other purported apnea risk factors in the literature were not significantly different between apneics and normals in our study: SNA, SNB, and ANB angles. This may be due to our subject selection: non-retrognathic subjects with normal occlusions. However, our data demonstrated that apneics have shorter, wider mandibles and a relatively lower hyoid bone than controls. Males have longer, wider mandibles than females in both apneics and normals. Apneic males had the widest mandibles and apneic females had the shortest mandible bodies. Normal males had the longest mandible bodies and normal females had the smallest mandible body angles. These data suggest that MR cephalometrics are useful for examining craniofacial structures.

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0670.J

Automated Detection of OSA using Peripheral Arterial Tone: In-Lab Polysomnographic Validation on a VA Medical Center Population

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Introduction: Introduction: The VA Healthcare System must manage a growing number of veterans suffering from undiagnosed OSA. Ambulatory testing for sleep apnea has allowed our lab to reduce the long waiting list for the standard diagnostic test, attended polysomnography (PSG) within the sleep laboratory. Ideally, ambulatory testing should have adequate sensitivity and specificity to minimize the number of inconclusive tests requiring a follow-up PSG. The objective of the present study is to compare the accuracy of the Watch-PAT100 (WP100), a portable device based on Peripheral Arterial Tone (PAT), to detect respiratory events with the standard PSG.
Methods: Methods: We recruited eligible, consecutive patients referred for suspected OSA to the sleep laboratory. Subjects underwent an in-lab PSG with a simultaneous WP100 recording. PSGs were performed and sleep staged according to standard criteria. Respiratory events were scored according to AASM guidelines (1999) with the scorer blinded to the WP100 results. The WP100 recordings included the PAT signal, heart rate, oxygen saturation, and actigraphy. A PAT respiratory disturbance index (PRDI) was calculated using automated analysis of the WP100 signals. The unedited PRDI was then compared to the PSG-RDI

using linear regression and the receiver-operator characteristic (ROC) curve. Subjects with OSA were differentiated from non-OSA using a PSG-RDI of 10 events per hour of sleep to define the abnormal population for ROC curve analysis. We classified OSA severity in each subject as normal (PSG-RDI < 5, PRDI < 10), mild (5 < PSG-RDI < 20, 10 < PRDI < 20), moderate (20 < PSG-RDI and PRDI < 40), or severe (PSG-RDI and PRDI > 40).

Results: Results: The study consisted of 11 subjects, all men, age (64 ± 9 years), BMI (30.4 ± 5.0 kg m-2). Based on the PSG criteria above to classify OSA, the prevalence of OSA in the study population was 73%. PRDI (27.0 ± 21.9) measured with the WP100 correlated with PSG-RDI (23.7 ± 26.4) across a wide range of RDI values (R=0.96, p<0.0001). The area under the ROC curve for the PRDI was 0.93.. The severity of OSA was accurately classified by both methods in 10/11 cases (2 normal, 3 mild, 2 moderate, 3 severe). In one case classified as normal by PSG, the WP100 detected more respiratory events than the PSG. This case turned out to have upper airways resistance syndrome detected by Nasal cannula pressure transducer.

Conclusions: Conclusions: Based on these results, the WP100 accurately detects and quantify the degree of severity of OSA in a Veterans population. The WP100 device is simple to use and allows automated calculation of the RDI. The ability to discriminate wake from sleep (rest activity cycle) should reduce the number of false negatives associated with screening sleep tests.

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0671.J

Novel Airflow Sensor Demonstrates Linear Relationship With Pneumotachography

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Introduction: Polysomnographic airflow monitoring traditionally utilizes heat-sensitive sensors. Pressure-sensitive sensors attached to nasal prongs, which demonstrate a more sensitive response, have recently found favor in clinical practice. Both of these techniques, however, exhibit non-linear relationships with pneumotachography – the recognized standard airflow monitoring technique. We evaluated the peak flow and volume properties of a dual-microphone noise-canceling acoustic flow sensor (AFS) to determine the response relationship with pneumotachography using a published test methodology.

Methods: 10 healthy adults (mean age 38, range 23-56) underwent airflow monitoring with the NovaSomQSG acoustic airflow monitor with simultaneous pneumotachographic monitoring with the Hans Rudolph pneumotach system. Each subject produced three trains of 20 breaths wherein rates or volumes were independently varied from minimal to maximal, including the full range between these levels. Peak expiratory flow and signal integrated area under-the-curve (AUC) values for each expiratory phase of the respiratory cycle were calculated for the AFS airflow signal. Similarly, expiratory peak flow and expiratory flow volume for each respiratory cycle were calculated for the pneumotachograph signal. Peak flow and AUC/volume measurements were compared and correlation statistics generated for all respiratory cycles collected. A sub-analysis was performed on the range of flow rates and volumes expected during sleep, including those likely to occur with various sleep-related breathing disturbance syndromes ranging from mild to severe. The sub-analysis was necessary because a high frequency noise-reducing filter in the AFS limits its response at high flow rates.

Results: Of the 10 subjects, one was eliminated due to pneumotachograph mask incompatibility. Comparison of peak flow and AUC/volume responses between the AFS signal and the pneumotachograph signal in the remaining nine subjects revealed linear relationships through all flow rates and volumes captured with the exception of the highest possible peak flows due to the noise filtering function of the AFS. Correlation coefficients for peak flow: r = 0.77, r2 = 0.59 and AUC/volume: r = 0.91, r2 = 0.83. Analysis of signals from both sensors in the expected physiologic ranges of normal sleep-related breathing and SRBD breathing (including flow cessation, limitation, and recovery breathing) demonstrated a linear relationship with both peak flows and AUC/volume measures between the AFS and pneumotachography. Correlation coefficients for peak flow: r = 0.85, r2 = 0.73 and AUC/volume: r = 0.88, r2 = 0.78.

Conclusions: The AFS demonstrated a highly linear relationship versus pneumotachography for both peak respiratory flows and AUC/volume measures in this preliminary trial. Due to this linear relationship, we hypothesize that incorporation of this signal into nocturnal polysomnography could be useful in providing for a more accurate qualitative assessment of increments or decrements in airflow. Additionally, a linear relationship with pneumotachography becomes critical for any airflow signal incorporated into automated airflow change analysis systems, many of which have been, or are in development for SRBD syndrome evaluation.

0672.J

Long Term Outcome of Apnea Related Advanced A-V Block. Is the Treatment of Sleep Breathing Disorder (SDB) Enough to Control the A-V Block?

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Introduction: Introduction: In sleep studies performed to evaluate SDB, patients with severe bradyarrythmias, like advanced AV block, are often encountered. It has been mentioned in the literature that 1) bradyarrythmias respond effectively to positive pressure therapy (PPT) or other effective treatments for SDB, 2) A sinus pause of more than 5 seconds has been suggested as a criteria to choose pacemaker therapy, irrespective of the treatment, response or adherence to SDB therapy. The objective of this study was to find out if SDB related advanced A-V block would respond to apnea therapy and thus avoid a pacemaker.

Methods: Methods: Six patients were studied (5 consecutive new cases and one old case). All of these cases satisfied the criterion of having advanced A-V block (Mobitz II or 3rd degree AV Block) and significant sleep apnea. All of them had a PSG proven temporal association of the apneic events with the A-V Block.

Results: Results: All 6 patients were men, age 61years ± 15 [41-80], Epworth Sleepiness scale: 11. ± 6 [6-19], BMI: 39 ± 8[27.2-45.8], RDI 68 ± 53. [23-172] (1 case of central apnea, 1 case of obstructive and central apnea and 4 cases of obstructive apnea), lowest nocturnal oxygen saturation:70. % ±12% [60-90], length of sinus pause established by PSG or Holter Monitoring was 4.1 seconds ± 1.82 [3.1-7]. In 2 patients the apneas significantly improved with SBD therapy (one on CPAP and the other with tracheostomy), but the A-V block in REM sleep persisted in the follow- up sleep study. Two patients failed to tolerate PPT upon its first exposure and 2 patients abandoned PPT afterwards. Out of these six patients only one did not need pacer therapy. Of note, that patient is on one of the most modern BIPAP units. His AV Block responded significantly to PPT, as documented by telemetry and PSG.Despite what is published in the literature, the length of the sinus pause did not differentiate patients with reversible vs. non-reversible AV Block. In fact, the only responder to BIPAP therapy had the longest sinus pause (7 seconds).

Conclusions: Conclusions: We were able to avoid pacer therapy in only one of the six patients treated for apnea related advanced A-V Block. Although SDB responded either to PPT or tracheostomy, we were forced to prescribe pacer therapy in the majority of the patients. The acceptance to PPT is low in this population with SDB. There may be new features with modern PPT devices, which can help to improve the acceptance and tolerance of treatment. These patients should be followed closely to determine the optimum need for pacer therapy rather than reliance on

sinus pause length as the guide to therapy.

0673.J

Should Women with Obstructive Sleep Apnea Syndrome be Screened for Hypothyroidism?

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Introduction: Hypothyroidism has been considered a possible independent risk factor for the development of obstructive sleep apnea syndrome (OSAS). These considerations are based upon individual clinical observation and supportive pathophysiological changes known to occur in patients with hypothyroidism. Investigation of the prevalence of hypothyroidism in women with OSAS has not been undertaken. The aim of this study was to determine if there is a significant increase in prevalence of hypothyroidism in women with OSAS such that screening might be warranted.
Methods: Charts of all women undergoing polysomnography (PSG) at Duke University between January 1, 2000 and August 31, 2001 were reviewed. Women with a respiratory disturbance index (RDI) greater than or equal to 10 were included for further analysis. Those women with an RDI less than 10 but thought to have significant OSAS that needed treatment with continuous positive airway pressure (CPAP) were also included. Charts of these patients were reviewed to obtain demographic data, height and weight, and documentation of thyroid testing or evidence of treated hypothyroidism. Only thyroid stimulating hormone (TSH) and free thyroxine levels obtained within one year of the PSG were used for this study. Women without documented TSH values were excluded from the study. Patients with a TSH value greater than 5.66 mIU/L were considered to have hypothyroidism, as were those on thyroid supplementation. Demographic data of the euthyroid and hypothyroid groups were compared by using two-tailed Student's t-tests. Prevalence of hypothyroidism was calculated and compared to the prevalence of hypothyroidism in the Framingham study with a two-tailed Chi-square analysis.
Results: A total of 459 women were evaluated for OSAS in the time period specified. Of these, 118 patients had OSAS per PSG. Seventy-five of these patients had thyroid function testing completed within 1 year of polysomnography evaluation. The mean age, body mass index, and RDI in the euthyroid and hypothyroid groups were: 50.5 yrs, 35.7, and 37.3 vs. 57.0 yrs, 41.5, and 28.0, respectively. These were not significantly different. The prevalence of hypothyroidism in this population was 9.3% (7 of 75). The established prevalence of hypothyroidism in the general female population was determined to be 5.9% by the original cohort of the Framingham Study. No difference in prevalence (p=0.232) was observed when comparing these two study groups.
Conclusions: These data states that women diagnosed with OSAS without signs or symptoms of hypothyroidism would not benefit from hypothyroidism screening.

0674.J

Novel Airflow Sensor Provides Linear Measure Of Airflow In The Laboratory

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Introduction: Polysomnographic airflow monitoring traditionally utilizes heat-sensitive sensors. Pressure-sensitive sensors attached to nasal prongs, which demonstrate a more sensitive response, have recently found favor in clinical practice. Both of these techniques, however, exhibit non-linear relationships with pneumotachography – the recognized standard airflow monitoring technique. We evaluated the peak flow of a dual-microphone noise-canceling acoustic flow sensor (AFS) to determine the response relationship with pneumotachography using a published test methodology.
Methods: Airflow produced by an automated bellows system was monitored with the NovaSomQSG acoustic airflow monitor with simultaneous pneumotachographic monitoring with the Hans Rudolph pneumotach system. The bellows system produced series of five simulated fixed-volume breaths at variable levels of peak flow up to 69.1 L/min. Two hundred series were measured for a total of 1000 simulated breaths. Peak expiratory flow values for each respiratory cycle were calculated for both the AFS airflow signal and the pneumotachograph signal. Peak flow measurements were compared and correlation statistics generated for all respiratory cycles collected.
Results: Comparison of peak flow between the AFS signal and the pneumotachograph signal revealed linear relationships over the full range of peak flow levels. Correlation coefficients for peak flow: r = 0.99, r2 = 0.98.
Conclusions: The AFS demonstrated a highly linear relationship versus pneumotachography for peak respiratory flows. We do not know if the demonstrated linear relationship between the AFS and pneumotachography would occur in humans during sleep. If such a relationship were to be found, incorporation of this signal into nocturnal polysomnography could be useful in providing for a more accurate qualitative assessment of increments or decrements in airflow. Additionally, a linear relationship with pneumotachography becomes critical for any airflow signal incorporated into automated airflow change analysis systems, many of which have been, or are in development for SRBD syndrome evaluation. Further exploration of this signal during nocturnal polysomnography, in subjects suffering sleep-related breathing disturbance syndrome, is warranted.

0675.J

Central Sleep Apnea in Patients Receiving Narcotics for Chronic Pain VS Those not Receiving Narcotics

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Introduction: Increased risk for sleep-related central apnea has been demonstrated in stabilized methadone program patients1. This effect is compounded by midazolam2, and possibly other sedative hypnotics. The pathogenesis of these apneas is non-specific, and may include disturbances in regulatory activity related to medullary centers and brain stem structures, afferent influx to CNS, sleep stages, upper airways, lungs and respiratory muscles. The purpose of this study was to compare reasons for referral, sleep architecture, and sleep-related breathing parameters in stable-narcotic Pain Clinic patients with central sleep apnea vs non-narcotic patients with central sleep apnea.
Methods: 22 consecutive patients with a central apnea-hypopnea index greater than 10/hour of sleep were divided into two groups, those taking stable doses of a narcotic analgesics for chronic pain (n=11, mean age=47.1yrs, sd=13.1; 8M,3F) and those free of narcotic medications (n=11, mean age=58.2yrs, sd=4.8; 6M,5F). One sleep recording (C3A2 & C4A1, OzA2 EEG, right & left occulogram, submental EMG, EOG, right and left anterior tibialis, respiratory effort, airflow and oximetry) was performed on all subjects. The sleep studies were staged according to standard criteria of Rechtschaffen and Kales, 1968. T-tests were performed to examine differences in age, BMI, %stage 1, %stage 2, %SWS, %REM, sleep onset latency, sleep efficiency, RDI, obstructive apnea index, central apnea index, hypopnea index, movement arousal index, low SaO2, periodic leg movement index, and %alpha EEG during sleep. Chi-square analysis was performed on symptoms of apnea, insomnia, non-restorative sleep, and excessive daytime sleepiness.
Results: There were no significant differences between the two groups with regard to age, BMI, or any polysomnographic parameters. Signifi-

cant group-related differences were found for symptoms of apnea (Pain Clinic-narcotic=2/11, non-narcotic=7/11; p<.01) and insomnia symptoms (Pain Clinic-narcotic=8/11, non-narcotic=2/11; p<.01). There were no significant differences regarding symptoms of non-restorative sleep or daytime sleepiness.
Conclusions: Central apnea patients from Chronic Pain Clinics taking stable daily doses of narcotics are more likely referred for investigation of insomnia, as compared with patients from other medical clinics, who are referred for investigation of sleep-related respiratory symptoms. Further studies are required to determine the prevalence of sleep-related breathing disorder in patients who receive narcotic analgesics for chronic pain.

0676.J

CPAP Adherence: Experience of a CPAP Clinic in Low-Middle Class Patients of Mexico City

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Introduction: CPAP is to date the treatment of choice for most cases of OSA. Mexico has a limited social Security system, and often patients must purchase the device. We know the economical and social situation are important factors influencing adherence to treatment. The altitude of Mexico City conditions hypoxemia in some patients, Which adds supplementary oxygen to the cost of treatment. The aim of this study was to better determine what factors influence the initial adherence to treatment and the needed actions to be taken to improve treatment
Methods: All patients referred to the Sleep Clinic with a high clinical suspicion of OSA underwent either a polysomnography or a simplified respiratory study during the night (Snoresat). Those with a confirmed diagnosis who had daytime somnolence using the Epworth Sleepiness Scale > 7 points, and / or a cardiovascular risk factor or disorder, were elegible to initiate treatment with CPAP. CPAP titration was done at the sleep lab. 2-5 weeks after the sleep study was done, patients attended to the Sleep Clinic for the results. A 20 minute educative session about CPAP, was given to all patients. The clinic is open daily to all patients, to attend whenever they feel keen to. A follow-up visit was mandatory after one month, and 6 months. A questionnaire on the symptoms related to the use of CPAP was applied during all visits.
Results: 97 patients were recruited. The mean age was 50.3±12.2 years. Gender distribution was 28.8% females, 71.3% males.Mean weight was 94 /pm 18.6 Kg. The mean respiratory index (RI) was 75.4 /pm 38. Mean basal oxygen saturation was 84.7 /pm 12.9%, and 87.3 /pm 13% with CPAP. The average pressure level required to normalize the breathing pattern during sleep was 9.6 /pm 2.26 cmH2O. 33% of the patients required to add supplementary oxygen. Epworth Sleepines Scale before CPAP usage was on average 12±6.3, after one month of treatment it was 7.34 /pm 6.5. After one month only 48% returned to the clinic for a control visit. 16% directly purchased the device, 9% rented it, and 18% received it from the social security system. Only 10% returned to the CPAP Clinic after six months, all of them had bought it. We lost contact with the rest of the patients. In Mexico a CPAP device cost ison average $600.00 USD, and $80-100.00 USD for one month rent. The average annual salary of our group is $3,000.00 –5,000.00 USD. Patients admitted that the main reason for not using the CPAP was inability to pay for it, the second was dryness of the upper airway.
Conclusions: Less than half of low-middle class patients with OSA have a good adherence to CPAP treatment for OSA. The main reason being the high cost

0677.J

Physiologic Changes During Inspiratory Loading In Obstructive Sleep Apnea And Control Subjects

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Introduction: Evidence suggests that autonomic control mechanisms are impaired in obstructive sleep apnea (OSA) patients. Sympathetic outflow is elevated, heart rate responses to a Valsalva maneuver are impaired, and excessive bradycardia is found in a subset of patients to a cold pressor challenge. The nature of autonomic impairment in OSA, however, is unclear; questions remain whether the interaction between respiratory action and autonomic output are principally affected, whether deficits principally emerge in heart rate, or whether the major effects are exerted on blood pressure control. We examined beat-by-beat blood pressure and heart rate responses to a waking challenge that simulates aspects of OSA, inspiratory loading.
Methods: Twenty-one healthy male subjects and 21 OSA subjects were recruited. Procedures were conducted with the approval of the Institutional Review Board at the University of California at Los Angeles and with the informed written consent of the subjects. Subjects were excluded if they were taking cardiovascular medications or they breathed around the mouthpiece during the trial. Twelve control subjects and nine OSA subjects were used in the subsequent analysis. Continuous blood pressure measurements were obtained using a Colin 7000 monitor for six control subjects and four OSA subjects. Heart rate was determined from beat-to-beat intervals. Subjects breathed through a two-way nonrebreather respiratory valve while wearing nose clips. Subjects breathed through the mouthpiece for the duration of the trial while lying supine. Baseline physiologic measures were recorded for 60 s; recording continued during a 90 s period in which the inspiratory arm of the rebreather valve was partially occluded.
Results: Baseline blood pressure was higher in OSA cases (Mean baseline blood pressure Control: 87 $\pm$ 5 mm Hg, OSA: 95 $\pm$ 12 mm Hg). Blood pressure initially declined (by 6%) in Controls, and then rose by 4% by the end of the challenge. In OSA cases, blood pressure did not show the initial decline, but increased to the challenge by 6% twenty s into the challenge, and by the end of the challenge had increased to 13% over baseline. Heart rate increased similarly in controls (5%) and OSA (8%) compared to baseline, but the increase was earlier in OSA.
Conclusions: We conclude that blood pressure responses to a respiratory challenge that simulates aspects of airway obstruction are impaired in OSA, that the deficit appears to follow a two stage pattern, with the initial decline in blood pressure absent, and an enhanced long term component. The deficits likely develop from delayed neural responses in sympathetic control areas previously described in OSA cases. The absence of overall heart rate differences between groups may relate to preferential deficits in sympathetic over parasympathetic neural areas in the syndrome.

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0678.J

Blood Pressure Changes During Expiratory Loading in Obstructive Sleep Apnea and Control Subjects

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Introduction: Obstructive sleep apnea (OSA) occurs in 2-4% of the population and is associated with autonomic dysfunction, in addition to physical characteristics of obesity, small upper airway and hypertrophied tongue or tonsillar structures. Expiratory loading is an autonomic challenge that simulates an aspect of obstructive apnea, and cardiac responses of OSA patients and control subjects may help further define the nature of the disorder.

Methods: Eight OSA and six control subjects were recruited. Procedures were conducted with the approval of the Institutional Review Board at the University of California at Los Angeles and with the informed written consent of the subjects. Subjects lay supine and breathed through a mouthpiece connected to a two-way non-rebreather respiratory valve, with nose-clips blocking the nasal airway. Various physiologic signals were recorded: blood pressure was continuously monitored using a Colin 7000 monitor, thoracic wall movement using an air-filled bag strapped to the thoracic wall, and oxygen saturation using a Nonin oximeter. Expiratory load pressure was measured using a pressure transducer connected to the valve. All signals were digitized and stored on a laptop computer. Following 60 s of baseline recording, an expiratory loading challenge was applied for 90 s, during which the expiratory arm of the rebreather valve was restricted. Calibration signals for blood pressure and expiratory load pressure were generated immediately after the challenge, and used to calibrate these signals. Mean blood pressure was calculated by smoothing the continuous blood pressure signal over a 5 s window. Heart rate was calculated by applying a peak detection algorithm to the raw continuous blood pressure signal. Response relative to baseline and group differences were assessed for statistical significance using repeated measures ANOVA.
Results: Average blood pressure during baseline was higher in OSA (OSA = 95 mmHg, SD = 14 mmHg; control = 80 mmHg, SD = 8 mmHg), as was heart rate (OSA = 72 bpm, SD = 9 bpm; control = 65 bpm, SD = 12 bpm). During the expiratory loading challenge, subjects extended the duration of the expiratory phase of each breathing, taking from three to seven breaths during the 90 s challenge period. Load pressure generated during these expiratory phases was between 10 and 20 mmHg. Mean blood pressure increased in control subjects throughout the challenge to a level approximately 15% above baseline. However, OSA patients showed only a temporary, mild increase of approximately 5 %, and their BP was significantly lower than controls after the first 30 s of the challenge. When four OSA subjects who were taking cardiac-related medications were removed from the analyses, the results were unchanged.
Conclusions: OSA patients have autonomic deficiencies compared to normal, healthy control subjects, and these deficiencies are apparent in the response to expiratory loading.

Research supported by HL-60296

0679.J

Mood Predicts Response to Placebo Continuous Positive Airway Pressure

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Introduction: Continuous positive airway pressure (CPAP) therapy is an effective treatment for obstructive sleep apnea (OSA). However, some researchers have questioned the specificity of the CPAP effect, in light of beneficial effects of placebo CPAP (CPAP administered at subtherapeutic pressure). In this study, we investigated what baseline psychological factors were associated with beneficial effects from the placebo CPAP treatment.
Methods: Twenty-five subjects were studied with polysomnography at baseline and after treatment with placebo CPAP. Baseline mood was assessed with the Profile of Mood States (POMS). Total mood disturbance (POMS-Total) was obtained by summing the six POMS subscale scores, with Vigor weighted negatively. The dependent variable was ¡§change in respiratory disturbance index¡¨ (£GRDI), which was calculated by subtracting the Pre- from the Post-CPAP RDI. Negative values implied improvement. Hierarchical regression analysis was performed, with Pre-CPAP RDI added as a covariate to control for baseline OSA severity.
Results: POMS-Total at study entry was negatively associated with £GRDI (R2=0.434, F=5.361, p=0.007), meaning that patients with greater distress at baseline showed the best improvement in response to placebo CPAP. The High Distress group showed a 34% drop (i.e. improvement) in RDI.
Conclusions: Baseline emotional distress predicts the drop in RDI to placebo CPAP. Highly distressed patients show a greater placebo response. These findings underscore the importance of placebo-controlled studies of CPAP treatment.

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0680.J

Modafinil Adjunctive Therapy Improves Excessive Sleepiness and Quality of Life in Obstructive Sleep Apnea: A 12-Month Open-Label Extension Study

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Introduction: Obstructive sleep apnea (OSA) is a common cause of excessive sleepiness, which is associated with an increased risk of accidents and reduced quality of life. Standard treatment for OSA is nasal continuous positive airway pressure (nCPAP). Despite the effectiveness of nCPAP, some patients experience residual excessive sleepiness despite regular nCPAP use. The wake-promoting agent modafinil has been shown to significantly improve wakefulness during short-term and chronic (12-week) treatment in OSA patients who were regular users of nCPAP. This 12-month, open-label (OL) extension study evaluated modafinil for OSA patients with residual excessive sleepiness despite regular nCPAP use.
Methods: Following a 12-week randomized, double-blind, placebo-controlled, parallel-group study, patients were enrolled into a 12-month OL extension period. Patients entering the double-blind study had OSA and residual daytime sleepiness (Epworth Sleepiness Scale [ESS] score ≥10 at screening), were using a stable nCPAP regimen (for ≥4 weeks), and were regular (≥4 h/night on ≥70% of nights) or partial (<4 h/night on >30% of nights) users of nCPAP. Patients entering the OL study period completed ≥8 weeks of double-blind treatment and did not withdraw from the double-blind treatment period because of adverse events. All patients received 200 mg/d of modafinil for Week 1 of the OL period, 300 mg/d for Week 2, and 200, 300, or 400 mg/d thereafter. Sleepiness was assessed using the mean change in ESS scores at Months 3, 6, 9, and 12. Quality of life was assessed using the Functional Outcomes of Sleep Questionnaire (FOSQ) and the Short-Form 36 (SF-36) at Months 6 and 12.
Results: Of the 266 patients enrolled in the OL phase, 175 (66%) completed the 12-month OL treatment period. Modafinil significantly improved subjective sleepiness at all time points, as assessed with the ESS. Mean changes (±SD) in ESS scores from baseline (baseline score, 14.5±3.6) at Months 3, 6, 9, and 12 were –5.7±4.5, –5.3±4.4, –5.4±4.6, and –4.5±4.7, respectively (P<.0001). Modafinil also significantly improved quality of life, as shown by total score on the FOSQ and mental and physical component scales of the SF-36 (P<.01). Long-term modafinil treatment was well tolerated. The most frequently reported treatment-emergent adverse events were infection (11%), nervousness (9%), headache (9%), accidental injury (8%), sinusitis (7%), rhinitis (7%), depression and anxiety (6% each), and insomnia and dizziness (5% each); most adverse events were mild or moderate in severity. Modafinil did not adversely affect clinical laboratory, ECG, or physical examination findings or vital signs.

Conclusions: Modafinil decreased subjective sleepiness and improved quality of life during 12 months of OL treatment in patients with OSA who experienced residual sleepiness despite regular nCPAP therapy. Long-term modafinil therapy was well tolerated.

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0681.J

Epworth Sleepiness Scale does not Predict Sleep-Disordered Breathing in a Community-Based Population

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Introduction: The Skaraborg Hypertension Project comprises a community-based sample of 940 patients with hypertension and a random sample of the population (n=1,109, 80% participation rate) in Skara, Sweden. The surveillance included assessment of CVD risk factors, gene typing, sleep, QoL and other health related measures. In a nested case-control study 100 men and 100 women with hypertension and equal numbers of normotensive subjects were selected for a standard polysomnography (ambulatory recordings). The current study aimed to evaluate how well Epworth Sleepiness Scale (ESS) predicts sleep-disordered breathing (SDB) in a community-based sample with/without hypertension.
Methods: Subjects with a total sleep time of at least four hours at the investigation night (n=322; 160 men, 162 women, 44% hypertensives, mean age 61.0±6.5 years, mean body-mass-index [BMI] 28.5±4.8 kg/m2) were included in the analysis.
Results: Mean apnea-hypopnea index (AHI) was 25.1±23.3 (assessment by nasal pressure), mean oxygen desaturation index (ODI) 14.0±15.9 and mean ESS score 5.9±3.6 in the whole population. Excess sleepiness (ESS score >10) was prevalent in 36 subjects (11.2%). In a multiple logistic regression model, age, male gender and BMI predicted SDB (AHI >20/h) but excess sleepiness did not. In cases with more severe SDB (n=91, AHI >30/h, mean AHI 55.6±20.7) only 7 reported excess sleepiness (7.7%). No significant relationship was found between ESS score and AHI or ODI. The results were similar in the hypertensive and normotensive subgroups.
Conclusions: ESS was not a useful tool for prediction of SDB in a community-based sample of hypertensives and random sample of normotensive controls.

0682.J

Diagnosis of Obstructive Sleep Apnea Syndrome in a General Population Using an Automatic Ambulatory Device for Home Recordings

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Introduction: Ambulatory devices for the diagnosis of obstructive sleep apnea (OSA) are widely used but their accuracy has been questioned. The Watch_PAT100 device is a 4-channel wrist-worn device, based on the fingertip Peripheral Arterial Tone (PAT) signal, and addition, pulse rate, pulse oximeter and a built-in actigraphy. This device uses automatic algorithms to detect respiratory events (Apnea/Hypopnea and Respiratory Effort Related Arousal (RERA), without specific distinction), and identifies sleep-wake states. The accuracy of the respiratory event detection and the sleep-wake analysis of the device was assessed by comparison of this device with simultaneously recorded full polysomnography (PSG) in the home environment.
Methods: Ninety-seven subjects (63 male, age 60 ± 6.5 years, BMI 28 ± 4.2 kg/m2) from the Skaraborg Sleep Study project (general population cohort of 400 subjects in Skara District, Sweden) underwent unattended-home simultaneous recording with the device and full PSG. The device recordings were automatically analyzed for respiratory events and sleep-wake state. The PSG data were manually scored using standard criteria, and respiratory events, including RERA, were assessed according to the recommendations of the ASDA (1999). The respiratory disturbance index (RDI) of the device (PRDI) was compared with the RDI obtained by PSG (PSG-RDI). Area under the receiver operator characteristic (ROC) curves for three different PSG-RDI thresholds were calculated. Scored actual sleep times (device versus PSG) were compared and an agreement analysis between the device and the PSG was performed for sleep time based on 30 second bins.
Results: The range of the PSG-RDI was 0-124 events/hr. Sleep apnea was very prevalent in this sample but the majority of subjects (59%) had a PSG-RDI below 30 events / hour. The PRDI was highly correlated to PSG-RDI ($r=0.85$, $p<0.0001$), and the areas under the receiver operator characteristic (ROC) curves were 0.91, 0.87 and 0.87 for PSG-RDI thresholds of 10, 15 and 20, respectively (for all $p<0.0001$). The mean sleep times assessed by the device and the PSG were 86±5.5 and 81±7.7%, respectively, and the mean absolute difference between assessments was 6 ± 7%. The agreement of sleep times between the two systems in 30 seconds bins was 86%.
Conclusions: The Watch_PAT100 provided acceptable accuracy for unattended-home diagnosis of OSA in this unselected population sample. It is likely that not only an accurate detection of respiratory events but also reasonable identification of sleep time contributed to the performance of the device.

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0683.J

Evaluation of Pharyngeal Airway Dimensions with Three Dimensions Computer Tomography and Pharyngeal Echo in Patients Treated with an Adjustable Dental Appliance for Obstructive Sleep Apnea Syndrome

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Introduction: Tho goals of this study was evaluating the clinical success and failure rates of the treatment ofObstructive Sleep Apnea Syndrome with adjustable dental appliance and compare the clinical data with the pharyngeal airway changes, measured objectively by3dimension computer tomography and pharyngeal echo.Forty consecutive patients wereselected(ages between 32 to 75who were referred to the Pain Center with a diagnosis of Obstructive Sleep Apnea, from an Accedited Sleep Disorders Center of Southern California who failed nasal CPAP treatment or primarily choose the dental appliance treatment. The gender distribution was 4 women and 36 men.
Methods: After a clinical evaluation, adjustable dental appliance(modifyed Herbst appliance) was made individually for every patients in the UCLA Dental Laboratory.The patients used at home with a dentist supervision and gradually advanced by millimeter by millimeter until they reached an optimum of 6 to 7 mm mandibular advancement.Our clinical group evaluated the patients after a trial periode of using the device for a four week period.After four weeks every patients had a standard polysomnography at the SleepMed of California, Century City Hospital Sleep Center at the same designe: during the first half of the study without the debtal applinace,during the second half with the dental appliance in place.The polysomnography was repeated after 6 month

after a questionnaire was completed by the patients regarding the use, compliance of the device during the 6 months period. After the control polysomnography every patients were sent to an x-ray study and the airway dimensions were computed with three dimensuions computer tomography.At the samen week a pharyngeal echo study was done for every patients in the Pain Center.

Results: We found a 55% success rate using the dental appliance aned evaluating objectively ythe patients with polysomnography when the dental appliance was in place.Our criteria was, that the Respiratory Disturbance Index(RDI)should be below 10, and the Blood Oxygen Saturation more than 90 %.With using these criteria we found that the success rate was not related to the severity of the Obstructive Sleep Apnea. Among the patients who were improved were mild ,moderate and svere disease. The success and failure rate is related to the anatomic dimensions and pharyngeal airway volumes,especially the cross sectional airway changes behind the tongue.were

Conclusions: 1.Adjustable Dental Appliance is an excellent treatment alternative for patients who failed other treatments (i.e.nasal CPAP or upper airway surgeries).2.Objective evaluation of pharyngeal airway will predict the patients population who will benefit from this type of treatment.3.Compliance is improving with meticulous clinical follow up and control polysomnography.

0684.J

Predictors of Daytime Hypercapnia in OSA Patients with Normal Pulmonary Functions

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Introduction: Obstructive sleep apnea syndrome (OSAS) refers to the occurence of episodes of pharyngeal obstruction during sleep with fluctuations in nighttime blood gas composition. There is still conflicting data on the daytime blood gas composition. The aim of this study was to evaluate the predictors of daytime hypercapnia in OSA patients with normal pulmonary functions.

Methods: 133 patients who had been referred to Pulmonary Medicine Department suspected of having OSA enrolled the study. Each patient was assessed with arterial blood gas analysis, seated pulmonary function tests and full- night polysomnography. Demographic data of the patients (age, body mass index, tobacco comsumption), complaints on admission and Epworth sleepiness scale were recorded. Patients with underlying lung disease and congestive heart failure were excluded. The characteristics of groups according to daytime hypercapnia (PCO2>45 mmHg) were studied.

Results: Seven (5.3 %) patients with 'Pure OSAS' had daytime hypercapnia. The mean PCO2 level in hypercapnic patients was 50.8± 9.7 mmHg, while normocapnic patients had a mean PCO2 level of 38.0±2.7 mmHg. Pulmonary function tests were in normal range in both groups (Hypercapnic vs normocapnic): FEV1 97.0±15.8 % vs 104.4±14.9 %; FVC, 95.9±20.7 % vs 105.4±14.8 % and FEV1/VC was 80.4 ± 6.4 % vs 81.5± 6.3 %. Hypercapnic patients had an AHI of 44.5±32.5 (5.2-93.2), and normocapnic patients had an AHI of 32.6±26.4 (5.1- 103.2). BMI of hypercapnic group was 29.8±5.8 kg/m2 and was 30.3±4.8 kg/m2 in normocapnic patients. We found a positive correlation between neck circumference (hypercapnic: 41.9±4.6 cm vs 42±3.6 cm) and daytime pCO2 level. But there were no correlation between PCO2 and BMI. In multiple regression analysis the main predictors of daytime hypercapnia were AHI, FEV1 and lowest nocturnal oxygen saturation.

Conclusions: The mechanism of daytime alveolar hypoventilation in pure OSAS patients is still unknown. In this study we found that 5.3 % of pure OSAS patients with normal pulmonary function tests had daytime hypercapnia. AHI, FEV1 and lowest nocturnal oxygen saturation parameters were found to be important predictors of daytime hypercapnia.

0685.K

'Weak With Laughter': Emotional Or Respiratory Motor Inhibition?

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Introduction: Cataplexy, the hallmark symptom of narcolepsy, is characterized by a sudden loss of muscle control evoked by emotions, particularly laughter. It is thought to be due to supraspinal depression of spinal alpha motor neuron activity. Searching for a subclinical expression of cataplexy, we found a considerable decrease of H-reflex amplitude in both narcoleptics and controls when they laughed out loud. Our hypothesis prompted some researchers to propose an alternative explanation: the reflex depression occurring with laughter might be due to the respiratory movement of laughter rather than to its emotional content. In the present study, we compared the effects of laughter and a variety of respiratory movements on H-reflex depression, in an attempt to unravel their respective influences.

Methods: We measured H-reflexes in thirteen healthy volunteers (8 men, aged 18-35 years) during various conditions. During each task, 15 H-reflexes were evoked at a 2-second interval. Respiratory movements were recorded concomitantly. The subjects completed 10 different tasks, including a neutral task, laughter, simulated laughter and various in- and expiratory movements (with different depth and frequency). The mean H-reflex amplitude during each task was expressed as a percentage of the mean amplitude of the inital three H-reflexes (a low percentile value thus reflects a high degree of H-reflex depression). To quantify the effects of various conditions, we compared the percentual degree of H-reflex depression during each task with that during the neutral task. H-reflex percentages were compared using ANOVA for the neutral task, true laughter and simulated laughter, followed by paired t-tests in case of statistical significance ($p<0.05$). The effect of the remaining variables was assessed by comparing them with the neutral task using the paired t-test.

Results: H-reflex percentage differed between the neutral task (79.4 ± 4.5%), true laughter (43.7 ± 5.0%) and simulated laughter (66.6 ± 6.7%, $p<0.0005$), and between the two latter tasks ($p=0.01$). Single deep inspiratory and expiratory movements caused H-reflex percentage to remain significantly higher compared to the neutral task, or in other words prevented habituation. The factors depth and frequency did not have a significant effect on H-reflex percentage ($p=0.46$ and $p=0.88$ respectively), and neither did their interaction ($p=0.26$). Again, mean values during all four tasks tended to be higher than in the neutral task.

Conclusions: We conclude that laughter has a depressing effect on spinal motor neuron excitability, and suggest that this effect is exerted through two pathways. The main pathway concerns mirth -the emotional content of laughter- and the second is respiratory in nature. As such, our findings in normal healthy subjects parallel the situation in narcolepsy, in which cataplexy is never evoked by coughing, sneezing or straining, but requires an emotional charge, i.e., laughter. It is tempting to speculate that the suppressing effect of mirth we found in healthy subjects is also implicated in cataplexy.

0686.K

Food Consumption Patterns in Narcolepsy

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Introduction: With the discovery of hypocretin abnormalities in narcolepsy there is a new interest in appetite and food consumption patterns in people with this sleep disorder.

Methods: The three day food intake patterns of 22 people (13F, 9M, mean age= 53.3)with narcolepsy/cataplexy were compared to 20 age and socioeconomic status matched control participants (11F, 9M, mean age = 56.3). Details of all medication, food and drink intake were recorded, with particular attention to quantities. Scoring was 'blind'. Thirty minutes after each meal participants rated their level of hunger/satisfaction on a 5 point scale.
Results: A series of MANOVAs yielded the following results.(a) People with narcolepsy had a higher frequency of sweet and snack intake than controls. (b) Total kilojoule (KJ) and carbohydrate (CHO) consumption was significantly more for those with narcolepsy than controls. (c) KJ and CHO intake through meals was significantly higher in narcolepsy, but this difference was not significant for snack or drink consumption. (d) Increased CHO consumption with narcolepsy was found for lunch and dinner CHO, but not breakfast CHO. KJ intake showed a similar trend. (e) Those with narcolepsy taking stimulants (MedicN, n=10) had significantly more lunch CHO and KJ intake than the unmedicated (UnmedN) but no other differences were found.(f) Although a trend was found for people with narcolepsy to weigh more than controls, this did not attain significance. A significant correlation was found in the control group between hunger/satiety ratings and both lunch CHO and KJ, although no such correlations were found in the narcolepsy group.
Conclusions: People with narcolepsy were found to initiate sweet consumption and snacking behaviour more frequently than controls but did not consume more CHO or KJ through snacks than controls. Thus, the large intake of CHO through snacking that is reported in some obese people is not evident in this sample. More frequent sweet and snack consumption was not a consequence of stimulant medication, but may relate to the condition of narcolepsy itself. Those participants with narcolepsy clearly consumed more food overall than controls, with the main differences occurring in meal intake. A larger sample may show significant body weight differences between those with and without narcolepsy, as has been reported in the literature. The issue of whether satiety signals operate normally in narcolepsy may be worth pursuing, given the finding of group differences after lunch. Consideration of the mechanisms that may underlie some or all of the differences found include: appetite control abnormalities, metabolic rate differences (with both potentially related to the role of hypocretins), stress induced eating (eg from the need to maintain wakefulness), and blood sugar irregularities (as seen with the higher rate of diabetes in narcolepsy that has been argued to be independent of obesity). More research is required to tease out where robust group differences may lie.

0687.K

Atypical Presentations of Narcolepsy due to Dissociation of Activation of Centers Controlling REM related Behaviours
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Introduction: Introduction: The clinical and electrophysiological effects of cataplexy in patients with narcolepsy involve the inappropriate activation of centers controlling REM sleep in wakefulness. The usual pattern of activation of the REM centers leads to the EEG changes, concurrently with the atonia and phasic components. The dissociation of activation of these three components can lead to behavioural characteristics, which may lead to atypical presentations of narcolepsy.
Methods: Methods: This paper present the clinical examination, video recording and polysomnographic investigations performed on 3 patients with atypical presentations of narcolepsy. In first case, the clinical examination was performed during the period of status cataplexicus.
Results: Results: All three patients satisfied the clinical and laboratory criteria for narcolepsy including REM fractionation, short REM latency and pathological excessive daytime sleepiness during Multiple Sleep Latency Tests (MSLT). During the attacks of atypical cataplexy, one patient exhibited the phenomenon of prolonged cataplexy in the form of status cataplexicus with atonia, REM sleep without phasic components. The second patient demonstrated prolonged cataplexy with atonia but with the ability to maintain verbal communication and answer questions suggesting incomplete activation of the cortical components of REM sleep. The third patient presented with recurrent episodes of dysarthria without impaired consciousness. This is interpreted as a state of incomplete atonia with incomplete activation of the cortical component of REM sleep. This patient's episodic dysarthria responded to pharmacological treatment of cataplexy.
Conclusions: Conclusions: Cataplexy typically involves the activation of the three components of REM sleep concurrently resulting the classical clinical features of loss of awareness, loss of postural tone with phasic myoclonic components. This paper demonstrates that these mechanisms can become dissociated resulting in atypical and prolonged behaviour disturbances which may not trigger the clinical suspicion of a diagnosis of narcolepsy.

0688.K

Does Pupil Noise Discriminate Between Control and Sleep-Disordered Subjects?
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Introduction: Differences in pupil noise, i.e., fluctuations in pupil diameter caused by the Edinger-Westphal nucleus in response to light that putatively reflect level of sleepiness, recently have been reported to reliably (90%) discriminate between narcoleptic and control subjects, although earlier reports indicated mixed results in measuring sleepiness when the pupil light response (PLR) was recorded. The purpose of this study was to determine if these findings for the narcoleptic and control subjects could be replicated when the PLR methodology was used with three subject groups.
Methods: The sample consisted of 12 untreated narcoleptics (6 F & 6M, mean age=29.3) and 10 untreated OSAs (5 F & 5 M, mean age=36.8) diagnosed with PSG and MSLT, and 15 normal controls (7 F & 8 M, mean age=30.7) without clinical evidence of a sleep disorder. About 12 hours after their nighttime mid-sleep period, subjects participated in the pupillographic PLR test during which they were seated in a quiet, dark room in a lounge chair and instructed to try to minimize blinking while looking at a red dot. Pupil diameters were recorded at 256 Hz for 1 minute in response to pseudo-random light stimuli that varied in intensity from 0.3-3.7 foot-candles following 2 minutes of dark adaptation. Digitized horizontal pupil diameters were later cleaned of artifact and down-sampled to 16 Hz for further analyses. Since we were concerned here with relative changes in pupil diameter, and not differences in diameter among subjects, measurements were standardized for each subject. Standard z-scores were computed on the measured diameters and a linear transform was performed to eliminate negative values. Recursive least squares was used to estimate nonstationary moving average (MA) functions of pupil diameter as a function of light stimulus for each subject at six different time lags. An ARIMA time-series analysis was performed on each function to remove serial autocorrelation effects and obtain unbiased estimates of residual noise.
Results: Linear discriminant analyses was performed in an attempt to predict diagnostic group membership using these noise estimates as predictors. Results for discriminating among three groups resulted in the following correct classification rates: 8 of 15 control subjects, 6 of 12 narcoleptic subjects, and 7 of 10 OSA subjects. With narcoleptic and OSA subjects collapsed into a single sleep-disordered group, rates were: 11 of 15 control subjects and 13 of 22 SD subjects.
Conclusions: These results suggest that differences in residual pupil noise are not specific to narcolepsy, but may reflect differences generally applicable to persons experiencing EDS. At the present time, the discriminatory power of this approach is insufficiently specific to provide a useful screening tool. We are currently performing another study with

larger samples, using improved equipment which is capable of more accurate measurement. It is expected that data obtained will provide more conclusive evidence regarding the utility of this method.

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0689.K

Mucle Atonia In NREM Sleep (MAN) In Narcoleptics And Normal Controls

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Introduction: Narcolepsy is characterized by excessive daytime sleepiness and associated features such as cataplexy (CP), sleep paralysis (SP) and hypnagogic hallucination (HH). Entering sleep through REM sleep (SOREM) is an additional hallmark of narcolepsy. CP, SP, HH and SOREM are thought to result from inappropriate triggering of REM sleep. Nielsen postulated that covert REM sleep processes occur within nonREM sleep (Nielsen 2000). According to this hypothesis, muscle atonia in nonREM (MAN) sleep might represent a REM sleep equivalent (Werth et al. 2002). Here, MAN was studied in a selective REM sleep deprivation protocol in narcoleptics (NCs) and healthy controls (Cs).
Methods: Submental EMG recordings from a selective REM sleep deprivation study in narcoleptics and normal controls were analyzed (Hurni et al. 2000). The study includes habituation sleep, baseline sleep (B), two night of selective REM sleep deprivation and recovery sleep (R) from 6 patients with narcolepsy with cataplexy (NCs, age$\pm$SD, 29$\pm$3.7) and 6 healthy age-matched controls (Cs, 28$\pm$2.6). Polysomnographic recordings were obtained during sleep episodes, and sleep stages were scored according to standard criteria. MAN was identified using a threshold determined on EMG variance level in REM sleep. Epochs of MAN were defined when at least 75% of a 20s epoch was below the threshold. Atonia latency (AL) was defined as the first appearance of muscle atonia after sleep onset.
Results: Baseline: All NCs had SOREM with REM sleep latencies (RL) close to sleep onset (mean$\pm$SE, 0.0$\pm$0.0), whereas no SOREM was found in Cs (RL: 95.7$\pm$3.8). All NCs had AL below 15 min, whereas all Cs had AL > 15 min. The amount of REM sleep and MAN was similar in NCs and Cs. Recovery: All NCs showed SOREM (RL: 0.3$\pm$0.1), whereas no SOREM was found in Cs, however, RL was shorter than during baseline (RL: 61.4$\pm$0.4). All NCs and 2 out of 6 Cs had AL<15 min. A REM sleep rebound was present in NCs and in Cs. Compared to baseline the amount of MAN was increased in Cs but decreased in NCs.
Conclusions: We confirm that episodes of MAN may contribute to the compensation of a REM sleep deficit in normal subjects. This seems not to be the case in narcoleptics, where MAN -while being present at baseline- decreased after selective REM sleep deprivation. Our data suggest the possibility that the inappropriate triggering of REM sleep in narcoleptics (e.g. SOREM) may not be caused by an increased REM sleep propensity.

0690.K

Modafinil Improves Executive Function In Narcolepsy Patients With Excessive Sleepiness

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Introduction: Patients with excessive sleepiness associated with narcolepsy frequently experience cognitive impairment. The novel wake-promoting agent modafinil has been shown to improve wakefulness in patients with excessive sleepiness associated with narcolepsy, OSA despite regular nCPAP use, and shift work sleep disorder. Modafinil has also been shown to improve cognitive performance in models of acute sleep loss. In addition, in a randomized, placebo-controlled, double-blind imaging study, modafinil increased frontal cortex activity and improved working memory in a model of acute sleep loss. This randomized double-blind study evaluated the effects of modafinil on both cognitive function and wakefulness in narcolepsy patients.
Methods: Twenty-four patients with narcolepsy who experienced residual late-afternoon/evening sleepiness despite a satisfactory response to modafinil earlier in the day were included in this study. Following a 1-week placebo washout period, patients received double-blind treatment for 3 weeks with either modafinil 400 mg once daily (400 mg at 0700h and placebo at 1200h) or 600 mg as a split dose (400 mg at 0700h and 200 mg at 1200h). Cognition/executive function was assessed by changes from placebo baseline in the Wisconsin Card Sort Test (WCST) scores at Week 3. Wakefulness was assessed using a modified Maintenance of Wakefulness Test (MWT), consisting of 30-minute sessions every 2 hours from 0900h to 2100h.
Results: Both doses of modafinil improved cognitive performance/executive function, as shown by reductions in the total number of errors on the WCST at Week 3 versus placebo baseline ($P < .01$ for the 600 mg split-dose regimen). Modafinil 600 mg reduced total errors raw score on the WCST by 8.8 $\pm$ 9.4 ($P < .01$), whereas modafinil 400 mg reduced total errors raw score by 7.5 $\pm$ 16.6, compared with baseline. Similarly, modafinil 600 mg significantly reduced total errors raw percent scores on the WCST by 6.3 $\pm$ 7.0 ($P = .01$), whereas modafinil 400 mg reduced these scores by 5.5 $\pm$ 11.3 (P = NS). Both doses of modafinil significantly improved patients' ability to sustain wakefulness, as assessed by mean increases from baseline at Week 3 in MWT sleep latency of 10.7 $\pm$ 7.2 ($P < .001$) for modafinil 600 mg and 6.2 $\pm$ 6.6 ($P <.01$) for modafinil 400 mg. Modafinil was well tolerated. Adverse events included headache (n = 1), emotional lability (n =1), bronchitis (n = 1), and accidental injury (n = 2). The majority of adverse events were mild to moderate in severity, and no patients discontinued the study because of an adverse event.
Conclusions: Modafinil significantly improved executive function and wakefulness in patients with excessive sleepiness associated with narcolepsy. Modafinil was also well tolerated in this population of narcolepsy patients. Additional research should be done to characterize the effect of modafinil on cognition and executive function in other clinical models associated with excessive sleepiness.

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0691.K

Monozygotic DQB1*0602 Positive Twin Pair Concordant for Narcolepsy with Cataplexy and Normal CSF Orexin-A Levels

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Introduction: Only six monozygotic twins concordant for narcolepsy are reported in the literature. A detailed presentation of clinical, PSG and MLST finding is available in only two of these six twin pairs. Measures of CSF orexin-A were never tested before in narcoleptic twins. We report on clinical and laboratory features of a monozygotic twin pair concordant for narcolepsy with cataplexy.
Methods: At time of presentation the two female patients were 37 years-old and had never been treated for narcolepsy. Our assessment included clinical history, standard sleep questionnaire, structured neuropsychological and neuropsychiatric examinations, 1-week actigraphy, overnight polysomnography (PSG), multiple sleep latency test (MLST), HLA-typing, measurement of CSF orexin-A, and brain MRI scanning.
Results: Both sisters (ID and JD) worked as secretaries, were never separated in life, and lived together at time of presentation. In both of them past neurological history was unremarkable, neurological examination

and standard brain MRI were normal. In both sisters narcolepsy started around the age of 7-9 years with sleep paralysis and hypnagogic hallucinations. Full narcoleptic tetrade appeared in both sisters during adolescence, although excessive daytime sleepiness and sleep paralysis remained the most disabling symptoms. One sister (ID) was more severely affected, had a higher Epworth sleepiness score (17 vs 11) and a higher body mass index (28 vs 24). Clear-cut (definite) cataplexy provoked by laughter or strong fear was reported by both sisters to occur less than weekly. Mean sleep latency on MSLT was 4.4 min (ID) and 5 min (JD), respectively. Only one sister (ID) had sleep onset REM periods occuring in nap 4 and nap 5. Both sisters were positive for the narcoleptic HLA-markers DQB1*0602, DQA1*0102, DRB1*15, DRB5* and had normal CSF-orexin levels (546 pg/ml and 530 pg/ml, respectively).

Conclusions: We present a monozygotic twin pair concordant for narcolepsy with cataplexy that is positive for DQB1*0602, DQA1*0102, DRB1*15, DRB5* but had normal CSF orexin-A levels. This unique observation demonstrates the existence of genetically determined narcolepsy with cataplexy not associated with a CSF-orexin deficiency.

0692.K

Exploring the Cytokine and Endocrine Involvement in Narcolepsy

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Introduction: Narcolepsy is a disabling neurological sleep disorder characterized by excessive daytime sleepiness and abnormal REM sleep manifestations. A genetic predisposition with HLA DQB1*0602 has been identified as well as a strong association with absent or abnormally low levels of the neuropeptide, hypocretin. It is thought that narcolepsy is resultant from the destruction and depletion of hypocretin. Recently, the role of cytokines in the regulation of sleep and narcolepsy has been considered, and data suggest that proinflammatory cytokines may be involved in sleep and narcoleptic symptoms. For example, tumor necrosis factor-a (TNF-a) and Interleukin-1 (IL-1) are involved in regulating sleep and they have been shown to increase the amount and intensity of slow wave sleep (SWS). Similarly, data suggests that interleukin-6 (IL-6) may be related to sleep and sleepiness in man. In addition to cytokine involvement in sleep, the role of Growth Hormone has been shown to have temporal associations with SWS epochs and, like IL-1, it is involved in sleep-wake regulation.

Methods: Serum and clinical data were obtained from the Stanford Center for Narcolepsy Research for 40 Narcoleptics (22 Females, 17 Males, age 39 ± 14.9) and 40 controls (12 Females, 27 Males, age 46 ± 17.9). Plasma levels of TNF-a, IL-6 and GH were measured by ELISA.

Results: TNF-a showed a significant increase in narcoleptic subjects, ($p = 0.03$), while IL-6 showed a trend toward elevated levels in narcoleptics, ($p = 0.07$). Interestingly, GH was significantly increased in narcoleptic subjects, ($p < 0.0001$). There was also a significant difference in the ESS (18.03 ± 4.2 vs. 5.13 ± 3.0, $p < 0.0001$). Additionally, more narcoleptics are HLA+ than controls (24 vs. 6).

Conclusions: Narcoleptics, relative to controls, had higher serum levels of TNF-a, IL-6, and GH. Although this was a convenience sample, there are several implications this research acknowledges. First, the dysregulation of sleep observed in narcoleptics correlates with the immune and endocrine dysregulation seen in these subjects. Moreover, the observed changes may in fact contribute to the higher likelihood of disturbed sleep and/or increased incidence of infection. The cytokine and GH alterations may be explanatory variables for the diverse variations seen in narcoleptic sleep patterns. It is well established that narcoleptics have fragmented sleep architecture with non-normal SWS patterns in the first third of the night, often accompanied by frequent daytime naps. The shortened REM latency may contribute to the altered levels of cytokines and GH observed since IL-6 is secreted during Stage 1 & 2, and REM sleep, and GH secretion is associated with SWS. A possible explanation of the extreme levels of GH may be a result of the additional SWS acquired via the frequent daytime naps. This may also lend an explanation to the elevated levels of TNF-a and IL-6.

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0693.K

A Comparison of Psychosocial Impact: Narcolepsy, Obstructive Sleep Apnea, and Idiopathic Hypersomnia

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Introduction: Diseases associated with excessive daytime sleepiness (EDS) have significant impact on psychosocial functioning. We compared psychosocial impairment in patients with narcolepsy (Narc), idiopathic hypersomnia (IH) and obstructive sleep apnea (OSA). We also tested the hypothesis that age of onset mediates the disruptive effects of these disorders.

Methods: The data was gathered by a questionnaire survey in randomly selected patients from each disease category. The questionnaire included approximately fifty targeted (mostly Yes/No) and seven open-ended questions. We received responses from: 20 patients with narcolepsy, 12 with IH, and 21 with OSA. Between-group differences on each of the closed-ended questions were analyzed using 2-sided Pearson Chi-square tests. First, we tested for overall differences between the three diagnostic groups. To test the mediation hypothesis, the questions that showed significant between-group differences were reanalyzed using hierarchical logistic regression. Age of onset (measured as a continuous, ordinal variable with 4 levels) was entered at Step 1 and the diagnostic group was entered at Step 2. The mediation hypothesis was supported if the age of onset significantly predicted the dependent variable and if its inclusion reduced or eliminated the significance of the diagnostic group.

Results: Our findings included: • Job loss due to EDS – Narc 25% - IH 0% - OSA 0% (P<.05) • Reduced job performance (EDS) – Narc 85% - IH 75% - OSA 47% (P<.05) • Illness started in childhood – Narc 55% - IH 42% - OSA 10% (P<.01) • Problems with teachers (EDS) – Narc 65% - IH 36% - OSA 15% (P< .01) • EDS/embarrassment in class – Narc 69% - IH 67% - OSA 11% (P<.001) • Poor grades in school – Narc 67% - IH 64% - OSA 22% (P<.05) • Married – Narc 47% - IH 81% - OSA 67% (P=.08) • Disturbed parent-child relationship – Narc 71% - IH 36% - OSA 25% (P<.05) • Experienced depression – Narc 74% - IH 50% - OSA 35% (P = .05)Occupational problems did not significantly differ regarding rates of present employment in narcolepsy (45%) and OSA (48%) however, 83% of patients with IH were currently employed.

Conclusions: Narcolepsy patients had significantly more abnormal psychosocial profiles when compared to patients with OSA. Patients with IH differed from the other groups only in their greater likelihood of being employed and their increased likelihood of suffering embarrassment and poor grades in school (compared to OSA). The mediation of the effect of age of onset was supported for 7 of 13 variables: problems with teachers, embarrassment in class, poor grades, marriage / children and considering suicide. An earlier age of onset was associated with greater impairment.

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0694.K

Narcolepsy - A Survey of UK Clinical Practice

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Introduction: Many clinicians encounter problems in diagnosing and managing a condition as infrequent and variable in its presentation as narcolepsy. This situation is compounded in the UK by the tendency for patients to be managed by a variety of specialists. The objective of this survey, therefore, was to gather information on diagnostic and management practices among clinicians involved in the care of patients with narcolepsy within the UK.
Methods: This 23-question survey was sent to 120 UK clinicians (mainly neurologists, respiratory physicians and psychiatrists) known to have experience in the management of narcolepsy. The questions addressed issues of diagnosis and referral patterns (3 questions), patient numbers (3), preferred treatment options and dosages (4), assessment criteria for success or failure of treatment (3), success or failure rates for specific treatments (5), reasons and strategies for switching treatments (4) and other areas of related experience (1).
Results: Responses were received from 46 of the 120 clinicians mailed (38.3%), who reported caring for a total of 658 patients with narcolepsy (mean 14.98, range 0 – 80). The principal findings were: With 11 of the 46 respondents caring for ³20 patients (vs mean of 4.2), 69% (451 / 658) are clearly being managed in a few centers Only 58% of clinicians believe the presence of cataplexy to be essential to the firm diagnosis of narcolepsy. While 84% of responding clinicians have access to sleep laboratory facilities, 62% will diagnose narcolepsy without laboratory data The preferred choice of medication for cataplexy is clomipramine (61%). The first-choice medication for EDS is modafinil (ProvigilÒ) – 86% of clinicians for patients <20 years old and 89% for patients >20 years old. Patient subjective report is the only consistently used assessment of efficacy. Only 54% of clinicians 'formalise' this through use of the Epworth Sleepiness Scale. Drug tolerance is reported in 38% of patients on amphetamine, vs 4.5% of patients on modafinil. 1 in 4 clinicians routinely use doses of modafinil and dexamphetamine significantly above those recommended in the labeling (23 and 25%, respectively). These 'higher dose prescribers' tend to be the clinicians caring for larger numbers of narcoleptics. They routinely use average daily doses of modafinil 142 mg/day higher than the rest (mean of 389 mg/day vs 247 mg/day), and highest daily doses 188 mg/day higher than the rest (591 mg/day vs 403 mg/day)
Conclusions: These findings indicate that patients with narcolepsy are managed in the UK on predominantly clinical grounds, and that many clinicians (particularly those caring for larger numbers) believe that some patients benefit from higher doses of modafinil and dexamphetamine than those recommended in the labeling.

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0695.K

ELISA Determination of Antibodies Reactive to Elements of the Hypocretin (Orexin) Neurotransmission System in Patients With Narcolepsy

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Introduction: There is clear evidence that the hypocretin (orexin) neurotransmission system is involved in narcolepsy. Human narcolepsy is rarely familial or related to a specific mutation but is highly associated with the HLA DQB1*0602. It is rarely associated with mutation. Three canine species with narcolepsy were found to have mutations of hypocretin receptor 2. A preprohypocretin knock out mouse model also exhibited narcolepsy-like behaviors and EEG activity as did a murine model with genetic ablation of hypocretin neurons. Hypocretin 1 is frequently undetectable in the CSF of patients with narcolepsy. Narcoleptic brains have been found to have loss of perifornical hypocretin content by RIA and in situ hybridization and immunostaining. One hypothesis is that an autoimmune diathesis exists for human narcolepsy although one has not been found to date. Here we describe a pilot study using enzyme linked immunosorbant assays (ELISAs) with sera of 12 patients with narcolepsy with cataplexy compared to 12 control subjects.
Methods: Twelve HLA DQB1*0602 positive patients with Mayo Narcolepsy Research Diagnostic Criteria (MNRD) category A narcolepsy (cataplexy positive and laboratory confirmed) who have undetectable CSF levels of hypocretin 1 (age range 25-77 years, average 48.5±18.11) were compared to 12 controls subjects (age range 29-66 years, 43.3±10.1) using ELISAs designed to determine the presence of anti-hypocretin 1 and anti-hypocretin 2 antibodies in serum. ELISA plates were coated with 12.5pmole of synthetic human hypocretin 1 and hypocretin 2 peptides. A commercially available positive control primary antibody controls as well as antibody 2 and reagent only negative controls were run for each assay. Patient and control sera were studied with doubling dilutions beginning at 1:40 and ending with a 1:2560 dilution. Detection was accomplished using a horseradish peroxidase system. Results were read on an automated plate reader. Control vs. narcolepsy optical density (OD) readings were compared for each dilution using Student's t test using 2 tailed distribution and assuming two-sample equal variance.
Results: Hypocretin 1 and 2 antibody levels were not significantly different in sera from narcoleptic patients vs. controls in all titers studied. The p values ranged from 0.097 to 0.417 for hypocretin 1 antigen and from 0.464 to 0.968 for hypocretin 2 antigen.
Conclusions: These preliminary results showed no statistically significant difference in ELISA OD readings for plates coated with synthetic human hypocretin 1 and 2 in serum tested from 12 HLA DQB1*0602 narcolepsy patients with undetectable CSF hypocretin 1 levels compared to 12 controls. This implies that patients with narcolepsy do not have increased serum antibody levels against these two components of the hypocretin neurotransmission system. However, it is possible that with a larger number of patients, a subtle difference may be detectable. ELISA examination for antibodies reactive to preprohypocretin, hypocretin receptor 1 and hypocretin receptor 2 are in progress.

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0696.K

Narcolepsy and Idiopathic Hypersomnia in Children

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Introduction: Narcolepsy (NAR) and idiopathic hypersomnia (IH) are well described in adults, but very little is known about either condition in children. The purpose of this study was to examine these two conditions in a pediatric sleep center population.
Methods: A retrospective chart review was conducted at the Sleep Disorders Center at Children's Hospital, Birmingham, Alabama.
Results: A total of 83 children had been diagnosed with either NAR

(46%, n=38) or IH (54%, n=45) from 1994 to mid-2002 with the majority (78%, n=65) diagnosed since 1999. The sample included both African-American (58%, n=48) and White (42%, n=35) children in comparable numbers, but significantly more boys (65%, n=54,Chi-Square, p= .006) than girls. Analysis of variance testing showed significant differences (p< .05) in sleep characteristics between the two diagnostic groups. NAR children were older (NAR: Mean=13.2(SD=3.2) vs IH:11.5(3.7) years), and had more REM periods overnight (NAR:4.8(1.0) vs IH:3.6(1.5) periods). During MSLT studies NAR children had shorter mean sleep onset latency (NAR:5.1(4.5) vs IH:8.3(4.8) minutes), and shorter mean REM onset (NAR:3.9(2.5) vs IH:5.9(3.6) minutes). Parental concerns elicited from open-ended questions focused on declining school performance, academic failure, and negative behaviors (e.g. irritable, hostile, grouchy, rude), which became evident after the onset of excessive daytime sleepiness. However, parental responses to specific items on a paper and pencil sleep symptom survey used to screen for NAR and IH were not consistent with the degree of sleepiness evident on the MSLT studies.

Conclusions: These findings reflect both the nature of these similar conditions as well as clinical practices in the sleep center. Firstly, the increase in number of diagnoses for these conditions parallels the increase in referrals to the sleep center since 1999, which also reflects increased awareness by local pediatricians about the benefits of evaluating excessive daytime sleepiness. Secondly, because the diagnosis of NAR carries lifelong ramifications, the specialists in this clinic are conservative when diagnosing NAR over IH in young children. Family history and family sleep hygiene practices also play a part in diagnosis of children under age 10 who have borderline MSLT findings. These practices may account for the higher number of children diagnosed with IH. Thirdly, the center's sleep technicians have taken an active role in identifying inconclusive overnight studies among excessively sleepy children. Thus, physicians are better able to order MSLT studies immediately after the overnight study and before the children and their parents have departed. Lastly, a brief valid and reliable questionnaire for quantifying excessive daytime sleepiness in children is greatly needed, as is community education for parents, teachers and primary care providers about sleep disorders in children.

0697.K

Olfactory Dysfunction in Patients with REM Sleep Behaviour Disorder

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Introduction: Impaired olfactory threshold and discrimination have previously been reported in patients with Parkinson´s disease (PD). It has been suggested that this olfactory dysfunction manifests already in the early stages of PD. No correlation between the degree of olfactory impairment and age, duration of disease or disease severity could be found. 38% of patients with REM sleep behaviour disorder (RBD) have been shown to develop parkinsonism (PD or multiple system atrophy / MSA) after a mean interval of 13 years. A recent study further showed that PD developed in 26,9% and MSA in 15% of 93 RBD patients. Olfactory dysfunction in patients with RBD might thus have some value as an early diagnostic marker for PD. The objective is to investigate olfactory function in patients with RDB.

Methods: Olfactory threshold, odor discrimination and odor identification were investigated in RBD patients and control subjects using standardized "sniffing sticks". We routinely investigated 1) the left nostril, 2) the right nostril, 3) both nostrils together and generated a mean score. For the "sniffing sticks" test sex and age dependent normal values are available.

Results: 28 patients (19 male, 9 female, 47.1 ± 13,0 years, range 19-69) suffering from RBD and 28 age and sex matched controls (47.1 ± 13,1 years, range 20-69) were investigated. The mean olfactory threshold of the control subjects was 7.7 ± 2.1, the discrimination score 11.0 ± 3.3 and the identification score 13.2 ± 3.5 (maximum score in each subtest 16). All values of the control subjects were within the normal range. In contrast, 92,9 % of the RBD patients had a pathologically decreased olfactory threshold (3.2 ± 2.4), 64,3% an impaired odor discrimination score (9.0 ± 3.7) and 46,4% a decreased identification score (11.8 ± 3.3). Direct comparisons of RBD patients and controls subjects showed a significantly lower olfactory threshold (p = 0.0001), lower discrimination score (p = 0.040), and lower identification score (p = 0.034) for the RBD. It should be noted that only 10 patients subjectively considered their olfactory capability to be diminished. There were no side-to-side differences in both, RBD patients and controls.

Conclusions: Patients with RBD showed marked olfactory deficits, mainly concerning the olfactory threshold. Our results suggest that olfactory dysfunction in RBD antedates the onset of clinical PD.

0698.K

Narcolepsy/Cataplexy Patients are Accurate Assessors of their Excessive Daytime Sleepiness

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Introduction: Assessment of sleep disorders uses both subjective and objective measures of sleepiness. Here, we studied the correlation between these measures of sleepiness in narcolepsy/cataplexy patients and in healthy volunteers by comparing Stanford Sleepiness Scale (SSS) scores with the Maintenance of Wakefulness Test (MWT, 20min protocol) latency.

Methods: We studied 10 patients with untreated narcolepsy/cataplexy recruited from the Walton Centre neurological sleep clinic, and 10 healthy volunteers who had no evidence of a covert sleep disorders on screening. Investigations were performed in controlled surroundings. Each individual had 4 MWTs, starting two hours after waking and leaving 2 hours between each test. With sleep onset the MWT was stopped and the subjects used the SSS to rate their level of sleepiness during the preceding MWT.

Results: Four data sets were collected: a MWT sleep latency score and the corresponding SSS score for the narcolepsy/cataplexy and control subjects. Non-parametric analysis was used, as the data was not normally distributed.Kendalls rank correlation (r) was then used to compare the MWT and SSS scores in each of the 2 study groups. In the narcolepsy/cataplexy group r =-0.43, p<0.0001. In the control group r = -0.023 p=. 8258. These results indicate that the narcolepsy group shows a significant inverse relationship between the MWT and SSS scores. The control group, by contrast, does not show any significant correlation between the MWT and SSS scores.

Conclusions: Our results suggest that narcolepsy/cataplexy patients are accurate at assessing their levels of excessive daytime sleepiness using the SSS.The control group did not show a correlation between the MWT and SSS. This is because of the 'ceiling effect' with most control subjects staying awake for the full 20mins.

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0699.K

Narcolepsy And Driving - Analysis By Questionnaire Among Patients

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Introduction: Daytime sleepiness and cataplexy as main symptoms in narcolepsy may account for motor vehicle accidents. Several studies in various countries revealed increased accident rates in narcoleptic patients. Therefore there are legal permissions regarding driving licenses. Physicians are asked to assess a narcoleptic patient's ability to drive a car. They have to include study results and neuropsychological investigations.
Methods: In order to gain data regarding automobile accidents of narcoleptic patients in Germany a questionnaire regarding driving performance was presented at the yearly conference of the German Narcolepsy Society 1999. 100 patients (57 women, 48.6 $\pm$ 15.7 years old, 43 men, 50.4 $\pm$ 16.7 years old) and 95 controls (47 women, 37.5 $\pm$ 10.8 years old, 48 men, 41.5 $\pm$ 11.9 years old) took part in the study. Data were compared by the Mann-Whitney U-test.
Results: 43 patients had 1 to 8 accidents. In patients and controls persons younger than 40 had higher accident rates than older ones without difference between the groups. Narcoleptic patients older than 40 had significant reduced number of accidents (women: 0.1$\pm$ 0.3 versus 1.3 $\pm$ 1.7 in controls, $p < 0.01$, men:0.7 $\pm$ 1.2 versus 1.9 $\pm$ 1.4 in controls, $p < 0.01$). If the car was needed for the job more narcoleptic patients than healthy controls were without accidents (28out of 39 versus 21 out of 63, $p < 0.001$, Chi-square test). In order to avoid crashes patients developed various coping strategies (preferred: preparation for driving by taking a nap before driving or taking medication [45 out of 80], stop over to take a nap [41 out of 80]).
Conclusions: The study could not reveal increased automobile accident rates in narcoleptic patients when they have been informed about their disease. Coping strategies even led to less crashes in patients older than 40 compared to controls. Regarding driving licence individual ability in driving practice has to be considered. Coping strategies should be imparted

0700.K

Symptoms and Health Status of Young Adults with Narcolepsy

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Introduction: While narcolepsy tends to manifest in adolescence or young adulthood, most of what is known about the effects of this disorder on quality of life during these important developmental stages comes from retrospective recall of adults who were middle aged or older. Treatment with stimulants and/or antidepressants often incompletely controls the symptoms of this disorder so that difficulties can arise in reaching academic and occupational potential for young narcoleptics. The purpose of this presentation is to describe the effects of narcolepsy on the health and functional status of young adults 18-35 years of age compared to healthy controls in the same age range. The sample consists of 121 young adults with narcolepsy (YAWN) (27 M, 94 F, mean age = 27±4.7) solicited from a Center for Narcolepsy Research (CNR) mailing list who reported meeting the ICSD diagnostic criteria, and 94 young adult healthy controls without any clinical evidence of a sleep disorder (34 M, 60 F, mean age = 25.6±3.9).
Methods: YAWN participants completed a mailed, nine section Young Adults Health Questionnaire (YAHQ) that had been previously piloted with 10 YAWN respondents previously seen by CNR professional staff. Control participants are acquaintances of the YAWN respondents who solicited their participation, and volunteers solicited through campus advertisements who completed a similar mailed questionnaire without the Narcolepsy History and Treatment section. The YAHQ consists of investigator-designed and standardized instruments commonly used to describe the health status and symptoms of sleep disorder and normal subjects for research purposes.
Results: YAWN rated their general health status as significantly less healthy than controls on all 8 scales of the SF-36 (independent group t-tests, corrected $p = .006$). Compared to controls, YAWN reported getting more sleep on weekdays (7.5 versus 7.3 hrs) and weekends (8.7 versus 8.2 hrs, $p = .001$), but reported significantly less sleep quality on the Pittsburgh Quality Index (median score = 15 versus 9.5, Mann-Whitney U, $p = .000$). All YAWN reported experiencing sleepiness as symptoms developed (63% reported EDS and 11% reported sleep attacks as the first symptom) with a mean time from symptom onset to the time of diagnosis of 4.8±5 years. While a significant improvement was reported in their sleepiness on treatment compared to the initial onset of the disorder, about two-thirds of the sample rated their treatment as only partially or not effective. Narcoleptic respondents compared to controls rated themselves as currently significantly more sleepy on the Epworth Sleepiness Scale (mean 16.1±4.6 versus 7.7±4.5, $p = .000$), and currently significantly less able to function in daily life on the Functional Outcomes of Sleepiness Questionnaire (13.3±3.1 versus 18.3±1.9, $p = .000$).
Conclusions: While the time from symptom onset to diagnosis in this sample of YAWN is encouraging compared to earlier reports, our data suggest that the respondents continue to experience significant sleepiness that limits ability to function compared to their healthy peers.

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0701.K

Low CSF Hypocretin (Orexin) Levels in Two Girls with Narcolepsy

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Introduction: Narcolepsy is a chronic sleep disorder characterized by excessive daytime sleepiness (EDS) and cataplexy. This disease usually develops in the second or third decade of life. Recently, Nishino et al reported that most human narcoleptic patients have undetectable level of hypocretin-1 in their cerebrospinal fluid (CSF)(Nishino 2001). We studied two narcoleptic girls with undetectable levels of CSF hypocretin-1.
Methods: Hypocretin-1 in CSF was measured using radioimmunoassay kits (Phoenix Pharmaceuticals, Belmont, CA) as previously reported [3, 5]. Either patients or families gave informed consent for the lumbar puncture.
Results: Case Reports: Patient 1, a 7-year-old Japanese boy, was referred due to a 6-month history of muscle weekness and daytime sleepiness. Laughing provoked episodes of sudden loss of muscle tone of the lower extremities. The daytime naps had occurred once or twice per day. He fell asleep even while eating a lunch. His nocturnal sleep was unremarkable and he did not have sleep paralysis or hypnagogic hallucination. Birth and psychomotor development were uneventful, and neurological examination at the first consultation was normal. His height was 123.5 cm; weight was 26.4 kg and %BMI was calculated as 111%. He had no family history of narcolepsy and EDS. Multiple sleep latency test (MSLT) revealed that the mean sleep latency was 4.5 min with twice of sleep onset REM periods (SOREMPs). The human leukocyte antigen (HLA) assay revealed positive results for DRB1*1501 /DQB1*0602. Other blood examination and biochemical analysis were normal. The lumber puncture was undergone 6 months after the onset of EDS and cataplexy. The concentration of hypocretin-1 was below the

lower detection limit of the assay. The girl was diagnosed as a narcolepsy by these examinations. The patient was given clomipramine for the cataplexy and methylphenidate for the hypersomnia . Patient 2
Patient 2, a 14-year-old girl, was evaluated for an 4 your history of EDS. Subsequently, laughing provoked episodes of sudden loss of muscle tone of the extremities. Hypnagogic hallucinations was also observed. HLA typing indicated positive results for DR2. The lumber puncture was undergone when she was 14 years old. The concentration of hypocretin-1 was below the lower detection limit of the assay. The girl was diagnosed as a narcolepsy by these examinations. Methylphenidate was prescribed for the excessive daytime sleepiness.
Conclusions: Narcolepsy is a disabling neurological disorder characterized by EDS and cataplexy. Although the onset typically occurs during adolescence, when school work and social interactions are more important to personal and professional development, diagnosis is usually made years later (up to 10 years)(Nishino 2001). The narcoleptic patients in prepubertal are rare, but retrospective studies have shown that the first symptoms may appear in childhood (Navelet 1976). The diagnosis has been primarily based on clinical impression, assisted by sleep EEG recordings and HLA typing, but these tests lack specificity and/or sensitivity (Nishino 2001). If a new, sensitive and specific diagnostic tool became available, many patients would stand to benefit. In our prepubertal patients, the CSF hypocretin-1 levels were below the detection limit (40 pg/ml). The measurement of hypocretin-1 levels seemed to be valuable for conclusive diagnosis of narcolepsy, which tends to be overlooked on routine examinations, expecially in prepubertal children.

0702.K

Validity of Neural Network in Predicting Narcolepsy from Clinical Data

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Introduction: The only validated epidemiological tools for the diagnostic screening of narcolepsy are English and Finnish questionnaires. We assembled an Italian language form (GINSEN form) based on validated questionnaires on symptoms of narcolepsy and other sleep disorders, and developed an artificial neural network (ANN) using the clinical information from the form. ANN are computer programs that can be trained to predict outcomes based on experience. This study was conducted to test the hypothesis that the ANN could accurately classify patients with narcolepsy from clinical data.
Methods: Five hundred and ninety-nine adults (mean age 44.9 years; 56.4% men) from 17 Italian sleep medicine centres were enrolled. Subjects were prospectively and retrospectively selected on the basis of suspicion of four main diagnostic groups: 1. narcolepsy; 2. other hypersomniac sleep disorders (including idiopathic hypersomnia and obstructive sleep apnea syndrome - OSAS); 3. other sleep disorders and neuropsychiatric disorders confounding for symptoms of narcolepsy; 4. healthy age-matched people. With a blind procedure and according to the standard international diagnostic criteria (ICSD-R), sleep medicine trained experts classified subjects as having or not having narcolepsy. All subjects self administered the GINSEN form, a collection of Italian validated questionnaires, investigating daytime sleepiness, cataplexy, snoring, sleep apnea symptoms and insomnia symptoms. The ANN was trained with a back- propagation algorithm and tested to diagnose narcolepsy. Seventeen variables were used as inputs.
Results: In our sample, 18.0% of subjects had narcolepsy (mean age 43.2 years; 57.4% men; 87.0% of subjects with cataplexy). The trained ANN had a diagnostic accuracy of 95.0%. The sensitivity was 79.6% for having narcolepsy and the specificity was 98.4% (positive likelihood ratio was 49.75 and negative likelihood ratio was 0.21). Most false negative subjects were subjects with narcolepsy without cataplexy; most false positive subjects were people with OSAS referring severe subjective daytime sleepiness and tiredness.
Conclusions: The trained ANN accurately classified subjects with suspected narcolepsy using clinical data from a self administered form (GINSEN form). The ANN can be of epidemiological value, for instance in preliminary screening for narcolepsy in the general population. Prospective validation of the ANN for the diagnosis of narcolepsy is now required.

Research supported by Dompé Biotec spa, Italy: On behalf of the GINSEN

0703.K

Health-related Quality of Life in Subjects with Narcolepsy: Results of the SF-36 Health Survey and Correlation with Subjective Symptoms

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Introduction: Increasing interest is being given to health-related quality of life in chronic sleep disorders. In narcolepsy both physical functioning and mental well-being may be altered, but few studies have addressed the correlation between subjective symptoms and the impairment of health-related quality of life. We investigated the psychometric performance and clinical validity of the 36-Item Short Form (SF-36) health survey in a sample of subjects with narcolepsy and other hypersomniac disorders.
Methods: With a blind procedure and according to the standard international diagnostic criteria (ICSD-R), sleep medicine trained experts classified 599 adults from 17 Italian sleep medicine centres as having or not having narcolepsy. The diagnosis of obstructive sleep apnea syndrome (OSAS) and idiopathic hypersomnia (IH) were also verified in people without narcolepsy. One hundred and eight people had narcolepsy (mean age 43.2 years; 57% men), 115 OSAS (mean age 52.5 years; 88% men) and 42 IH (mean age 43.1 years; 55% men). They filled in a self-administered Italian form (the GINSEN form) including the SF-36 and other validated questionnaires investigating excessive daytime sleepiness (EDS) and cataplexy. A standard psychometric analysis and the scoring of the 8 scales of the SF-36 (physical functioning, PF; role functioning-physical, RP; bodily pain, BP; general health, GH; vitality, VT; social functioning, SF; role functioning-emotional, RE; mental health, MH) were performed. In the group of narcoleptics the r Pearson' s correlation coefficient were calculated between the scales of the SF-36 and the scales investigating narcolepsy symptoms.
Results: The recommended psychometric standards were satisfied and the Cronbach's alpha were always greater than 0.70. In narcoleptics, all but BP resulted lower than the Italian norm. Narcoleptics performed worse than OSAS patients in the following domains: RP, VT, SF and RE. No differences between narcolepsy and IH were observed in any domain. The self reported EDS (according to the Bologna questionnaire on sleepiness related symptoms) showed a moderate inverse correlation with PF, RF, VT and SF (r in the range of – 0.30 and – 0.41, $p<0.05$). The self reported occurrence of cataplexy (according to a scale based on frequency) showed a weak inverse correlation with PF, RF, SF (r in the range of – 0.17 and – 0.22, $p<0.05$).
Conclusions: According to the SF-36 health survey, narcolepsy impacts patients' health-related quality of life in terms of physical and mental well-being and impairs physical and emotional functions, restricting social and interpersonal life. Narcoleptics showed the same reduction of quality of life as people with IH and a worse impairment of social and emotional domains than OSAS patients. EDS and cataplexy showed only a weak to moderate inverse correlation with SF36. Further studies

are needed to explore other aspects of narcolepsy that could impact subjects' quality of life.

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0704.K

Prostaglandin-D-Synthase (b-trace) In Narcolepsy

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Introduction: The prostaglandin-D-system has a crucial role in animal sleep. Recently it could be shown that prostaglandin-D-synthase (PGDS) (b-trace) is also involved in normal human sleep regulation. Alterations of the prostaglandin-D-system were found in diseases that present with hypersomnia as the prominent symptom (trypanosoma infection, bacterial meningitis, systemic mastocytosis, major depression, obstructive sleep apnea). The findings encouraged us to investigate its role in the pathophysiology of narcolepsy.
Methods: Salivary, urinary and serum concentrations of PGDS, melatonin, and cortisol in 12 narcoleptic patients (NP) and one patient with idiopathic hypersomnia (IH) were measured at 4-hour intervals over a period of 5 days and nights covering physiological sleep, REM- and total sleep deprivation. Nocturnal blood sampling was performed by a through-the-wall tube system without affecting quality of sleep. PGDS was measured simultaneously with albumin as a reference protein by an automated immunonephelometric assay.
Results: PGDS serum concentrations of 12 NP (41.33 $\pm$ 17.77 years) and one patient with IH (65 years) have been analysed. Results were expressed as means $\pm$ standard deviation (SD). The statistical analyses of serum PGDS levels were based on a two-way analysis of variance (ANOVA), followed by a two-sided student´s t-test, alpha-adjusted for repeated measures using the method of Cross and Chaffin. In contrast to 14 healthy subjects (24.21 $\pm$ 2.42 years), who were previously studied, NP had significantly increased baseline PGDS concentrations (0.58 $\pm$ 0.09 vs. 0.45 $\pm$ 0.10 mg/l; $p < 0.01$) and showed a clear circadian modulation with evening increases, highest values at 8.00 a.m. (0.66 $\pm$ 0.11 vs. 0.49 $\pm$ 0.09 mg/l; $p < 0.01$), and a prolonged elevation in the day (12.00 a.m.) without any impact of total or REM sleep deprivation. There was no relationship between frequency or extent of cataplexy and circulating PGDS-levels. In the IH patient PGDS serum concentrations were likewise higher than those of healthy controls with peak excretion at 4.00 p.m. (0.58 mg/l).
Conclusions: Increased baseline level and amplitude of circulating PGDS in narcolepsy without any suppression by total sleep deprivation indicates that the prostaglandin-D-system has an important role in the pathophysiology of narcolepsy. The results imply that narcolepsy may be ruled by two different mechanisms: Hypocretins for regulation of cataplexy and PGDS for regulation of hypersomnia. In contrast to hypocretins PGDS seems to be unspecific as it exerts influence on the symptom hypersomnia in other disorders as well.

0705.K

Narcolepsy Without Cataplexy: Should it be Classified as Narcolepsy?

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Introduction: The diagnosis of narcolepsy remains a controversial issue among investigators, and full international agreement on its definition has still not been attained. The classification systems of sleep disorders in North American (ICSD, DSM-IV) lump together patients with and without cataplexy, whereas other investigators have proposed that patients without cataplexy should be categorized as having idiopathic (primary) hypersomnia. The nighttime sleep of patients with narcolepsy and cataplexy is characterized by increased wakefulness and amount of stage 1 sleep. The objective of this study was to evaluate whether the nighttime and daytime sleep of patients with narcolepsy without cataplexy is similar to patients with narcolepsy with cataplexy or patients with idiopathic hypersomnia.
Methods: We compared the polysomnographically-recorded nighttime and daytime sleep characteristics of 52 consecutive untreated narcoleptic patients without cataplexy; 53 narcoleptic patients with cataplexy; 64 idiopathic hypersomnia patients, and 50 normal controls.
Results: Sleep latency (SL), wake time after sleep onset (WTASO) and percent sleep time (% ST) of nighttime sleep of patients with narcolepsy without cataplexy were similar with those of patients with idiopathic hypersomnia, as well as normal controls. In contrast, the nighttime sleep of narcoleptic patients with cataplexy had significantly increased WTASO and total wake time (TWT) and decreased % ST compared to the other two groups of EDS and/or normal controls ($P < 0.05$). REM latency was significantly shorter in narcoleptics with and without cataplexy compared to idiopathic hypersomniacs and controls ($P < 0.05$). Daytime sleep for both narcoleptics with and without cataplexy compared to normal controls had significantly shorter sleep latencies and higher % ST. Also, patients with narcolepsy and cataplexy demonstrated significantly higher amount of % REM sleep compared to the other two EDS groups and normal controls ($P < 0.05$).
Conclusions: According to these findings, classifying narcolepsy with and without cataplexy in one category may not be appropriate. Further studies focusing on the clinical features, familial genetic patterns, HLA-typing or other biological markers, course of the illness, and response to treatment are needed to clarify whether narcolepsy without cataplexy should be categorized together with narcolepsy with cataplexy or with idiopathic hypersomnia. In the meantime, we propose that narcoleptic patients without cataplexy should be classified separately from the other two disorders of EDS.

0706.K

A Drug Distribution System Which Supports The Safe Use And Patient Adherence To Sodium Oxybate Oral Solution, A Novel Drug For The Treatment Of Cataplexy

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Introduction: Sodium oxybate (the medicinal form of gamma-hydroxybutyrate; GHB) was discovered to be a valuable medication for the treatment of narcolepsy over 25 years ago. Commercial development followed passage of the Orphan Drug Act, first with a generic company who abandoned development in 1994, followed by Orphan Medical who sponsored the product upon request from FDA that same year. By that time, illicit forms of GHB and related compounds had emerged as popular drugs of abuse and were being implicated in cases of drug-facilitated sexual assault. Further clinical development of the drug was hindered by fears of wide-spread diversion and abuse of any approved form of sodium oxybate. Indeed, federal legislation threatened to make all forms of GHB, including sodium oxybate, a Schedule I controlled substance, preventing further development of this potentially valuable medication for patients with narcolepsy.
Methods: During the clinical development of sodium oxybate, Orphan Medical worked closely with a variety of organizations including state and federal legislators, law enforcement groups, governmental agencies and medical organizations to develop a system that ensures the respon-

sible distribution of sodium oxybate while educating patients and physicians about the unique aspects of the product. Successful lobbying efforts on behalf of physicians and patients lead to modification of the Hilary J. Farias and Samantha Reid Date-Rape Drug Prohibition Act of 2000, creating the first ever bifurcated or split Schedule for GHB/sodium oxybate. Provisions to this act allowed sodium oxybate for medicinal purposes to be controlled under Schedule III following FDA approval and permitted Schedule III storage conditions for investigational drug product with harsh Schedule I penalties for illegal use under the controlled substances act.

Results: A comprehensive drug distribution system was created which satisfies the needs of patients, physicians and other stakeholders. Components of the system include centralized distribution, a physician and patient registry, educational materials for patients and physicians and a specially trained pharmacy team who provides dedicated support to physicians and patients regarding the safe use of sodium oxybate. The centralized pharmacy staff works closely with patients to guarantee delivery of sodium oxybate only to the patient or their appointed designee.

Conclusions: In July 2002, the United States Food and Drug Administration approved Xyrem® (sodium oxybate) oral solution for the treatment of cataplexy in patients with narcolepsy. The development of a centralized drug distribution system has alleviated concerns of widespread diversion of sodium oxybate. In addition to verifying the legitimacy of all sodium oxybate prescriptions and ensuring safe delivery of the medication, it has created a unique opportunity to provide both physician and patient education and ongoing patient counseling to support patient adherence to treatment with their medication and enhance drug safety.

0707.K

Effect of Increasing Doses of Sodium Oxybate on Attributes of Nocturnal REM Sleep

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Introduction: In the past, the effects of sodium oxybate on REM sleep characteristics (REM latency, REM duration, REM%, REM density and REM efficiency) were usually performed on a small number of patients treated by a fixed dose of drug. Recent study examined the dose-response effect of sodium oxybate on polysomnographic findings (dose escalation from 4.5-9.0g/night). A dose-response increase in delta sleep and delta power was documented, as was reduction of subjective and objective daytime sleepiness. We performed an analysis of data of the same group of patients for possible dose-related effects of sodium oxybate on features of REM sleep.

Methods: A post-hoc analysis of REM efficiency and REM density was performed on PSG data from 21 patients with narcolepsy treated with sodium oxybate in an open-label forced dose-titration protocol (from 4.5 to 9.0 gms) over 10 weeks. PSG data were collected with patients previously on TCA's or SSRI's, then during a treatment-free baseline period, then at each respective dose. Patient-specific Spearman's correlation coefficients were generated using all paired comparisons between six parameters (REM sleep, REM latency, REM efficiency, REM density, Stage 3-4 sleep, and Delta Power). Quantitative variables were analyzed using a two-way ANOVA with patient and treatment as the main factors. All inferential statistics performed were descriptive only.

Results: The mean REM-sleep time at baseline was 87 ($\pm$ 29 SD) minutes. A dose-related reduction in REM-sleep time was observed with a mean reduction to 53 minutes at 9 gm. Sodium oxybate caused a dose-related decrease in REM density. REM-sleep time was positively correlated with REM density. Both REM-sleep time and REM density decreased with increasing dose. REM density and REM efficiency were found to be positively correlated. There was an inverse correlation between stage 3-4 sleep time and REM-sleep time as well as with REM density. A positive correlation between REM latency and duration of stage 3-4 sleep was also found. A strong inverse correlation occurred between delta power and REM density. REM efficiency was unaffected by sodium oxybate.

Conclusions: The dose-related inverse correlations between both slow-wave sleep and delta power and both REM sleep time and REM density are of interest and suggest a probable competitive REM sleep limitation as a function of CNS delta activity induced by sodium oxybate. Alternatively, sodium oxybate may directly inhibit REM sleep activity similar to the inhibition seen with TCA's and SSRI's. Direct inhibition is less likely in view of the lack of rebound cataplexy at treatment discontinuation (typical of these other agents) when sodium oxybate is abruptly discontinued. The post-hoc findings of this study will be confirmed in a larger, blinded, placebo-controlled PSG study currently underway.

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0708.K

Body Mass Index And Narcolepsy

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Introduction: Several studies have reported an increased prevalence of obesity and increased Body Mass Indices (BMI) in narcoleptic patients. Possible causes are decreased activity due to excessive daytime sleepiness, or a side-effect of the medication used. Recent research on hypocretin and leptin in narcolepsy, however, has given growing evidence that altered energy homeostasis in narcolepsy plays a role. The objective of our study is to explore further the association of narcolepsy and BMI.

Methods: Two hundred forty-four patients referred to the sleep center of Kempenhaeghe because of suspicion of narcolepsy participated in the study. Patients were included only when they had not yet received previous medical treatment for their sleep complaints, and when they did not have symptoms or signs suggestive for a Sleep Related Breathing Disorder (SRBD). BMI and Epworth Sleepiness Scale (ESS) were assessed as part of the routine intake procedure. All patients got MSLT and full polysomnography during the preceding and the following night. Patients which appeared to have a SRBD at the sleep registration were as yet excluded. Diagnoses were made according to the International Classification of Sleep Disorders. Narcolepsy was diagnosed in 124 patients. The remaining 120 patients had the following diagnoses: Idiopathic Hypersomnia (6), Parasomnia (10), RLS/PLMD (12), Circadian Rhythm sleep disorder (38), sleep disorder secondary to Psychiatric (24) or Medical disease (30).

Results: Mean age of the group of narcoleptic patients was 35.6 ± 14.9 years, of the non-narcoleptic patients 35.0 ± 12.9 years. Age and sex differences were not significant. Mean BMI of narcoleptic patients was 26.3 kg/m2, of non-narcoleptic patients 24.1 kg/m2. The difference was significant ($p<.005$). The difference remained significant when controlled for age, sex, duration of complaints, and ESS score. Within the group of narcoleptic patients patients with a higher BMI appeared to have more MSLT abnormalities and a longer duration of their complaints ($p<.05$).

Conclusions: Our study shows that BMI is increased in medication-naive narcoleptic patients and that this increase is independent of age, disease duration, and amount of daytime sleepiness. This underscores the notion that obesity in narcolepsy is part of the disease process itself. Thus, the elevated BMI's appeared not to be secondary to behavioral consequences of narcolepsy or medication status. BMI's in narcolepsy have been reported not to be related to symptom severity. However, our data suggest that this is not correct for at least the amount of MSLT abnormalities and the duration of complaints, as both parameters

appeared to have a (weak) association with BMI.

0709.K

Decreased CSF Hypocretin-1 (Orexin-A) Level In Narcolepsy Without Cataplexy

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Introduction: There is controversy concerning the criteria necessary for the diagnosis of narcolepsy in patients with excessive daytime sleepiness without cataplexy. CSF hypocretin-1 level is markedly decreased in most narcolepsy/cataplexy patients but rarely decreased in narcolepsy without cataplexy. However, clinical characteristics of narcolepsy without cataplexy in terms of CSF hypocretin-1 has not been discussed. The aim of the study was to examine whether there is a clinical difference depending on cerebrospinal fluid (CSF) hypocretin-1 level in patients with narcolepsy without cataplexy.
Methods: Seven patients (1 male, 6 female) fulfilled the diagnostic criteria of narcolepsy according to the International Classification of Sleep Disorders (ICSD) without having cataplexy were employed in the study. CSF hypocretin-1 level was measured using a radioimmunoassay kit. Clinical features, sleep studies, and HLA typing were correlated with CSF hypocretin-1 level.
Results: Two patients showed a markedly decreased CSF hypocretin-1 level (<40 and 53pg/ml), while five showed normal level (ranged 204-356, mean 277.2 pg/ml). Between these two groups, mean age of onset of hypersomnia was significantly younger (13.0 years vs 18.0 years) and mean ordinary sleep time was shorter (5.8 hours vs 7.7 hours) in the former group. MSLT findings including mean seep latency, number of SOREMPs and REM latency did not show any difference between these two groups. HLA DR-2 was positive in all patients with low CSF hypocretin-1 while three were DR-2 positive among patients with normal CSF hypocretin-1.
Conclusions: We presented decreased and normal CSF hypocretin-1 level in patients of narcolepsy without cataplexy. Narcolepsy without cataplexy may share a common feature between narcolepsy/cataplexy and idiopathic hypersomnia, and CSF hypocretin-1 level can aid in clarifying the dissimilarity.

0710.K

CSF Hypocretin (Orexin) in Disorders of Excessive Daytime Sleepiness

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Introduction: The deficiency of, the REM modulating neuropeptide, Hypocretin-1 (hcrt-1) in HLA positive patients, with narcolepsy is now established. The role(s) of hcrt-1 in other disorders of excessive daytime sleepiness (EDS) is less well understood. We report the characteristics of patients presenting with EDS including CSF HCRT levels.
Methods: This prospective study was undertaken to study the characteristics of patients with EDS presenting to our regional referral centre. We set out to measure CSF hcrt-1 in this sample of patients with narcolepsy-cataplexy (NC), in monosymptomatic narcolepsy (MN) and primary hypersomnia (PH)Patient assessments included the following: Epworth Sleepiness Score (ESS); Clinical Evaluation by a senior sleep physician; HLA typing; Conventional Nocturnal Polysomnography (NPSG); Multiple Sleep Latency Testing (MSLT) and CSF hcrt-1 levels using a standardised RIA kit.Inclusion Criteria were as follows: NC - the presence of Excessive daytime sleepiness (EDS) > 6 months, an ESS > 10 and the presence of cataplexy; MN - EDS > 6months; ESS > 10; No cataplexy; Sleep Latency (SL) < 10 minutes; MSLT with > 1 Sleeponset Rapid Eye Movements (SOREMs); No other evident cause(s) of EDS and Apnea-Hypopnea Index (AHI) < 10; No improvement in EDS following sleep extension; PH - patients who fulfilled the criteria for MN but who had no SOREMs.
Results: NC: n = 23 (F = 16, M = 7) ESS - mean score of 19.6, MSLT analysis - mean sleep latency of 3.9 minutes. All the patients were HLA DQB1*0602 positive; Mean Body Mass Index (BMI) was 31.1kg/m2 ± 6.2 kg/m2, similar to previous published findings; CSF hcrt-1 was below the detection limit (40 pg/ml) in the 12 patients analysed to date. MN: n = 18 (F = 8, M =10); ESS mean = 18; MSLT - mean SL of 5.4 minutes. Thirteen of the patients were HLA DQB1*0602 positive; The mean BMI was 25.6kg/m2 ± 5.24kg/m2 ;Very low levels of CSF hcrt-1 were found in the eight HLA positive patients analysed to date.PH: n = 33 (F = 14, M =17); Mean ESS = 18; Mean SL of 5.7 minutes 8 patients were HLA DQB1 * 0602 positive; Mean BMI = 22.7kg/m2 ± 1.2kg/m2.Mean CSF hcrt-1 was 67.9pg/ml ± 12.4pg/ml in the 6 patients analysed to date.
Conclusions: Our early results confirm the previous findings that hcrt-1 is deficient in patients with NC and indicate that there may be a graded deficiency of hcrt-1 in disorders of excessive daytime sleepiness.

0711.K

Clinical and Polysomnographic Findings of Narcolepsy with and without Cataplexy: A Population-Based Study

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Introduction: Most information regarding clinical and polysomnographic features of narcolepsy is reported from series of patients seen at specialized clinics. The nosologic status of narcolepsy without cataplexy is uncertain; previous data suggests that it differs in many ways from narcolepsy with cataplexy. We used our population-based prevalence study of narcolepsy in Olmsted County, Minnesota (Sleep 2002;25:197-202) to investigate the frequency of associated clinical and laboratory phenomena in a population-based sample of narcoleptic patients with and without cataplexy. We hypothesized that the two groups would differ in many characteristics.
Methods: All patients with narcolepsy resident in Olmsted County, Minnesota on January 1, 1985 were identified. Patients were divided into those with cataplexy (C+) (excessive daytime sleepiness and cataplexy) and those without (C-) (EDS and an MSLT with mean sleep latency of <8 minutes and >1 SOREMPS). MSLT data was available for 51% of the cataplexy group. Charts were reviewed and data abstracted and analyzed. Chi-squared and T-tests were used for statistical comparisons.
Results: Fifty-five patients met criteria. Thirty-five had cataplexy (64%). Sleep paralysis was present in 66% of the C+ group and 11% of the C- group ($p<0.0001$). Hypnagogic/hynopompic hallucinations were present in 59% of the C+ group and 32% of the C- group ($p=0.06$). PSG data was available for 41 patients. Mean sleep efficiency was 82.4±10.4% in the C+ group and 90.9±6.2% in the C- group ($p=0.004$). There were no other significant differences between the 2 groups and the remaining data is reported for the 2 groups combined. Mean sleep latency was 4.9±4.2 minutes (range 0-17 minutes); 87% had sleep latencies <10 minutes. Mean REM latency was 74.5±77.1 minutes; 27% had REM latencies minutes. The mean periodic limb movement index was 20.3±27/ hour; 45% had PLMI >10/hour. MSLT data was available for 37 patients. Mean sleep latency was 4.2±2.2 minutes; 68% had mean latencies minutes. The mean number of naps showing SOREMPS was 2.4±1.2; 84% had >1 SOREMPS.
Conclusions: The C+ group had a significantly higher frequency of sleep paralysis and a borderline higher frequency of hypnagogic/hypnopompic hallucinations compared to the C- group. PSG sleep efficiency was significantly lower in the C+ group. This suggests that the two disorders are different, with narcolepsy without cata-

plexy being closer to idiopathic hypersomnia. The descriptive data from this population-based study presents a more accurate picture of the associated features of narcolepsy in the community than from previous clinic-based samples. Thirty six percent of patients with narcolepsy did not have cataplexy. PSG sleep latencies were very short in both groups. REM latencies were variable, with 27% of patients having a SOREMP on PSG. Almost half the patients in both groups had PLMI >10 per hour. The MSLT data revealed that about 2/3 of the patients (combined groups) had mean latencies minutes and 84% had >1 SOREMP.

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0712.K

Month Of Birth And Month Of Symptom Onset In Narcolepsy

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Introduction: Analysis of the seasonal patterns in month of birth and month of symptom onset for a disorder can provide an indication of the environmental factors that may precipitate its onset. Two studies have examined month of birth in narcolepsy and both found an increase in March (Carlander et al., 1993; Okun et al., 2002). This study sought to replicate this finding and to determine if seasonal trends are also present in the month of symptom onset.
Methods: Archival data from the 301/302 trials assessing the safety and efficacy of modafinil in the treatment of narcolepsy were used in this study. Patients without cataplexy were excluded to obtain a homogeneous patient group (n=429). The observed number of births per month was compared to the expected number of births per month in the general population. These control frequencies were obtained from 1997 data on number of live births from the National Center of Health Statistics. From the overall group, 14% (n=61) could recall the month in which their symptoms first began. Due to data misclassification, it was necessary to exclude January from the month of onset analysis.
Results: The month with the most births was March with 56 (OR=1.6, p<.05) and the value of 2 was marginally significant (2s11s=18.02, p<.1). When only cases with age of onset less than or equal to 30 were considered (n=345), the odds ratio associated with a March birth increased (OR=1.8, p<.05) and the value of 2 became significant (2s11s=22.19, p<.05). The month in which the most patients reported their onset was September with 12. Although the value of 2 for these data was non-significant (2s10s=12.03, p=.28), September was 2.5 standard deviations above the mean number of onsets per month (M=5.6, SD=2.6).
Conclusions: The finding of an excess of March births in narcolepsy replicates earlier studies. The finding of an excess of September onsets in narcolepsy is a new finding that needs replication. While the relation of these findings to each other is equivocal, attempting to reconcile them could point to potential environmental triggers in narcolepsy. For example, September corresponds to the beginning of the cold and flu season and a March birth would indicate that the fetus was in the second trimester (a critical period of brain development) during the flu season. Consequently, an infectious agent could be the link between these two findings and could be triggering the putative autoimmune process in narcolepsy. Similar seasonal findings for month of birth and month of symptom onset have been reported for leukemia (Olsen et al., 2001; Westerbeek et al., 1998), which is suspected of having an infectious origin. The fact that the effect size for month of birth increased when only cases with age of onset less than or equal to 30 were considered is consistent with the idea that these individuals experienced an environmental trigger for narcolepsy in utero rather than later in life.

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0713.K

Epidemiology of Narcolepsy: Inter-Ethnic Differences or Similarities?

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Introduction: There is much controversy about the exact prevalence rate of narcolepsy across various ethnic groups. Whereas Japanese researchers reported the prevalence rate to be as common as one in 200, the Israeli group suggested that it could be as rare as one in 500,000. Such a wide range of difference in the reported prevalence rate is likely contributed by the lack of well-designed epidemiological study.
Methods: Recently, we reported a two-phases general population study in our Chinese population. We carried out a random telephone survey with a validated screening instrument (Chinese version of Ullanlinna Narcolepsy Scale) and followed by a secondary clinical-polysomnographic-HLA confirmation of the questionnaire-positive subjects.
Results: Among 9,851 subjects interviewed, 0.28% were screened positive by questionnaire criteria. With further clinical-PSG-HLA investigations, only one-tenth of the subjects were found to be suffering from genuine narcolepsy. The prevalence rate of narcolepsy in Southern (Hong Kong) Chinese was found to be at 0.034% (95% CI 0.010% - 0.117%). Upon review of previous published studies, the range of prevalence rate was reported within 0.3-0.7% across most of the studies if solely based on single-phase questionnaire studies. However, with more stringent design employing a certain degree of secondary clinical confirmation, most epidemiological studies (including Arabs, Finnish, British) reported a prevalence rate of narcolepsy in the range of 0.026-0.04%.
Conclusions: The current study suggested that for future epidemiological study of sleep disorder, a two-phase design with secondary clinical and laboratory confirmation is indicated. The prevalence rate of Chinese narcolepsy is comparable to other population studies using stringent epidemiological design and suggests that previous reports of major cross-ethnic differences in the prevalence rate of narcolepsy may likely be a result of methodological limitations.

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0714.K

HLA Study in Korean Patients with Narcolepsy-Cataplexy

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Introduction: Narcolepsy is a chronic sleep disorder and it has the clinical characteristics of excessive daytime sleepiness and abnormal manifestations of REM sleep including cataplexy, sleep paralysis and hypnagogic hallucinations. Although narcolepsy has been shown to be tightly associated with HLA-DR and DQ genes in many ethnic groups, very few studies have been performed in Asian populations, other than Japanese. We have studied HLA-DRB1 and DQB1 associations in Korean patients with narcolepsy-cataplexy.
Methods: A total of 60 patients with narcolepsy-cataplexy diagnosed during a period of 8 years in the Seoul National University Hospital were enrolled. The clinical diagnosis was confirmed by nocturnal polysomnography and Multiple Sleep Latency Test (MSLT). HLA-DRB1 genotyping was performed in two steps: first, DRB1 generic typing using a PCR-reverse SSO (sequence-specific oligonucleotide) typing kit, and then DRB1 genotyping using the PCR-SSCP (single strand conformation polymorphism) method. HLA-DQB1 genotyping was performed using the PCR-RFLP and PCR-SSCP methods. The phenotype frequencies of HLA-DRB1 and DQB1 alleles were compared with those

of a control group of 200 normal Koreans, using chi square test or Fisher's exact test. P values were corrected (corrected P, Pc) for multiple comparisons by multiplying P values by the number of alleles found in each locus.
Results: HLA-DRB1*1501 was found in all patients, showing very strong association with the disease (100% vs 17% in controls, Pc=2.3 x10–30). Three DRB1 alleles were significantly decreased in the patients compared with controls, showing protective effect: DRB1*0101 (1.7% vs 13.5%, P=0.010), *0405 (1.7% vs 16.5%, P=0.003), and *0901 (5.0% vs 17.5%, P=0.016). Besides DRB1*0405, other DRB1*04 alleles were also decreased in the patient group resulting in a markedly decreased DRB1*04 frequency compared with controls (8.3% vs 37.5%, Pc=0.0003). In HLA-DQB1 analysis, those alleles known to be in strong association with the above mentioned susceptible and protective DRB1 alleles in Koreans showed significant changes. DQB1*0602, which is almost exclusively in association with DRB1*1501, was also found in 100% of the patients (vs 17% in controls, Pc=3.0 x 10–30). Four DQB1 alleles were significantly decreased in the patients compared with controls, showing protective effect: DQB1*03032 (6.7% vs 20.6%, P=0.013), *0401 (1.7% vs 16.0%, P=0.004), *0501 (3.3% vs 17.5%, P=0.006) and *0601 (5.0% vs 15.5%, P=0.035). Strong association of HLA-DRB1*1501 and DQB1*0602 with the disease and protective effect of DQB1*0501 and *0601 found in Koreans are similar to those found in Japanese or Caucasians. However, the strong protective effect of DRB1*04 found in Koreans is quite different from the findings in Japanese or Caucasians, showing increased DRB1*04 frequency in the patients.
Conclusions: These results indicate the similarity of narcolepsy-cataplexy in Koreans to the disease in Japanese or Caucasians. We also found a new protective DRB1 allele, DRB1*04 (*0405), indicating the heterogeneity of immunogenetic background underlying the disease.

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0715.K

CSF Hypocretin Levels in Korean Narcoleptic Patients

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Introduction: Narcolepsy is a sleep disorder, characterized by excessive daytime sleepiness, cataplexy, sleep paralysis, hypnagogic hallucination. The cause of narcolepsy is still unknown. However, recent studies suggested hypocretin level is strongly associated with its pathophysiology. This study was designed to investigate the level of CSF Hypocretin-1 and to confirm the Hypocretin deficiency in narcoleptic patients. Additionally we attempted to suggest the level of hypocretin as a valuable diagnostic tool.
Methods: We selected 18 patients(mean age 20.7¡¾7.6, 12 men and 6 women) who have narcolepsy confirmed by the polysomnography and multiple sleep latency test(MSLT) as well as clinical history and symptoms at the St. Vincent Hospital Sleep Disorder Clinic. Any subjects comorbid with other hypersomnic sleep disorders such as sleep apnea or periodic limb movements during sleep were excluded. All patients and 8 controls (mean age 35.4 ¡¾ 10.7, 3 men and 5 women) did spinal tapping for the level of hypocretin. Clinical data were collected by semi-structured interview for narcolepsy.
Results: Results obtained were as follows:1) Average sleep latency was 2.6±2.0 minutes and average frequency of sleep-onset REM periods was 2.7±1.4 by MSLT. 2) Characteristic symptom of narcolepsy investigated were as followed: excessive daytime sleepiness(100%, n=18), cataplexy(83.3%, n=15), sleep paralysis(66.7%, n=12), hypnagogic hallucination(72.2%, n=13) and disrupted nocturnal sleep(55.6%, n=10).3) In narcoleptics, compared with the normal control, hypocretin-1 level was found to be significantly decreased(P=0.002). Hypocretin-1 was detectable in all controls(227¢¦321 pg/mL). But, in 15 of 18 patients(83.3%), hypocretin-1 levels were decreased(91pg/mL) or below the detection limit of assay(<40 pg/mL). And the hypocretin-1 levels of the other patients were 149 pg/mL, 275pg/mL and 284 pg/mL.
Conclusions: High frequency hypocretin deficiencies in narcoleptic patients suggest that hypocretin level could be a valuable diagnostic marker of narcoleptic patients.

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0716.K

The Thyreotropic Axis In Hypocretin Deficient Human Narcolepsy: Decreased Total And Pulsatile Secretion Of TSH

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Introduction: Narcolepsy with cataplexy is strongly associated with disruption of hypocretin (orexin) neurotransmission. Narcoleptic patients show, once suffering from the sleep related narcoleptic complaints, a tendency to grow obese suggesting a reduced metabolic rate. Orx-ataxin3 transgenic mice demonstrate the narcoleptic phenotype when they are over 12 weeks of age and almost all hypocretin cells have disappeared. From that moment they also start growing obese despite a reduction in food intake, suggesting an acquired lowered metabolic rate.The thyroid hormone system is a key effector of energy balance, and may be compromised in the absence of hypocretin. Hypocretin administration would be expected to upregulate the thyroid hormone system since hypocretin deficiency is associated with a lowered metabolic rate. Experiments in rats however, showed inconclusive results, and data from hypocretin deficient mice have not been reported yet. We therefore explored whether hypocretin deficiency disrupts the circadian timing and level of thyroid-stimulating hormone (TSH) secretion in humans, in addition to T4 and T3 levels.
Methods: We measured 24 hour serum concentrations of TSH, total T4 and total T3 in 7 hypocretin-deficient narcoleptic males (N) and 7 controls (C), matched for age and Body Mass Index. We deconvolved the 24-h profiles of TSH to estimate secretion rates, and determined TSH circadian rhythmicity by cosinor analysis. Data are expressed as mean ± SEM.
Results: The mean 24 hour TSH concentration was significantly lower in narcolepsy patients (1.58±0.27 (N) vs. 2.88±0.36 (C) mU/L, p=0.014), while T4 and T3 concentrations were unaffected (T4 85.9±3.5 (N) vs. 90.6±4.7 (C) nmol/L, p=0.44; T3 1.58±0.04 (N) vs. 1.62±0.05 (C) nmol/L, p=0.58). Total TSH secretion was lower in narcoleptics (41.5±8.55 (N) vs. 78.5±7.56 (C) mU/L, p=0.007), which was caused by a 50% reduction in pulsatile secretion (37.2±7.31 (N) vs. 74.7±7.70 (C) mU/L, p=0.004). The acrophase of TSH was shifted forward (~ 01.5h in narcolepsy patients, and the amplitude of the nocturnal TSH surge was blunted.
Conclusions: The present study suggests that hypocretin deficiency is accompanied by reduced serum TSH concentrations through a reduction in pulsatile TSH release, in the absence of a change in T4 and T3 levels. Furthermore, the amplitude of the nocturnal surge in TSH is blunted and the circadian rhythm of TSH is time-advanced in narcolepsy patients. These findings indicate that hypocretin deficiency resets the dynamics of the pituitary-thyroid axis in human narcolepsy.

0717.K

Narcolepsy-related Symptoms in a Population-Based Sample

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Introduction: Symptoms used as narcolepsy's diagnostic criteria have heretofore been primarily investigated in clinical samples. Narcolepsy's clinical symptoms (cataplexy, hallucinations, sleep paralysis, automatic-behavior) were investigated in a population-based sample to assess their possible relation to narcolepsy, using self-reported excessive daytime sleepiness (EDS) as a proxy. Aims were to: 1) determine prevalence of narcolepsy-related symptoms in a sample representative of a general adult population; 2) test hypotheses that each symptom's self-reported presence is associated with the presence of EDS, oft-considered narcolepsy's most debilitating symptom.
Methods: Our sample consisted of 3023 Wisconsin Sleep Cohort Study Survey participants. Point prevalence rates were calculated. Using EDS as the outcome (presence: ≥ 5/month; absence: £ 2-4/month), each multivariate logistic regression model run included the symptom-of-interest (presence: <1/month, ≥ 1/month but <1/week, ≥ 1/week; absence: 0, "only a few times ever"), and age, sex and BMI. For each symptom 'x,' 2 model types were examined, with 0 occurrence of narcolepsy-like symptoms as the reference group in both: (1) 2 dummy variables represented 'x': "'x' regardless of other symptoms," "symptoms excluding-'x'"; (2) 3 dummy variables represented 'x': "isolated 'x' (with no other symptoms)," "'x' with other symptoms" and "symptoms excluding-'x.'"
Results: Prevalence: Prevalence (%) of at least one symptom was 26.13%. Rates for total symptoms were: paralysis- 5.16%; hallucinations- 9.16%; automatic-behavior- 18.19%; cataplexy- 2.42%; for isolated symptoms (without other symptoms) were: paralysis- 1.56%; hallucinations- 4.53%; automatic-behavior- 12.27%; cataplexy- 0.76%.Odds Ratios (ORs): Presence of any symptom, with or without others (type 1 model), was strongly significantly associated with EDS. ORs (95% confidence intervals) were: paralysis = 3.36 (2.30, 4.90), hallucinations = 3.80 (2.83, 5.10), automatic-behavior = 3.77 (3.00, 4.75), and cataplexy = 5.19 (3.14, 8.58).In type 2 models, combined with other symptoms, associations were strong and statistically significant: ORs (95% confidence intervals) were 4.61 (3.01, 7.04) for paralysis, 6.91 (1.93, 4.78) for hallucinations, and 8.08 for cataplexy (4.54, 14.38). The three symptoms in isolation had lower ORs: for paralysis, hallucinations, and cataplexy, ORs were, respectively, 1.23 (0.51, 2.04), 1.69 (1.05, 2.72), and 0.97 (0.22, 4.22). Even for automatic-behavior, for which the isolated effect seemed strong (OR= 2.90, 95% CI: 2.20, 3.81) and so might represent a non-narcolepsy construct (e.g. sleep deprivation), combination with other symptoms resulted in an increase to 6.13 (4.39, 8.57).
Conclusions: EDS is the principal behavioral morbidity marker for narcolepsy. Thus, strongly positive, statistically significant associations with EDS when any narcolepsy-related symptom was present suggest a narcolepsy spectrum. That only cataplexy combined with other symptoms (not cataplexy in isolation) was associated with EDS is striking, as the combination of cataplexy and EDS is considered narcolepsy's cardinal diagnostic criterion. Findings suggest future diagnostic foci on specific combinations of symptoms to be explored by further analyses on interactions between the 4 symptoms. Future studies will also evaluate the influence of HLA susceptibility alleles on narcolepsy-related symptoms.

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0718.K

Investigation Of The Autoimmune Basis Of Narcolepsy Using Western Blot Analysis Of Lateral Hypothalamus Protein Extract With Serum And Cerebrospinal Fluid (CSF)

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Introduction: Narcolepsy-cataplexy has recently been shown to be associated with deficiency in hypocretin neurotransmission. Because of its tight association with the HLA marker DQB1*0602, it is possible that narcolepsy results from autoimmune destruction of hypocretin neurons. In an autoimmune process, it would be expected that patients with narcolepsy have serum and/or cerebrospinal fluid (CSF) antibodies that specifically react to antigens expressed in the lateral hypothalamus (LH) where hypocretin neuronal cell bodies are exclusively located.
Methods: Using western blot, we screened binding of sera (1:500-1:5000) from 40 HLA DQB1*0602 positive hypocretin-deficient patients and 120 healthy controls to protein from LH of dogs, rats, and mice. The patients studied included recent onset cases, young patients, and patients prior to development of cataplexy. The sera from ten patients and ten controls were purified for IgG using protein G and tested on western blot at 1:100-1:1000. The possibility of intrathecal production of antibodies was tested next using neat CSF from 20 HLA positive hypocretin-deficient patients and 10 controls. Freshly frozen dog, rat or mouse brain was carefully dissected to remove the LH, where hypocretin cell bodies are concentrated. Protein extracted from LH cells was combined from 5 dogs, 10 rats and 10 mice. One hundred microgram to 1mg of extract from each species was denatured by addition of an equal volume of sample buffer, followed by incubation at 80ºC for 5min. Samples were run on 12% polyacrylamide gels at 120V/1hr. Protein was then transferred to a 0.45-micron nitrocellulose membrane at 300mA/1hr. The membrane was then stored in PBS containing 0.05% (v/v) Tween and 5% (w/v) blotting grade milk [PBS-Tween-Milk]. After blocking overnight, the membrane was exposed to sera/IgG from patients and controls diluted in PBS containing 10% normal horse serum for 1hr. CSF was used neat. After three 10-minute washes in PBS-Tween, the membranes were placed in PBS-Tween-Milk containing 1:10,000 HRP-conjugated donkey anti-human antibody for 1hr. After three 10-minute washes with PBS-Tween, the membrane was exposed to chemiluminescent peroxidase substrate followed by exposure to film.
Results: No specific or shared binding to any protein band in lateral hypothalamic blots from any animal species was noted using sera from patients at dilutions of 1:500-1:5000. Purified IgG at various dilutions (1:100-1:1000) did not reveal any specific or shared binding to lateral hypothalamic blots either. Neat CSF applied to blots did not reveal any specific or shared binding in narcolepsy.
Conclusions: Although the hypothesis that narcolepsy is an autoimmmune disorder is attractive, to date, there is little evidence to support this. The results presented, however, do not disprove an autoimmune basis for narcolepsy. It may be that because hypocretin neurons are few in number, it is difficult to isolate a highly specific antigen using currently available techniques. Further studies are underway to investigate this possibility.

0719.K

Hypocretins (Orexins) And CART Peptides Are Co-expressed In Human But Not In Rodents Hypothalamus

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Introduction: The hypocretins (Hcrt), also called orexins, are neuropeptides exclusively synthesized in the perifornical area of the tuberal

region of the hypothalamus. In regard to the neuroanatomical distribution of the Hcrt neurons and their terminal projections, Hcrt have been implicated in complex physiological functions including feeding behaviors, vigilance states, and neuroendocrine functions. More recently, convergent studies have shown that deficiency in the Hcrt system (ligand or receptors) is associated with a debilitating sleep disorder known as narcolepsy. In humans, typical narcolepsy was associated with a lack of signal for preprohcrt mRNA and its mature peptides. The current hypothesis regarding the etiology of human narcolepsy is that it is an autoimmune disorder with the Hcrt neurons as the target. This hypothesis is based on reports indicating that more than 85-95% of the patients with narcolepsy have the form DQB1*0602 for the human leukocyte antigen (HLA). Furthermore, Hcrt-1 is undetectable in the CSF of HLA DQB1*0602 positive narcoleptic patients examined to date. To test this hypothesis, it is crucial to determine whether Hcrt neurons have degenerated in narcoleptic patients.The objective of the present study is to identified peptides expressed in a large majority of Hcrt cells in controls in order to test further on post-mortem samples whether Hcrt cells would be labeled by the marker or would have degenerated in narcoleptic patients. A large variety of neuropeptides are present in the hypothalamus. Among them, cocaine and amphetamine regulated transcript (CART) is densely located in the paraventricular nucleus and through several hypothalamic areas partially overlaping the distribution of Hcrt neurons.

Methods: To determine whether CART peptides are co-expressed by Hcrt neurons, we conducted dual-labeling in situ hybridization and double-immunolabeling experiments.

Results: We found that a large portion of the Hcrt neurons co-expressed CART in the dorsal part of the parafornical nucleus, the adjacent areas of the dorsomedial and ventromedial nuclei and the lateral hypothalamic area in humans respectively. In contrast, we found in rodents that Hcrt and CART expressing neurons represent two distinct cell populations.

Conclusions: These results suggest that the labeling of CART on hypothalamic post-mortem samples from narcoleptic subjects is an appropriate approach to be taken in order to examine whether the cause of narcolepsy is due to a degenerative process targeting Hcrt cells.

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0720.K

Voxel-Based Morphometry In Narcolepsy - A Controversial Issue

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Introduction: Structural brain pathology has not been found in narcoleptic patients with conventional CT and MR techniques. Voxel-based morphometry (VBM), an observer unbiased volumetric tool, was used in this study to investigate gray matter changes in the entire brain of patients with narcolepsy without restriction of regions-of-interest.

Methods: Twelve patients (8 men and 4 women, mean age 35.8±13.2 years) with narcolepsy according to ICSD criteria and twelve healthy age-matched controls of the MRI data bank were included. Mean time since onset of narcoleptic symptoms was 15±13.2 years. Patients were studied on their usual stimulant and anticataplectic treatment. T1-weighted images of all subjects were normalized onto a template by a 12 parameter affine and a non-linear stereotactical normalization using discrete cosine (7x8x7) basis functions. Following normalization images were segmented in gray and white matter as well as cerebrospinal fluid. Finally gray matter was smoothed with a Gaussian filter of 10x10x10 mm FWHM. The general linear model as employed by SPM99 was used to compare the gray matter compartment between patients and controls. The significance level was set at $p<0.05$ corrected for multiple comparisons across the volume.

Results: Compared to controls patients with narcolepsy showed significant clusters of gray matter loss in the left medial frontal gyrus (cluster size: 717 voxels) and the left anterior cingulated cortex (cluster size: 146 voxels). Additional small clusters were found in both posterior parietal cortices corresponding to Brodmann´s area 7.

Conclusions: Using voxel-based morphometry we found gray matter loss particulary in medio-frontal areas of narcoleptic patients. In two recent VBM studies on this topic the authors reported contradictory results with volume loss in inferior temporal and inferior frontal regions (Kaufmann C, 2002) or no significant volume changes compared to controls (Overeem S, 2002). Further studies are required to investigate methodological bias (e.g. pre-statistical processing) or to assess a possible impact of symptoms, severity and duration of narcolepsy or stimulant treatment.

0721.K

Reduced Density of Hypocretin (Orexin) Axonal Varicosities in Human Narcolepsy

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Introduction: In previous work, we reported that human narcoleptics have an 85-95% reduction in the number of hypocretin (Hcrt) neurons and gliosis in the hypocretin cell and axonal projection regions (Thannickal et al., 2000). In the current study we analyzed the distribution of varicosities on surviving Hcrt axons in each hypothalamic nucleus, locus coeruleus, raphe dorsalis and raphe centralis of human narcoleptics and controls.

Methods: The hypothalamus and brain stem areas of four narcoleptic and four normal individuals were used. Death had occurred 31-51 years after symptom onset in the narcoleptics. The following nuclei were examined: anterior hypothalamus, periventricular, paraventricular, supraoptic, arcuate, dorsal, dorsomedial, ventromedial, lateral, posterior, tuberomammillary, and mammillary hypothalamus, thalamus, locus coeruleus, raphe dorsalis and raphe centralis. The number of varicosities and varicosity spacing within individual axons were counted using the Neurolucida program (Microbright Corp).

Results: We assessed regional differences by comparing the mean spacing of varicosities in each nucleus. Narcoleptics had a significant reduction in varicosities in Hcrt fibers ($t - 22.5$, $df - 30$, $p<0.00001$). The average density of varicosities decreased from 26.7/100 um in normals to 17.9/100 um in narcoleptics, a 33% reduction. The maximum percentage reduction in varicosity density occurred in dorsomedial (40.2%, $t - 5.69$, $p<0.001$, $df - 6$), arcuate (40.0%, $t - 5.7$, $p<0.001$, $df - 6$), ventromedial (37.3%, $t - 5.23$, $p<0.001$, $df - 6$), posterior (37.2%, $t - 3.98$, $p<0.007$, $df - 6$), anterior (36.9%, $t - 5.7$, $p<0.001$, $df - 6$), lateral (36.4%, $t - 5.03$, $p<0.002$, $df - 6$), and tuberomammillary hypothalamic nuclei (35.3%, $t - 4.2$, $p<0.005$, $df - 6$). The mean spacing of varicosities increased from 3.8 um in normals to 5.7 um in narcoleptics. There was no significant increase in varicosity spacing in surviving Hcrt axons in supraoptic, thalamus, locus coeruleus, raphe dorsalis and raphe centralis.

Conclusions: The reduced density and increased spacing of varicosities in Hcrt fibers may provide a clue to the nature of the degenerative process in narcolepsy. The regions with the greatest reduction in varicosity density are also those with the most pronounced gliosis (Thannickal et al., 2002). These findings suggest that certain Hcrt terminal regions may be targeted by the immune or toxic events that ultimately produce Hcrt cell loss in narcolepsy, whereas other Hcrt terminal regions are spared.

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0722.K

The Effects Of Hypocretin-1 (Orexin A) In Hypocretin Receptor 2 Gene Mutated And Hypocretin Ligand-Deficient Narcoleptic Dogs

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Introduction: Human narcolepsy-cataplexy is associated with loss of hypocretin-1 and -2 in the brain and CSF. In dogs, two forms of the disease have been reported: a sporadic form with hypocretin deficiency and a familial form with loss of function mutations in the hypocretin receptor 2 gene (Hcrtr2). Hypocretin-related gene mutations are rare in humans, but a loss of hypocretin peptides (possibly due to acquired cell death of hypocretin neurons), is likely involved in most cases. Hypocretin or hypocretin agonists may therefore be a promising and logical future treatment for human narcolepsy. John et al, recently reported that the intravenous (IV) administration of hypocretin-1 (up to 3 µg/kg) reduces cataplexy and consolidates sleep fragmentation in hypocretin receptor 2 (Hcrtr2) gene mutated narcoleptic Dobermans. This result is unexpected, as central penetration for hypocretin peptides is low, and Hcrtr-2, (the more important receptor subtype for narcolepsy), is nonfunctional in these animals. Using the same experimental design, we did not observe any effects of IV hypocretin-1 on cataplexy or sleep in control and narcoleptic Dobermans. We pursued this line of investigation and studied (1) the effect of intracerebroventricular (ICV) administration of hypocretin-1 in Hcrtr 2 -mutated narcoleptic and control Dobermans, (2) the central penetration of hypocretin-1 in the same animals, (3) the effect of IV hypocretin-1 (up to 384 of µg/kg) in two ligand-deficient narcoleptic dogs (a model equivalent to human narcolepsy). Our goal was to further evaluate hypocretin supplementation as a therapy for narcolepsy.

Methods: (1) ICV experiments: Two controls and 2 Hcrtr 2-mutated narcoleptic Dobermans implanted with EEG, EMG and EOG electrodes and ICV guide cannulae were used. After confirming spontaneous CSF outflow through the injection needle, artificial CSF or hypocretin-1 (10, 30 nmol) was injected in the lateral ventricle, and effects on sleep monitored over a 6- hour period. Two recording sessions (artificial CSF, 10, 30 nmol) were conducted in each animal. For cataplexy testing studies, ICV hypocretin-1 (30, 60 120 nmol) was administered in 2 narcoleptic Dobermans, and cataplexy was quantified using the FECT. (2) Central penetration study: 30 minutes after an IV injection of hypocretin 1 (saline, 24, 96, 386 µg/kg) in two Dobermans, plasma and cisternal CSF were collected. Hypocretin-1 levels were measured using a radioimmunoassay. (3) The effect of IV hypocretin-1 (3-384µg/kg) on cataplexy was evaluated in 2 hypocretin ligand deficient narcoleptic dogs (a 3 year old Schipperke, 3 sessions for each dose; a 2 year old Wermeier,1 session up to 96µg/kg).

Results: (1) An ICV injection of hypocretin-1 (up to 30 nmol) dose-dependently increased wakefulness, reduced SWS and REM sleep in control Dobermans. In contrast, no effect on sleep (up to 30 nmol) or cataplexy (up to 120 nmol) was observed after ICV hypocretin-1 in Hcrtr 2-mutated narcoleptic Dobermans . (2) IV administration rapidly increased plasma hypocretin-1 from undetectable (< 40 pg/ml) to very high levels (1.2 µg/ml). In contrast, no significant increase in CSF hypocretin-1 levels were observed at the dose range used in previous IV studies. Higher doses (96 to 384 µg/kg IV) increased hypocretin-1 levels in the CSF up to 2.4 fold, but this increase was small when compared to that observed in the plasma (>30,000 fold). (3) IV administration of hypocretin-1, up to 24 µg/kg, did not suppress cataplexy in ligand-deficient sporadic dogs. However, at doses higher than 48 µg/kg, hypocretin-1 partially suppressed cataplexy, but the effect lasted less than 30 minutes.

Conclusions: ICV administration of hypocretin-1 significantly increases wakefulness and reduces SWS and REM sleep in control, but not in narcoleptic Dobermans. Only a very small fraction of IV administered hypocretin-1 penetrates in the central nervous system. Higher IV doses of hypocretin-1 (48 to 386 µg/kg i.v.) induce only a short-lasting anti-cataplectic effect in hypocretin-deficient narcoleptic dogs. The development of more stable and centrally penetrable hypocretin analogs will be necessary to reverse the central hypocretin deficiency seen in human narcolepsy.

0723.K

Treatment Of Cataplexy With Sodium Oxybate: Transition From Tricyclic Antidepressants (TCAs) And Selective Serotonin Reuptake Inhibitors (SSRIs)

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Introduction: TCAs and SSRIs have been used for the treatment of cataplexy and other REM-related symptoms of narcolepsy with varied success. These agents may cause numerous side effects, tolerance and "rebound cataplexy" which limit their usefulness. A new medication, Xyrem® (sodium oxybate), Orphan Medical Inc. was recently approved by the FDA for the treatment of cataplexy associated with narcolepsy. The following clinical observations support initiation of sodium oxybate prior to discontinuing TCAs or SSRIs.

Methods: This 6-month study was conducted to evaluate safety and efficacy of sodium oxybate in narcolepsy patients. Patients entered the study while being treated with stimulants, TCAs and/or SSRIs. Sodium oxybate was added to these regimens at a total dose of 4.5 g nightly taken in equally divided doses, at bedtime and 2.5–4 hours later. Sodium oxybate was then titrated to an optimal dose with changes in dose occurring at 2–4 week intervals, in 1.5 g increments but staying within the range of 3–9 g. Investigators were encouraged to decrease or discontinue TCAs and SSRIs after the optimum dose of sodium oxybate was established. Patients were permitted to remain on stable doses of stimulant medications throughout the trial. Narcolepsy symptoms and adverse events were evaluated by clinical evaluation, laboratory measures and subjective reports using the Narcolepsy Symptom Assessment Questionnaire (NSAQ).

Results: One hundred eighty five narcoleptic patients participated in this study, at 26 sites (180 for efficacy analysis). Ninety-one patients (51%) were treated with TCAs and/or SSRIs during the study. Seventy-two patients used antidepressants for control of their REM-related symptoms and 19 patients used them for unrelated disorders. Forty-three patients used TCAs and 36 patients used SSRIs; seven patients were on both; one used two TCAs. The mean time to reach the optimal sodium oxybate dose was: 18, 17, 37, 60 and 80 days for patients requiring a 3.0 g, 4.5 g, 6.0 g, 7.5 g and 9.0 g dose, respectively. Changes in the antidepressants were allowed after the optimal dose of sodium oxybate was achieved. The following changes in antidepressant use were observed: 40% discontinued, 33% decreased, 21% had no change in TCA use while 2% had another TCA added; 28% discontinued, 25% decreased, 36% had no change in SSRI use, while 8 % had another SSRI added. Nine patients (12.5%) required an increase in sodium oxybate because of a mild increase in cataplexy attacks following discontinuation of their antidepressant.

Conclusions: These results indicate that the treatment of cataplexy with sodium oxybate can be initiated while patients remain on TCAs and/or SSRIs. The decrease or withdrawal of antidepressants may be recommended after the optimal dose of sodium oxybate has been achieved. The dose of sodium oxybate may need to be increased in some patients experiencing a mild increase in cataplexy following antidepressant withdrawal.

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0724.K

CSF Hypocretin (Orexin) Levels in Subjects Without Narcolepsy: Relationship to the HLA DQB1*0602 Allele

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Introduction: Reduced levels (110 pg/ml) of cerebrospinal (CSF) hypocretin are regarded as highly specific (99%) and highly sensitive (87%) for narcolepsy with typical cataplexy (Mignot, 2002). The association with the HLA DQB1*0602 is less understood, although in narcolepsy patients, with and without cataplexy, a statistically significant relationship has been observed (Krahn, 2002). This relationship is important because this HLA allele is suspected to confer susceptibility for narcolepsy. Previous work has shown an association between reduced initial REM latency and the DQB1*0602 allele in normal subjects (Mignot, 1999). We hypothesized that CSF hypocretin 1 levels would be lower in non-narcoleptic subjects with the DQB1*0602 allele compared to those without this marker.
Methods: This ongoing study examines CSF hypocretin 1 levels in 26 non-narcoleptic subjects. The patients were undergoing the lumbar punctures as part of a diagnostic assessment for a variety of neurologic disorders. Using the Wilcoxon rank sums test, the values from the 9 subjects with the DQB1*0602 allele (35%) were compared to the 17 without (65%). Hypocretin values were determined using extracted CSF utilizing a single radioimmunoassay kit (Phoenix Pharmaceuticals, Mountain View, CA). Assessing larger samples sizes by combining specimens run in different batches has been difficult because of inconsistent control data obtained with different lots of radioimmunoassay kits.
Results: Subjects with the DQB1*0602 allele had a median value of 688 pg/ml (range 584-855) as compared to 763 pg/ml (range 613-924) for subjects without this allele. There was not a statistically significant difference (p=0.22).
Conclusions: In this small sample, there is no statistically significant difference in CSF hypocretin levels in non-narcoleptic subjects. Larger sample sizes need to be examined in the future in order to understand if a relationship exists between lower hypocretin levels and the DQB1*0602 allele analogous to the association previously reported between this HLA allele and reduced REM latency in subjects without narcolepsy.

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0725.K

Pharmacological Rescue Of Narcoleptic Orexin-Neuron Ablated Mice

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Introduction: Human narcolepsy is a debilitating, lifelong neurological disease characterized by excessive daytime sleepiness and symptoms of abnormal REM sleep, such as cataplexy, sleep paralysis, and sleep onset-associated hallucinations. Excessive daytime sleepiness and cataplexy are currently treated using amphetamine-like stimulants or modafinil and antidepressants, respectively, although they have limitations in their therapeutic capability. Recent studies have established that human narcolepsy is caused by failure of signaling mediated by orexin (hypocretin) neuropeptides. This raises the possibility that orexins or orexin receptor agonists are useful for treatment of narcolepsy. In this study, we showed rescue of narcolepsy-like phenotype in orexin-neuron ablated mice (orexin/ataxin-3 mice) by ICV administration of orexin-A.
Methods: For scoring of cataplexy-like behavioral arrests, orexin/ataxin-3 mice (16-19 weeks old males, obtained from intercross between 129/SvEv and C57Bl/6J) were implanted with a guide cannula into the left lateral ventricle. Mice were injected with vehicle or orexin-A immediately before onset of dark phase, then transferred to the novel environment and videotaped for following 3 hr. For EEG/EMG recording following ICV administration, 3 wild type and 4 orexin/ataxin-3 mice were implanted with an EEG/EMG implant and a guide cannula. Mice were injected immediately before onset of dark phase or 3 hr after onset of light phase, then recorded for the following 24 hr. All experiments were carried out after at least 10-day recovery period of surgery using a randomized crossover design with vehicle or orexin-A.
Results: ICV administration of orexin-A clearly suppressed cataplexy-like behavioral arrests in orexin/ataxin-3 mice. Several episodes of behavioral arrests were seen in 5 orexin/ataxin-3 mice when administered with vehicle (2-37 episodes per 3 hr, median 5), while only one brief episode was observed in 1 out of the same 5 individuals when administered with orexin-A (3 nmol ICV). EEG/EMG recording revealed that ICV administration of 3 nmol orexin-A maintained wakefulness for more than 2 hours after administration and suppressed NREM and REM sleep in the first 3 and 4 hours, respectively, in orexin/ataxin-3 mice regardless of injection time. Orexin-A administration was less effective in wild type mice.
Conclusions: Here, we showed that ICV orexin-A administration suppresses cataplexy-like behavioral arrests and stabilized wakefulness, the latter indicating suppression of the possible sleepiness, in orexin/ataxin-3 mice. Therefore, orexin/ataxin-3 mice sustain ability to respond to orexin peptides and delivery of these peptides throughout the brain is sufficient to rescue the narcoleptic phenotype of these mice. This finding is consistent with our observation that ectopic overexpression of an orexin transgene rescues narcolepsy in orexin/ataxin-3 mice. As most human narcolepsy is thought to result from the specific degenerative loss of orexin neurons, orexin/ataxin-3 mice are the most pathophysiologically accurate model of narcolepsy available. Our results with this model suggest the therapeutic value of orexins and agonists of orexin receptors for the treatment of human narcolepsy.

0726.K

Polysomnographic Evidence For REM Dysfunction In Non-Narcoleptics

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Introduction: In 1978, REM periods in two or more naps during a multiple sleep latency test (MSLT) were proposed as indicative of narcolepsy. Subsequently, SOREMPs were shown to be much less specific for narcolepsy, being found in cases of moderate to severe obstructive sleep apnea (OSA). Rosenthal et al. found two or more SOREMPs during MSLT in 20 young, normal, asymptomatic men. Aldrich, however, found that 3 or more SOREMPs had high specificity for narcolepsy if sleep latency under 10 minutes, and that SOREMP on nocturnal polysomnogram (PSG) was also highly specific. Occurrence of SOREMPs in non-narcoleptics is still poorly understood and little has been written about contributing factors. The data of Rosenthal et al. have not been replicated. We searched our database for SOREMPs in patients who were not narcoleptic and did not have significant OSA.
Methods: Between 1998 and 2001, we found 8 patients out of 2000 who had PSG and MSLT, and who met inclusion criteria: 1) 3 or more SOREMPs on any combination of MSLT and PSG or 2 SOREMPs on MSLT with REM latency under 60 minutes on PSG; 2) apnea-hypopnea index (AHI) under 20; and 3) no cataplexy or ancillary symptoms. All patients snored and most reported excessive daytime sleepiness and witnessed apneas. Demographic and polysomnographic parameters were tabulated and clinical history and physical examination were reviewed.

Special attention was directed toward: 1) HLA typing: an absent marker would make narcolepsy much less likely; 2) Measures of sleepiness: an ESS < 10 or MSLT average latency > 5 minutes would argue against narcolepsy; 3) Age and duration of sleepiness: older age and shorter duration decrease the probability of narcolepsy.
Results: Age (eight patients) ranged from 24 to 64; five were older than 35. ESS was recorded in seven patients and was below 10 in five patients. MSLT average latency ranged from 1.9 to 9.8 minutes. Number of SOREMPs during MSLT was 2 in four patients and 3 in four patients. SOREMP during PSG occurred in three patients (1.5, 4, and 11 minutes). REM latency for remaining patients was 47.5 to 210 minutes. Duration of sleepiness was known in only five patients – five years or less in four patients. AHI was 0-15 (< 10 in four patients); lowest SaO2 was 75-93%. HLA testing was performed in six patients: negative in three. Six of eight patients had three SOREMPs: two had two SOREMPs on MSLT and REM latency between 20 and 60 minutes. Three patients reported head trauma with loss of consciousness. Two patients had bipolar disorder.
Conclusions: Our patients are distinctive because REM abnormalities were not accompanied by clinical evidence for narcolepsy. Even patients with 3 SOREMPs did not have convincing symptoms of narcolepsy. Further work is necessary to clarify how different mechanisms can lead to SOREMPs.

0727.L

Modifications Of Sleep Parameters Under An Intermittent Treatment Regimen With Zolpidem

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Introduction: There is growing evidence that the non-nightly use of hypnotic agents in chronic insomnia is as efficacious on subjective sleep quality as continuous medication. Limited information is available, instead, on the objective modifications of sleep parameters when hypnotic drugs are administered on a discontinuous basis.
Methods: Six patients (3 M and 3 F, aged 32.8 ± 9 yrs.), suffering from sleep-maintenance primary insomnia and accepting the protocol regimen, were recruited for the study. For each patient, an adaptation polysomnographic (PSG) recording (night 0) was carried out to allow acquaintance with the sleep lab and exclude the presence of sleep-related breathing disorders, periodic limb movements or other sleep disorders. A baseline recording (night 1), without placebo or active medication, was followed by 6 consecutive recordings based on the alternation of 3 nights with active treatment, i.e. Zolpidem 10 mg in tablet (nights 2, 4, 6), and 3 nights with placebo in tablet (nights 3, 5, 7). The patients were blind on the tablet content. A morning questionnaire evaluated the quality of the previous night sleep. Statistical analysis was based on a 2-way ANOVA test integrated by Bonferroni comparisons. Correlations with subjective sleep quality were measured for PSG parameters showing significant F values.
Results: Subjective sleep quality was globally modified ($p < 0.0001$). In particular, compared to baseline, sleep quality was reported as significantly improved under Zolpidem (nights 2, 4, 6) and as not worsened by placebo (nights 3, 5, 7). Overall, sleep latency and REM sleep showed no significant modifications, whereas sleep efficiency ($p < 0.0001$) and CAP rate ($p < 0.0001$) showed global changes with significant differences between baseline and all the Zolpidem nights. Significant overall modifications involved also slow wave sleep ($p < 0.0001$) and total arousals ($p < 0.0001$), but significant differences with baseline values were found only on night 4 for arousals and on nights 4 and 6 for slow wave sleep. Objective sleep parameters never worsened under placebo compared to baseline. Subjective sleep quality correlated linearly with CAP rate ($r = - 0.60$), slow wave sleep ($r = 0.48$) and sleep efficiency ($r = 0.47$).
Conclusions: Intermittent treatment allowed us to quantify the objective efficacy of the hypnotic agent on a multi-night basis. The present regimen indicated not only absence of objective rebound insomnia during placebo, but also lack of tolerance as PSG parameters improved during all Zolpidem nights. Compared to baseline, a significant increase of sleep efficiency and a significant reduction of sleep instability (CAP rate) occurred already during the first Zolpidem night. Significant improvement of slow wave sleep and sleep fragmentation (arousals) emerged only during the second night of active medication. This 1-week intermittent schedule can be the first step of an alternative procedure for monitoring the objective impact of long-term drug treatment in chronic insomnia.

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0728.L

Physiological Activation in Situational Insomnia

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Introduction: Situational insomnia (SI) is defined as poor sleep produced in an otherwise normal sleeper in response to specific environmental or stress factors. It has been hypothesized that chronic insomnia develops in response to repeated episodes of SI. However, little research has examined the nature of SI. Previous work has shown that SI, as defined by EEG criteria, is a robust and stable phenomenon. The current study examined physiological measures (heart rate, heart rate variability and VO2) in young adults identified as having SI in comparison with good sleepers.
Methods: Fifty normal young adults (age 23 +- 5) participated. Subjects slept in the lab for a screening night followed by a baseline night and advanced sleep night (advance of normal bed time by 3 or 6 hours). On the following week, Ss returned for another baseline and advanced sleep night (whichever advance was not given in the first week). Ss remained in the lab for the day after each night for MSLT and physiological measurements . Heart rate and metabolic data were collected for 20-minute periods immediately after awakening each morning and after each of the four MSLT observations.
Results: Extreme groups were formed based upon Ss with the best sleep (top 25%, n = 13; sleep efficiency was 97%) and the worst sleep (bottom 25%, n = 12; sleep efficiency was 82%) on the screening night. All subjects were required to display normal sleep on baseline nights (Sleep efficiency respectively 94 versus 91% - difference not significant). Significant group differences were not found for any mood or personality variable. Significant group by condition interactions were found for Heart Period ($F=11.02$), Low Frequency Spectral EKG Power (LFP: $F=12.81$) and High Frequency Spectral EKG Power (HFP: $F=18.10$). Newman-Keuls pairwise comparisons indicated that Heart Period was significantly shorter in SI Ss following baseline sleep nights (transformed to a heart rate of 64.3 versus 62.6 BPM in SI Ss versus best sleepers). SI Ss also had significantly increased LFP after both advance sleep nights and significantly decreased HFP after baseline and the 3-hour advance night. VO2 was increased in SI Ss compared to best sleepers but the difference (281 versus 271 ml/min) was not statistically significant.
Conclusions: These data indicate that normal sleepers predisposed to SI have elevated heart rate, increased LFP (an indicator of sympathetic nervous system activity), and decreased HFP (an indicator of parasympathetic nervous system activity) compared to good sleepers. Similar changes have been found in patients with psychophysiological insomnia. However, the finding of physiological activation in noncomplaining individuals with SI implies that physiological activation may precede the development of both chronic sleep problems and the subjective and personality symptoms associated with psychophysiological insomnia.

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0729.L

Management of Hypnotic Dependent Insomnia in Older Adults

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Introduction: Hypnotic-dependent insomnia is characterized by sustained hypnotic use and return of insomnia. The present clinical trial used psychological interventions and a placebo control to treat hypnotic dependence in older adults, a group that uses hypnotics at a disproportionately high rate and is particularly vulnerable to hypnotic side-effects. This is an update of preliminary data presented last year.

Methods: Volunteers were recruited by media announcements. Volunteers were age 50 or older, reported current insomnia, used prescription hypnotics for at least 6 months, and were free of sleep-active medical or psychiatric disorders or substances (other than the designated hypnotic). We now report on 28 participants. By meeting time, we will have data on at least 45 participants. The present sample is composed of 18 women and 10 men. They averaged 65 years of age (SD = 9), they have been taking hypnotics an average of 4 years (SD = 4), and they have experienced insomnia an average of 10 years (SD = 9). About half the participants were using benzodiazepines, a fourth nonbenzodiazepine hypnotics, and a fourth sedating anti-depressants. Participants were randomized to scheduled gradual hypnotic withdrawal (HW) supplemented by eight sessions of psychological treatment (PT, relaxation, stimulus control, and sleep hygiene)[designated HW/PT], hypnotic withdrawal supplemented by placebo EEG biofeedback, or hypnotic withdrawal only.

Results: ANOVAs on two weeks of sleep diaries comparing the three groups at baseline and posttreatment found significant interactions for wake time after sleep onset, sleep efficiency %, and sleep quality rating. In these three analyses, HW/PT exhibited improved sleep, and the other two groups changed little. For self-reported hypnotic consumption (mean number of daily units of a medication's lowest recommended dose, LRD), significant findings occurred only for the main effect of time. For the three groups considered jointly, medication use went from 2.1 LRD at baseline to 0.3 LRD at posttreatment, an 84% reduction. There were no significant pre-post changes in all 12 PSG measures including five sleep pattern variables and seven sleep stage variables. The absence of PSG change occurred despite a hypnotic advantage at baseline. 96% of participants took sleep medication during baseline PSG nights, compared to 21% during posttreatment PSGs.

Conclusions: Older adults who are chronic users of prescription hypnotic medication are receptive to gradual medication withdrawal, attained substantial medication reduction, and suffered no posttreatment worsening of sleep by their self-report. When withdrawal is supplemented by behavioral treatment, self-reported sleep improves. Similarly, PSG monitored sleep exhibited no deleterious effects concurrent with substantial hypnotic reduction. Both self-report and PSG data support the conclusion that chronic hypnotic use is therapeutically inert.

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0730.L

Insomnia as a Risk Factor for Depression in the Elderly

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Introduction: There are seven studies that provide evidence that insomnia is a significant risk factor for recurrent and new onset Major Depressive Disorder (MDD). Two of the seven studies suggest that, despite the increased prevalence of insomnia in the elderly, it remains a significant predictor of future morbidity. In the present study, we evaluated archival data from a community sample of 250 healthy elderly subjects (original data from grant MH01113, PI: JL) in order to further assess the extent to which insomnia predicts future illness in older adults.

Methods: Subjects age ³ 60 years were recruited from primary care settings (age 71.7 ± 7.2, 56.5% female, 94% Euro-American). Psychiatric diagnoses were determined at study intake and at one-year follow-up using the Structured Clinical Interview for the DSM-III-R. 131 subjects at study intake had no history of mental illness. This sub-sample was divided into three groups based upon the items on the Hamilton Rating Scale for Depression that pertain to sleep disturbance. The groups were (1) no insomnia; (2) transient insomnia (present at intake but not at follow-up); and (3) persistent insomnia (present at both intake and follow-up).

Results: Of the 131 individuals at study intake with no history of mental illness, 66 were classified as having "no insomnia" (50.4%), 31 had "transient insomnia" (23.6%), and 34 had "persistent insomnia" (25.9%). 11 new onset episodes of MDD developed during the one-year follow-up period. Of the 11, two of the people had no insomnia (18%), three of the people had transient insomnia (27%), and six of the people had persistent insomnia (55%). Thus, 9 out of the 11 (82%) new cases of depression were associated with some form of pre-existing insomnia. A contingency analysis of these data show that these increased proportions of morbidity relative to insomnia were significant ($p < 0.04$). Of the six people with persistent insomnia, none showed initial or mixed insomnia, two showed persistent terminal insomnia (33.3%), and four showed persistent middle insomnia (66.6%).

Conclusions: These data suggest that subjects with persistent insomnia are at five times greater risk for the development of new onset Major Depression. The measure however, while sensitive, does not appear specific. Approximately 50% of the subjects with no history of psychiatric illness reported insomnia and only about 17% (11 of 65) of these subjects went on to develop a new onset episode. It remains possible that the "surviving" group differed on type or severity of insomnia and/or that given a longer monitoring period more of the 32% of the subjects with insomnia would go on to develop MDD (and at a higher rate than subjects without insomnia).

0731.L

Use of Cognitive-Behavioral Treatment for Comorbid Insomnia in Older Adults: Preliminary Data

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Introduction: Controlled clinical trials have demonstrated the efficacy of cognitive-behavioral treatment (CBT) programs in the treatment of older adults with primary insomnia. However, in clinical practice, many older adults with insomnia also have co-morbid medical illness. These patients are presumed to have secondary insomnia, and the traditional approach to the treatment of their insomnia is to focus on the primary disorder. This clinical trial was designed to test the efficacy of CBT in the treatment of insomnia in older adults with medical illness.

Methods: Fifty patients over the age of 55 with insomnia and either COPD, osteoarthritis, or CAD were randomized to an 8-week CBT treatment program that incorporated sleep restriction, stimulus control, sleep hygiene, relaxation training, and cognitive restructuring, or to a wellness class that emphasized stress management skills, nutrition, and exercise. Sleep diaries, actigraphy, and in-home polysomnography were used to assess sleep pre-treatment, post-treatment, and at a one-year follow-up. Partial data are available as the trial is ongoing.

Results: Data from the sleep diary measures are presented here as the

actigraphy and polysomnography is still undergoing analysis. The pre-treatment sleep efficiency was 72.3% (SD=13.2) and 68.0% (SD=14.6) for the CBT group and wellness group, respectively. Sleep efficiency improved significantly (p's <.05) for both groups to 84.5% (SD=8.5) and 76.6% (SD=15.7). Total sleep time also improved significantly (p's<.05) from 345 (SD=68.9) minutes to 373 (SD=61.7) minutes for the CBT group and 323 (SD=82.5) minutes to 373 (SD=79.7) for the wellness group. Sleep onset latency was also significantly reduced (p's <.05) from 54 (SD=61.4) minutes to 24 (SD=20.7) minutes for the CBT group and from 36 (SD=26.6) minutes to 26 (SD=22.6) minutes for the wellness group. There were no significant differences in changes in self-report sleep variables between the two groups.

Conclusions: These preliminary data demonstrate that CBT is an effective treatment with older adults with comorbid insomnia. Contrary to our hypothesis, thus far the data suggest that a wellness class also provides a significant self-reported sleep benefit. Analysis of the objective measures of sleep, as well as the one-year follow-up data, is needed to further define the scope of this improvement in sleep. The study will ultimately enroll 120 patients and allow for sub-analysis of subject factors (e.g., medical condition, age, and insomnia severity) that may predict response to treatment.

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0732.L

Perceived Sleep Quality in Adult Population Residing in Mexico City

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Introduction: In several series insomnia or difficulty to sleep well has been reported in 30-50% of the population. Women are more frequently affected. There is no reason to believe that this should be different in residents of Mexico City. The aim of this study was to determine the prevalence of insomnia, snoring and to describe how sleep is perceived in a sample of the general population.

Methods: Mexico among other countries in the world celebrated the International Sleep Day on March 21st of 2002. A media campaign was conducted to increase the awareness and the importance health wise, of favoring a good sleep. The same week a survey was conducted during 2 days in malls. A booth was installed in 2 centrically located malls, and people was openly invited to complete a questionnaire on sleep habits, insomnia, snoring and daytime sleepiness.

Results: A total of 2353 subjects participated voluntarily. 917 questionnaires were excluded for important missing data, and those corresponding to subjects younger than 20 years old. The sample consisted in 1356 questionnaires. Mean age was 37.8 /pm 12.9 years (20-85). Distribution by gender was of 617 males (45.5%), and 739 females (54.5%). For females the referred sleep quality was as good in 52.2%, bad in 45.4%, and 2.4% did not answer. For the male group, sleep quality was considered as good in 54.4%, as bad in 43.4%, and 2.2% declined to answer. A slight higher proportion of females admitted a bad quality of sleep, but there was no significant difference between gender and sleep quality. 21% of the sample admitted taking longer than 30 minutes to fall asleep. 10.6% of the sample reported having more than 4 awakenings during the night. Sleep time was reported being on average > 7 hours per night in 45%, 5-6 hours per night in 46%, and < 5 hours per night in 10.5%. Only 8% of the sample admitted a visit to the doctor because of insomnia, but only 2.8% reported having taken an OTC medication or herbal remedies to help them to sleep. Snoring more than 3 nights per week was reported in 20%. Frequent witnessed apneas was reported in 6% of the sample, with a higher frequency in males.Daytime sleepiness assessed by a simple question was admitted in 30% of the sample. The mean score in the Epworth Sleepiness Scale was 7.74 /pm 4.82.

Conclusions: A high percentage of the general population perceives having a bad quality of sleep, and one third complain of feeling sleepy during the day. Half of the population in this sample sleep less than 6 hours per night. A small percentage visited a physician because of insomnia, and even less have taken a prescribed or OTC medication as an sleep aid.

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0733.L

Acupuncture Reduces Depressive And Insomnia Symptoms, And Increases Nocturnal Melatonin Secretion

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Introduction: The close relationship between insomnia and depressive symptoms is well established. Many studies have indicated that patients with chronic sleep problems have impaired mood and that effective management of insomnia in these cases can markedly reduce depressive symptoms. Benzodiazepines are often used in depressed patients. The side effects of benzodiazepines however are well known. The aim of the present study was to determine if acupuncture, which has a comparatively limited side effect profile, could address these concerns. Specifically we sought to ascertain if acupuncture could reduce insomnia and associated psychological conditions, including depressive symptoms, in subjects whose primary complaint was insomnia and "life stress". Another goal was to measure acupuncture's potential effects on nocturnal melatonin secretion, a biochemical marker of circadian activity which is also affected by depressive and anxious symptoms.

Methods: Eighteen adult subjects who complained of insomnia and who met test criteria for above normal anxiety on the Zung Anxiety Scale were assessed in an open clinical trial design. The subjects had sub-syndromal depressive symptoms, i.e., did not meet formal (DSM-IV) criteria for a depressive disorder. Their response to five weeks of acupuncture treatment (two treatments per week, ten treatments in total) was evaluated on a before and after basis. This included their responses to psychometric measurement of depressive and anxious symptomatology (CES-D and the STAI), polysomnographic recordings of their sleep profile, and 24-hr. measures of urinary melatonin secretion.

Results: Acupuncture treatment was associated with significant improvements in depressive symptoms on the CES-D (p = .001). Both state and trait anxiety scores were significantly improved (p = .049 and p = .004). Changes in urinary melatonin concentrations were also found. Post test analysis showed a significant increase (p = .002) of nocturnal urinary 6-sulphatoxymelatonin (aMT6s) concentrations over baseline values, while daytime (morning and early afternoon) levels dropped to below baseline levels (p=.037), both changes representing a trend toward physiological normalization. Improvements were found in most polysomnographic parameters of sleep architecture and continuity. Sleep onset latency and the arousal index dropped significantly (p = .003 and p = .001, respectively). The total sleep time and sleep efficiency were similarly improved (p = .001 and p = .002, respectively). Some improvement in sleep quality was confirmed by the increase in the amount of time spent in stage three sleep (p = .023), but the amount of stages one, two, four and REM sleep did not change significantly in the before-after comparison. There were no changes in REM sleep latency following acupuncture.

Conclusions: Objective findings of sleep improvement and the parallel reductions in depression and anxiety scores support the conclusion that acupuncture may represent an alternative to pharmaceutical therapy for some categories of patients with depressive symptoms. One of the limitations of the study however was its lack of a control group. The find-

ings thus need to be confirmed with a study using a more rigorous design.

0734.L

Polysomnographic and REMview Assessment of Treatment Outcomes in Patients with Insomnia

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Introduction: Outcomes assessment for insomnia treatment has been limited by treatment variability between patients, and subjective rather than objective measures of outcomes. The primary aims of this study were:1) To compare polysomnographic indices in patients with insomnia before and after a 9-week standardized and structured comprehensive insomnia treatment program2) To validate an ambulatory device (REMview, Respironics, Inc.) that estimates sleep parameters using recorded eye and head movements

Methods: The major inclusion criteria for the study were age 21 years or older and a diagnosis of insomnia, with symptoms (initiation or maintenance difficulties for greater than 30 min at least 3 nights per week, a sleep efficiency of less than 80 percent or a total sleep time less than 6 hrs, and at least 1 negative daytime complaint associated with insomnia) for at least 6 months.All subjects signed informed consent forms approved by the local institutional review board. A total of 19 subjects underwent comprehensive, laboratory polysomnograms (PSGs), during 2 consecutive baseline nights and 2 consecutive experimental nights. A standardized and structured 9-week (7 weeks of sessions with two 1-week breaks) insomnia treatment program occupied the interval between these two sets of polysomnograms. The program met once a week for 1.5 hours and was led by a psychologist specializing in behavioral treatment for insomnia. If a subject failed to participate in more than one of the weekly insomnia workshops, they were required to participate in a comparable make-up session.For the pre- and post-treatment PSG study, 76 PSGs (19 subjects x 4 studies apiece) were analyzed. For the REMview (RV) validation study, a total of 73 simultaneous PSG and RV recordings from subjects either enrolled in the study or who subsequently did not meet inclusion criteria were also evaluated.

Results: For the PSGs, using Wilcoxon matched-pair signed-rank test, following insomnia treatment (2-night pre- and post-treatment means, p values):1) A significant decrease in the sleep latencies (23.1 to 11.3 min, 0.014)2) A significant decrease in total sleep time (380.9 to 344.1 min, 0.001)3) Non-significant trends toward an increase in sleep efficiency (0.838 to 0.844) and NREM sleep percentages (62.7 to 65.8) and a decrease in REM sleep percentages (20.4 to 19.9)For the PSG versus RV data, using paired t-tests (sleep parameter means, p values):1) Significant differences in sleep latencies (17.3 vs 43.3 min, < 0.001) and REM sleep percentages (18.9 vs 38.0, < 0.001)2) No significant differences between total sleep time (342.3 vs 337.3 min), NREM sleep percentages (62.7 vs 70.8), and sleep efficiency (79.5 vs 78.3)The subjects reported subjective improvement in the quality of their sleep via analysis of sleep diaries.

Conclusions: PSG data revealed significant improvement in sleep latencies for 19 subjects following behavioral insomnia treatment. There was also a significant decrease in total sleep time, and a subjective improvement in sleep quality. The REMview device compared favorably with polysomnography, offering a new ambulatory tool for insomnia evaluation.

Research supported by Respironics, Inc.

0735.L

Prevalence of Insomnia in Patients with Obstructive Sleep Apnea Syndrome (OSAS)

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Introduction: OSAS and chronic Insomnia are both common disorders of sleep, and both have very significant associated health costs. Little is currently known about the prevalence or impact of Insomnia in patients with OSAS. Limited previous research has indicated a potentially high rate of comorbidity between these two disorders. OSAS disrupts sleep continuity and may therefore precipitate and perpetuate Insomnia. Sleep fragmentation due to Insomnia may increase respiratory instability, exacerbating OSAS. However, the interaction between these disorders is currently not well understood. This study examined the prevalence of Insomnia in OSAS patients, and assessed related health factors including mood and beliefs about sleep.

Methods: 110 consecutive OSAS patients (new & treated) attending an outpatient clinic attached to a public hospital sleep unit completed a brief battery of standardised and validated questionnaires, assessing sleep and mood. The battery included the Insomnia Severity Index (ISI), the Dysfunctional Beliefs & Attitudes about Sleep Scale (DBAS), Depression-Anxiety-Stress Scales, and the Survey Screen for Prediction of Apnea (SSPA). The Latin-square method was used to control for order effects. Habitual sleep was assessed with the Pittsburgh Sleep Diary (PghSD). OSAS status was further assessed via clinical interview and standard overnight PSG. The research criteria for Insomnia were designed to address DSM-IV and ICSD-R diagnostic criteria, and included: (a) ISI score > 15 (moderate severity), (b) length of insomnia complaint > 6 months, and (d) at least one negative daytime consequence of sleeplessness.

Results: 32% of all participants met criteria for Insomnia. Mean ISI rating for the OSAS only group was 3.5 ± 3.0(SD), and OSAS+Insomnia group 17.4 ± 1.5(SD). This proportion did not differ in patients who had been conventionally treated (typically CPAP). Reported levels of Depression, Anxiety and Stress were significantly increased in the OSAS+Insomnia group (95% CI: -9.1 to -3.0, -8.3 to -2.2 & -9.6 to -4.6). Reported apnea symptom ratings (SSPA), were also greater in the OSAS+Insomnia group (CI: -17.9 to -6.7). Both groups reported similar beliefs about the consequences of poor sleep (DBAS). There was no difference between the groups in RDI (Mean=31.1, CI: -7.5 to 28.2)

Conclusions: A high proportion of this OSAS population reported 'moderate' or greater levels of clinical Insomnia according to conservative criteria. That is, they had significant problems with getting to sleep or staying asleep, in addition to their reported OSAS symptoms. The proportion of patients with a significant complaint of Insomnia did not diminish with conventional treatment of OSAS. Thus, these patients had an ongoing significant sleep disorder. The increased levels of depression, anxiety and stress found in the OSAS+Insomnia group suggest that mood may be a factor in the management of this group. Comorbidity of Insomnia in OSAS patients may lead to increased symptom severity, and may also complicate standard treatment. Assessment and management of Insomnia should be incorporated into the standard clinical practice of sleep units.

0736.L

Studio Morfeo: Clinical And Therapeutic Management Of Insomnia By Italian General Practitioners

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Introduction: Insonnia is the most frequent sleep disorder among the general population and represents a heavy burden for the general practictioner (GP). The management of insomnia varies according to the national heath service of the single countries and therefore requires local epidemiological surveys. We present the findings of Studio Morfeo 2, an investigation carried out by the Italian Association of Sleep Medicine (AIMS) and GPs to explore the clinical and therapeutic management of insomnia in the primary care setting.

Methods: A total of 582 GPs, adequtely trained at 16 Centers of Sleep Medicine distributed across the national territory, administered a brief questionnaire (Q1) including 5 questions (4 on sleep symptoms and 1 on the habitual use of sleep-promoting medication) to the first 10 patients who visited their office each day of a standard working week. The first patient of each day classified as insomniac and providing written consent underwent a second more detailed questionnaire (Q2) investigating demographics, socio-economic status, medical situation and clinical characteristics of insomnia.

Results: Q1 was submitted to a total of 26,919 patients, 10.992 (41%) of which were classified as insomniacs. Q2 was appropriately administered to 2,755 (25%) of the insomniac patients interviewed with Q1. In most cases, insomniac patients complained of difficulty falling asleep, reported occurrence of the disturbance at least 3 times/week and 2 or more symptoms of insomnia. A total of 1,211 insomniac patients were treated (either drug or non-pharmacological therapy) and 1,544 were completely untreated (NT). Sixty-six patients were exclusively under OTC or a non-pharmacological regimen (behavioral therapy, psychotherapy). Of the 1,145 patients under medication for insomnia, 69% reported a favorable outcome (responders), while 31% were non-responders. GPs were not informed of insomnia in 15% of the treated patients and in 75% of the NT patients. In NT patients, the GP decided to refrain from treatment in 33% of the cases because the patient opposed to drug therapy and in 22% of the cases because insomnia was not considered by the GP as a severe disturbance. For 92% of responders, GPs decided to confirm the ongoing treatment (52% were taking hypnotics, 64% anxyolitics, 26% antidepressants) versus 27% of non-responders. For the remaining 73% of non-responders, additional solutions consisted of dosage increase (26%), drug change (22%), add-on (18%). In 44% of the NT patients, a treatment was introduced under direct request of the patient or for a worsening of insomnia and daytime dysfunction.

Conclusions: The present survey confirms that in the primary-care setting the complaint of insomnia is often underrated both by the patient, who covers the problem or rejects treatment, and by the GP, who limits intervention on the sleep disorder or poorly modifies the ongoing therapy. Anyway, the management of insomnia pertains to the GP, especially in the screening phase and in the initial approach. Thus, an appropriate educational operation based on the knowledge of the clinical and therapeutical procedures of GPs becomes mandatory.

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0737.L

A Pilot Study of Daytime Alertness And Mood In Insomnia Patients Using Ecological Momentary Assesment

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Introduction: Previous studies have not found consistent differences in daytime symptoms of insomnia insomnia compared to healthy controls. One reason for this may be that few studies have examined daytime symptoms of insomnia in the individuals' actual environment using frequent sampling (Ecological Momentary Assessment, or EMA). The goals of this pilot study were: 1) To examine mean levels of subjective alertness and mood in patients with primary insomnia and age-matched controls; 2) To examine variability of alertness and mood between insomnia patients and controls; and 3) To examine correlations between daytime symptoms and self-reported sleep characteristics.

Methods: Subjects included seven patients with primary insomnia (six women, one man; mean age 24.1 years) and eight healthy control subjects (seven women, one man; mean age 23.3 years). Patients and healthy control subjects monitored their sleep-wake habits with a sleep diary and rated their daytime symptoms using an Alertness and Mood Diary (AMD) four times per day for seven consecutive days, in their home environments. Individual items from the AMD were collapsed into five domains: concentration, mood, energy, alertness, and overall feeling. AMD results were analyzed using repeated-measures ANOVA to examine group differences, time of day effects, and group*time of day interactions.

Results: Compared to controls, insomnia patients had significantly lower scores on each of the five AMD domains ($F(1,13)>39.0$, $p<0.0001$ for each). Concentration, energy, and alertness varied significantly by time of day ($F(3,39)>10.5$, $p<0.0001$ for each). Significant group*time of day interactions were observed in each of the domains ($F(3,39)>3.3$, $p<0.05$ for each). Insomnia patients appeared to have particular impairment in the morning, shortly after awakening. Post-hoc testing on morning ratings confirmed lower values in each domain for the insomnia group ($t>5.0$, $df=15$, $p<0.001$ for each). The insomnia group also had significantly larger coefficients of variation on each domain compared to control subjects ($F(1,13)>12.3$, $p<0.004$ for each), with a significant group*time of day interaction only for the alertness domain ($F(3,39)=3.37$, $p<0.02$). No significant correlations were found between AMD ratings and sleep diary measures

Conclusions: EMA demonstrates significantly lower ratings and greater variability in subjective alertness and mood among insomnia patients compared to control subjects, as well as different patterns across the day. Our results raise the possibility that one specific characteristic of daytime symptoms in insomnia is their variability or unpredictability. Therefore, single assessments of daytime alertness and mood taken at random time points during the day may not be an accurate measure of the daytime alertness and mood dysfunction characteristic of insomnia. These pilot study results suggest that EMA may be an important methodology for measuring daytime symptoms in insomnia studies.

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0738.L

Sleep and Cognitive Performance: Gender Differences Among Older Adults with Persistent Insomnia

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Introduction: Insomnia is a prevalent sleep complaint, especially, among women and elderly individuals. Insomnia sufferers report negative daytime consequences associated with their sleep difficulties, complaints which are not always corroborated by objective findings. Objectively, some studies confirm these complaints. The aim of the present study is to examine whether elderly men and women differ in both subjective and objective sleep and daily cognitive performance.

Methods: 30 men and 30 women aged 55 and over were evenly assigned to one of three groups: 20 insomnia sufferers (INS), 20 insomnia sufferers using benzodiazepines (BZs) chronically (INSBZ) and 20 good sleepers (GS). Participants had a mean age of 62.5 years (SD 5.8 years) and a mean education level of 13.4 years (SD: 3.7 years). Insomnia sufferers reported a mean duration of insomnia of 25.8 years (SD:15.7 years). Chronic BZ users had been using medication for 13.5 years (SD: 10.0 years) for a mean average of 6.6 nights/week (SD: 1.1 nights/week). Subjectively, daytime sleepiness was evaluated with Stanford Sleepiness Scale and Visual Analog Scales while sleep was evaluated with sleep diaries. Objectively, cognitive performance was measured through neuropsychological testing and sleep with polysomnography. MANOVAs were run for between groups comparisons and multiple comparison tests were used when indicated.
Results: Objectively, significant groups differences in sleep were observed as well as between men and women. Men had greater objective sleep difficulties than women. Subjectively, both groups of insomniacs reported greater sleep difficulties than GS. Regardless of gender, between-group differences were observed in objective cognitive performance. Both groups of insomniacs evaluated more negatively the daily consequences than GS did. Men using BZs reported being less alert, more sleepy than GS. Women using BZs evaluated more negatively their daytime performance than women GS.
Conclusions: Sleep continuity as measured by PSG appears worse in men than in women, but no gender differences are noted in sleep diary measures. Both groups of insomnia sufferers appear to exhibit an altered cognitive performance on tasks measuring attention and working memory. However, objective cognitive deficits do not appear to be attributable to gender. These results also suggest that insomnia and the use of benzodiazepines might influence the evaluation of sleep and performance in daytime cognitive tasks differently according to the gender of the individual.

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0739.L

Phase II Study of the Selective ML-1 Receptor Agonist TAK-375 in a First Night Effect Model of Transient Insomnia

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Introduction: TAK-375 is a novel, highly selective ML-1 receptor agonist being studied for the treatment of insomnia and circadian rhythm sleep disorders. A randomized, double-blind, placebo-controlled design was used to evaluate the efficacy and safety of a single administration of TAK-375 in a first night effect model of transient insomnia.
Methods: Healthy adults (age, 35-60 years; n=375) naïve to a sleep laboratory were enrolled at 14 US sites. Subjects were randomized to receive placebo (PBO, n=123), 16 mg TAK-375 (n=126), or 64 mg TAK-375 (n=126). No group differences in mean age, gender, or race were present. All subjects received a single oral dose of study medication approximately 30 minutes before their habitual bedtime and were monitored by polysomnography for 8 hours. To evaluate residual effects, the digit symbol substitution test (DSST) and subjective measures of alertness and ability to concentrate were completed upon arising. The primary measure of efficacy was latency to persistent sleep (LPS), measured by polysomnography. Safety measures included adverse events (AEs), vital signs, laboratory tests, and electrocardiogram.
Results: Compared to the PBO group, the 16-mg and 64-mg treatment groups had significantly shorter mean LPS (22.6, 12.2, and 13.4 minutes, respectively, P<0.001 for both doses vs PBO) and significantly longer mean total sleep time (TST, 413.3, 427.3, and 424.7 minutes, P<0.05 for both doses vs PBO) as measured by polysomnography. No significant differences between groups were observed for time spent in any sleep stage. Compared to PBO, subjective sleep latency was shorter (P=0.013) and subjective TST longer (P=0.034) in the 16-mg group; there were no differences on these measures between PBO and 64 mg. There was no evidence of residual sedation on the DSST in either active drug group. However, on a post-sleep questionnaire, subjects in the 64-mg group reported small but significant reductions in subjective levels of alertness and ability to concentrate compared with PBO subjects (difference vs PBO, 0.3 point for both measures [7-point scale], P=0.020 and P=0.043, respectively). This effect was not observed with the 16-mg dose. The most common AEs were headache (1.6% [PBO], 7.1% [16 mg], 6.3% [64 mg]), somnolence (2.4%, 4.8%, 2.4%), fatigue (0.0%, 2.4%, 4.0%), nausea (0.0%, 2.4%, 1.6%), and dizziness (0.8%, 2.4%, 0.8%). There were no consistent or clinically important differences in vital signs, clinical laboratory values, or electrocardiogram among groups.
Conclusions: TAK-375 showed statistically significant reductions, at both doses investigated, in LPS in a laboratory model of transient insomnia. No dose-related differences in LPS were observed. There were no consistent differences between groups in number or type of AEs reported.

0740.L

Dysfunctional Beliefs and Attitudes About Sleep (DBAS): Validation of a Brief Version (DBAS-16)

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Introduction: Faulty beliefs and attitudes about sleep play an important mediating role in perpetuating insomnia and should be targeted in treatment. The DBAS was originally designed as an assessment device to identify dysfunctional sleep-related cognitions (Morin, 1993). In its preliminary form, the DBAS contained 30 items that were rated on 100-mm visual analog scales. To refine this instrument and increase its clinical usefulness, we have developed an abbreviated version with a different response format (0-10, Likert-type scale). This paper presents initial validation data of this abbreviated version.
Methods: The sample consisted of 237 individuals (60% of women) aged from 18 to 71 years old (M = 44.4) with a presenting complaint of insomnia (mean duration of 13.4 years, SD = 12.2). Of those, there were 124 clinical patients attending a sleep clinic and 113 research participants enrolled in insomnia treatment studies. Research participants met diagnostic criteria for primary chronic insomnia, whereas clinical participants had a primary insomnia complaint but they could also present comorbid depression or anxiety disorders. As part of their baseline evaluation, all participants kept daily sleep diaries for two weeks and completed the 30-item DBAS, the Insomnia Severity Index, and the Beck Depression and Anxiety inventories.
Results: A total of 16 items were retained for the final scale and their selection was based on psychometric, theoretical, and practical considerations. The abbreviated 16-item DBAS had adequate internal consistency, based on a cronbach alpha of 0.80 and item-total correlations ranging from 0.19 to 0.58 (M = 0.40, SD = 0.10). The 16 items were submitted to an exploratory factor analysis followed by a varimax rotation. A five-factor structure was retained since it explained about all data variance, it met criteria for simple structure, and yielded interpretable factors. Those factors were labelled "perceived consequences of insomnia" (F1: Items 10,17,18,25, 30),"helplessness and worry about sleep" (F2: 5,8,20,25), "sleep expectations" (F3: 1,2,18), "attributions to physical causes" (F4: 9,11,24,27), and "attributions to emotional causes" (F5: 10,12,21). There was no difference in total DBAS scores between participants who completed the version with visual analog scales (n = 186) and those using a revised numerical 0-10 Likert scale (n = 51). There was no significant correlation between DBAS total scores and demographics (age, education), insomnia duration or with sleep efficiency.

However, there were significant correlations with both anxiety (0.36) and depression (0.31) inventories and with the insomnia severity index (0.31).
Conclusions: These findings provide psychometric support for the revised/abbreviated version of the DBAS. The factor structure is similar to the 30-item version, although cross-validation with additional samples will be necessary. These preliminary findings would justify the use of this revised format in clinical and research programs on insomnia.

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0741.L

Dysfunctional Beliefs and Attitudes About Sleep in Older Insomniacs Discontinuing Benzodiazepine Treatment
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Introduction: Dysfunctional beliefs and attitudes about sleep are presumed to play an important mediating role in perpetuating insomnia. Cognitive-behavior therapy (CBT) has been shown to produce changes in these cognitions, which have been positively correlated with improvements in sleep efficiency. Erroneous sleep-related cognitions are however thought to be more difficult to change among insomniacs who rely on sleep medication. This study aimed at assessing CBT's usefulness in changing sleep-related beliefs and attitudes in older insomniacs discontinuing their benzodiazepine (BZD) hypnotic treatment.
Methods: Seventy-six older adults (38 women, 30 men; mean age, 62 years old) with chronic insomnia and prolonged use (mean duration, 14 years) of BZD for sleep, who wished to stop hypnotic usage, were randomized into 3 conditions : medically supervised TAPER alone (n = 24), CBT alone (n = 25), and COMBINED taper + CBT (n = 27). Erroneous sleep-related cognitions were evaluated using the 30-item Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS), a questionnaire assessing misconceptions about causes of insomnia, misattributions or amplification of its consequences, unrealistic sleep expectations, control and predictability of sleep, and faulty beliefs about sleep promoting practices. Items were rated on a 0-10 Likert-type scale. A higher overall score indicates either more erroneous cognitions or more intense ones. The DBAS was completed at baseline, at post-treatment and at 3, 12, and 24 months follow-ups (FU). Analyses of variance according to treatment condition and drug-intake status were computed at each level of time.
Results: Participants in the CBT and COMBINED conditions displayed lower DBAS scores compared to those in the TAPER condition at post-treatment and 3 month-FU. However, this difference was not maintained at 12 and 24 month-FUs. Participants who achieved and maintained a drug-free state, regardless of treatment condition, also displayed weaker dysfunctional beliefs about sleep, compared to participants who did not stop their BZD or, at some point, had resumed it. This was true at post-treatment, and at 3-, 12-, and 24-month FUs.
Conclusions: While CBT is helpful in diminishing dysfunctional beliefs about sleep in older insomniacs during BZD discontinuation, drug-free participants achieved and maintained lower levels of erroneous sleep-related cognitions independently of the treatment they received. It is still unclear whether the changes in beliefs led to the discontinuation of medication or resulted from it. Other mediating variables may also have influenced changes in both cognitions and medication use.

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0742.L

Insomniacs' Perception Of Wake Instead Of Non-REM Sleep
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Introduction: Insomniacs are more likely then good sleepers to report having been awake when woken following 5 minutes of Stage 2 sleep. However, 5 minutes following Stage 2 onset may not reflect the conditions of spontaneous awakening, and be too early in the sleep cycle to accurately sample sleep/wake perception. The present study investigated whether sleep state misperception persists when awoken from Stage 2 sleep later in the sleep cycle.
Methods: Twenty four insomniacs (15F, 9M) who reported SOL>30min, WASO>40min, and SEF<80% on a 7-day sleep/wake diary underwent 4 weekly laboratory PSG recordings and were compared to 10 good sleepers (6F, 4M, diary SOL<20min, WASO<20min, SEF>90%). Across the night subjects were delivered a tone through a speaker at the bed head. Following verbal acknowledgment of hearing the tone, a recorded question was presented through the speakers; "Just prior to hearing the tone, were you awake or asleep?" These sleep/wake probes occurred under four different conditions; Wake- after 5 minutes of wake without movement, Early Non-REM- 5 minutes after the first sleep spindle/K complex following sleep onset, Late Non-REM- 5 minutes after the return to Stage 2 following SWS, or 20 minutes of continuous Stage 2, REM- 5 minutes after REM onset. The schedule cycled through these four conditions to maintain sleep architecture and provide samples of each sleep/wake probe distributed evenly across the night.
Results: The probability of reporting being awake immediately prior to each type of probe was calculated for both groups. The probability of reporting prior wakefulness at Early Non-REM probes was higher for Insomniacs [Mean .561 (sd .301)] compared to Controls [.234 (.205)], $F = 9.81$, $p = .002$. Similarly, Insomniacs were more likely to report prior wakefulness at Late Non-REM probes [.511 (.244)] in comparison with Controls [.346 (.197)], $F = 3.61$, $p = .033$. A two-way, repeated measures analysis of variance of responses to both Non-REM probe types indicated a significant main effect of condition (Insomniac vs Control, $F = 83.8$, $p < .001$) but no significant main effect of probe type (Early Non-REM probe vs Late Non-REM probe, $F = .863$, n/s). A significant interaction of condition and probe type was observed ($F = 5.97$, $p = .020$), with the likelihood of both groups reporting prior wakefulness appearing to converge between Early and Late Non-REM probes. Post hoc related samples t-tests indicated no statistically significant variation between Early and Late Non-REM probes for either Insomniacs [$t(23) = 1.41$, n/s] or Controls [$t(9) = -1.95$, n/s].
Conclusions: These results further demonstrate that insomniacs are more likely than good sleepers to perceive having already been awake following nocturnal awakenings. The present study indicates that our previous findings on sleep state misperception early in Non-REM sleep extend to Stage 2 sleep later in the sleep cycle.

Research supported by NH&MRC

0743.L

Health and Safety Consequences of Insomnia Remain Significant after Controlling for Demographic and Socio-Economic Factors
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Introduction: Insomnia is likely to be a significant public health issue because of high symptom prevalence and potentially serious consequences for health, safety, and quality of life. However, previous studies linking insomnia symptoms and adverse outcomes have seldom taken into account potential confounding factors (such as age, gender, ethnicity, or socio-economic deprivation) that might be independently responsible for the reported statistical relationships.
Methods: A questionnaire was mailed to a stratified random sample of 4,000 people. The national sample was designed to recruit equal numbers of Maori (indigenous New Zealanders) and non-Maori, and equal numbers in the age decades from 20-60 years (response rate 72.5%). Participants were ascribed a socio-economic deprivation ranking using a

validated census-based small area index, and were asked if they were currently in paid employment, or worked at night. They indicated how often (never/rarely/often/always) they had difficulty falling asleep, getting back to sleep, woke too early, and woke refreshed, how many times they typically woke during the night, if they had a sleep problem, and for how long. Outcome measures included: general health status (1=excellent, 5=poor); ability to concentrate, to get things done, and to cope with minor problems, (1= poor, 4 = excellent); relationships with family/friends, physical wellness, and general quality of life (1= poor, 4 = excellent); trouble remembering things (never/rarely/often/always); and being the driver in a motor vehicle accident in the preceding 3 years (yes/no).A series of logistic multiple regression analyses were performed for each of the outcome measures, to assess the independent contribution of each insomnia symptom. Other variables included in the regression models were ethnicity, age, gender, deprivation score, employment status, and for motor vehicle accidents, average weekly driving hours. Outcome measures were dichotomised as follows: general health – poor/fair versus good/very good/excellent; quality of life measures - poor/fair versus good/excellent; trouble remembering things – never/rarely versus often/always.

Results: Reports of insomnia symptoms were significantly related to all of the outcome measures ($p<0.001$) except motor vehicle accidents, after controlling for age, gender, ethnicity, socio-economic deprivation, and employment status. The largest adjusted odds ratios were consistently found for people who reported never/rarely waking refreshed (adjusted ORs ranging from 2.0 to 4.5) or who had a current sleep problem (adjusted ORs ranging from 2.5 to 4.4). The smallest adjusted OR between having an insomnia symptom, or not, and the likelihood of poorer health or quality of life was 1.7.

Conclusions: Reports of insomnia symptoms are significant independent predictors of poorer health and quality of life, after controlling for demographic and socio-economic factors. The high prevalence of chronic (>6 months) sleep problems (29% for Maori, 26% for non-Maori) suggests that insomnia in New Zealand is a major public health problem with serious and expensive consequences.

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0744.L

Ethnicity And Insomnia: Implications For Treatment Services

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Introduction: Insomnia has been recognised as a serious public health problem with high human and economic costs. The aetiology of insomnia is complex, but it is important in determining the choice of treatment. This study provides the first population prevalence estimates for insomnia comparing ethnicity and gender after controlling for age, socio-economic deprivation, unemployment and night work.

Methods: A questionnaire was mailed to a stratified random sample of 4,000 New Zealand adults aged 20-60 years. Our aim was to compare Mâori (the indigenous people of New Zealand) and non-Mâori adults with equal statistical power in multi-variate analyses therefore the methods were designed to recruit equal numbers of Mâori and non-Mâori and equal numbers in each age decade. Socio-economic status was measured using a validated census-based small area index (NZDEP2001). Participants were asked how often they had difficulty falling asleep, woke too early in the morning, and woke feeling refreshed (never/rarely/often/always). They were also asked how often they woke during the night (never/1-2/3-4/>4 times) and if it was difficult to get back to sleep (didn't wake/no difficulty/bit difficult/very difficult). Participants also indicated if they thought they had a current sleep problem and for how long. Calculations of the population prevalences for each insomnia symptom and reports of sleep problems were performed by weighting the data by the population proportions of age, gender and ethnicity in the 20-60 year age group.

Results: An overall response rate of 72.5% was achieved (Mâori 64%; non-Mâori 81%). Mâori were more likely to report waking more than 3 times during the night and often/always waking too early ($p<0.0001$). Mâori were also more likely to report having difficulty going back to sleep and never/rarely waking feeling refreshed ($p<0.05$). Difficulty falling asleep often/always was more likely to be reported by Mâori than non-Mâori adults ($p<0.001$). Mâori were significantly more likely to report excessive daytime sleepiness (ESS >10) than non-Mâori ($p<0.0001$).33.0% of Mâori adults and 26.4% of non-Mâori adults in New Zealand reported a current sleep problem. It is estimated that 29.4% Mâori and 26.6% non-Mâori reported a chronic sleeping problem (> 6 months).

Conclusions: This study suggests that approximately one quarter of adults in New Zealand may suffer from a chronic sleep problem, highlighting insomnia as a major public health issue in New Zealand. Significant differences in the prevalence of insomnia symptoms and current sleeping problems with respect to ethnicity have implications in the purchase and development of treatment services, with the need for these services greater among Mâori than non-Mâori. Socio-economic deprivation is higher among Mâori and there are major disparities between Mâori and non-Mâori in other areas of health and life expectancy. A companion abstract examines the role of socio-economic deprivation and unemployment on the prevalence of self-reported insomnia symptoms in these groups.

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0745.L

Insomnia: A Problem Of Poverty?

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Introduction: Insomnia symptoms include difficulty with sleep initiation, maintenance, and gaining restorative sleep. Earlier studies have determined the prevalence of insomnia among populations, however they have not established the relationships with ethnicity, socio-economic deprivation and employment.

Methods: A randomly stratified sample of 4,000 New Zealand adults (20-60 years) was mailed a questionnaire (response rate 72.5%). The sample permitted equal statistical power in multi-variate analyses between Mâori (indigenous New Zealanders) and non-Mâori and equal numbers in each age decade. Socio-economic deprivation was measured using a validated census-based small area index (NZDEP2001). Current employment status was determined. Participants were asked how often they experienced difficulty falling asleep, waking too early in the morning, and waking feeling refreshed (never/rarely/often/always). They were asked how often they woke during the night (never/1-2/3-4/>4 times) and if it was difficult to get back to sleep (didn't wake/no difficulty/bit difficult/very difficult). Participants indicated if they thought they had a current sleep problem (yes/no) and for how long (< 4 weeks/1-6 months/> 6months).Logistic regressions analyses were performed to identify independent predictors of each insomnia symptom and of having a sleep problem. Regression models included ethnicity, gender, age, socio-economic status and employment status and for reports of a current sleep problem, daytime sleepiness (ESS>10).

Results: Socio-economic deprivation was an independent predictor of each insomnia symptom ($p<0.0001$) except never/rarely waking refreshed, after controlling for demographic and employment factors. Unemployment predicted difficulty falling asleep often/always (OR=1.39) and waking ≥3 times during the night (OR= 1.49). Night

work was significantly related to reporting difficulty falling asleep often or always. Having a sleep problem was predicted by unemployment ($p<0.001$), night work ($p<0.05$) and socio-economic deprivation ($p<0.05$). Gender (male vs. female) was significantly related to difficulty getting back to sleep (OR=0.82), waking too early often/always (OR=1.22) and never/rarely waking refreshed (OR 1.23). Mâori were more likely to report waking ≥3 times (OR=1.24) and waking too early often/always (OR=1.43).
Conclusions: Reports of insomnia symptoms and current sleeping problems are strongly predicted by socio-economic deprivation after controlling for demographics and employment. There is a significant relationship between unemployment and some insomnia symptoms and having a current sleep problem. In New Zealand socio-economic deprivation and unemployment levels are higher among Mâori and a companion abstract highlights the significant difference in the prevalence of insomnia symptoms and current sleep problems among Mâori and non-Mâori adults. Multi-variate analyses show that after controlling for other factors this difference is not always conserved, suggesting that prevalence differences are largely due to other factors rather than ethnicity per se. After controlling for socio-economic deprivation and employment, gender differences in having a sleep problem disappeared and it was not always an independent predictor of having an insomnia symptom.

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0746.L

Self-Report Predictors of Sleep Efficiency in Situational Insomnia
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Introduction: Situational insomnia (SI) is poor sleep experienced by an otherwise normal sleeper in response to environmental or stress factors. Identifying individuals sensitive to SI may provide clues to the development of chronic insomnia, and also may help in devising countermeasures for people forced to sleep in unusual situations. The present study evaluated self-reported sleep and personality variables for their use in predicting EEG sleep efficiency during SI conditions in the laboratory.
Methods: Forty-nine normal young adults (age 23 +- 5) slept in the lab for a Screening night followed by Baseline nights and Advance Sleep nights (where bed time was 3 or 6 hours earlier on alternating weeks). Prior to laboratory sleep, subjects completed a sleep and health history questionnaire and the MMPI. Variables from these instruments (e.g. usual sleep latency or time spent awake, sleep disorder symptoms) were entered into multiple regression equations to identify variables likely to predict sleep efficiency on potential SI nights (i.e., the Screening night and the 3- and 6-hour Advance Sleep nights).
Results: The 6-hour Advance night was the only SI condition with sufficient variance in sleep efficiency for regression analysis (Mean=76%, SD=20). Sleep efficiencies during the baseline and other SI nights were similar (93-96%) with narrow SDs (4-7). Multiple regression predictors (standardized beta weights) of sleep efficiency on the Advance-6 night included: subjective number of awakenings (0.33), the MMPI Depression (-0.48) and Mania (-0.26) scales, frequency of symptoms of circadian rhythm disturbance (-0.26), frequency of respiratory complaints (0.49), and positive responses to an alcoholism screening test (0.30). These variable explained 44% of the variance in sleep efficiency on the Advance-6 night. Similar results were observed on the Advance-3 night for subjective number of awakenings (0.23), Depression (-0.41), and Mania (-0.31), despite the restricted range of sleep efficiency in that condition.
Conclusions: The data suggest that SI sensitivity can be predicted from sleep/health histories and personality variables. These results were obtained in a relatively small sample of subjects carefully selected to be healthy, normal sleepers, with all screening responses in the normal range. Within that range, slight elevations in the MMPI scales, circadian rhythm disturbance, and respiratory symptoms were associated with poorer sleep in a manner consistent with more extreme patient populations. Whether these results are specific to phase-advance SI or are more generalizable requires further study. Additional modeling on larger, more diverse samples and on other SI conditions holds promise for a comprehensive characterization of the SI-sensitive individual using self-reports.

Research supported by Department of the Army and the Sleep-Wake Disorders Research Institute

0747.L

Eszopiclone, A Novel Non-Benzodiazepine Anti-Insomnia Agent: A Six-Week Efficacy and Safety Study in Adult Patients with Chronic Insomnia
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Introduction: Eszopiclone (ESZ) is a novel, isomerically pure, cyclopyrrolone, non-benzodiazepine agent. ESZ has been investigated to determine its potential, relative to the observed pharmacokinetic half-life of six hours, to rapidly induce sleep and improve sleep maintenance and total sleep time with an absence of residual next day effects and tolerance.
Methods: This randomized, double-blind, multicenter study evaluated the efficacy, safety, and potential for residual effects of ESZ in adult patients (21-64 years) with chronic insomnia. Patients received a nighttime dose of placebo (PBO) or ESZ 2 or 3 mg for 44 consecutive days (N=308) and assessments were performed at baseline, after the first dose, and at Weeks 2, 4, and 6. Efficacy was evaluated via polysomnography and morning questionnaires; next day residual effects were evaluated at 9-9.5 hours post lights-out using the Digit Symbol Substitution Test (DSST).
Results: ESZ produced sustained improvements in sleep onset, sleep duration, sleep maintenance, and the quality and depth of sleep over six weeks of treatment with no evidence of pharmacologic tolerance. Overall, the objective results were consistent with the subjective findings. Relative to PBO, both ESZ doses significantly improved LPS and sleep latency ($p<0.0001$), sleep efficiency and total sleep time ($p<0.0001$), and the quality and depth of sleep ($p<0.05$). Only the 3 mg dose of ESZ significantly improved objective and subjective wake time after sleep onset relative to PBO ($p<0.05$). DSST scores improved above baseline in the PBO and both ESZ dose groups and there were similar gains across all groups demonstrating an expected learning effect over time. The most common AE in any group was unpleasant taste.
Conclusions: Across six weeks of treatment, ESZ produced sustained objective and subjective improvements in sleep onset, sleep duration, sleep maintenance, and improved the quality and depth of sleep in adult subjects with chronic insomnia with no evidence of pharmacologic tolerance or next day residual effects.

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0748.L

Phase II Study of the Selective ML-1 Receptor Agonist TAK-375 in Subjects with Primary Chronic Insomnia

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Introduction: TAK-375 is a novel, highly selective ML-1 receptor agonist under investigation for the treatment of insomnia and circadian rhythm sleep disorders. This study examined dose-related safety and efficacy in subjects (age, 18-64 years) with primary chronic insomnia as defined by the DSM-IV.
Methods: For entry in this double-blind, placebo-controlled crossover study, subjects with chronic insomnia had to meet the following inclusion criteria: presence of insomnia complaints for >3 months, polysomnography (PSG)-defined mean latency to persistent sleep (LPS) >20 minutes and mean wake time >60 minutes on 2 consecutive screening nights in a sleep laboratory. Each subject (n=107) was randomized into a dosing schedule that included 4, 8, 16, and 32 mg of TAK-375 and placebo. Medication was administered 30 minutes before habitual bedtime on 2 consecutive nights. Each night, PSG monitoring was performed for 8 hours. Upon awakening, visual analog scale (VAS), digit symbol substitution test (DSST), memory recall tests, and post-sleep questionnaires were completed. Subjects underwent 5 treatment periods, with a 5- or 12-day washout period between treatments.
Results: There was a statistically significant reduction in objective LPS for every dose of TAK-375 compared to placebo (P<0.001). Least square (LS) mean LPS was 24.0, 24.3, 24.0, 22.9, and 37.7 minutes, respectively, for 4, 8, 16, and 32 mg TAK-375 and placebo. In all TAK-375 dose groups, a statistically significant increase was seen in LS mean total sleep time (TST) (411.0, 412.9, 411.2, and 418.2 minutes, respectively) and sleep efficiency (85.7%, 86.0%, 85.7%, and 87.1%, respectively) compared with placebo (400.2 minutes and 83.5%, respectively). Subjects in the 16-mg group reported a significantly shorter subjective sleep latency compared with placebo (P=0.015). There were no statistically significant differences between the five treatment groups in terms of awake time after onset of persistent sleep, subjective TST, and sleep quality. The only statistically significant change in sleep stage was a slightly lower percentage of total time in NREM stage 3/4 sleep with TAK-375 (difference from placebo: -1.3% [4 mg], -1.9% [8 mg], -1.4% [16 mg], and -2.1% [32 mg]). There were no statistically significant differences among treatment groups or between any treatment and placebo in terms of VAS, DSST, memory recall tests, or post-sleep subjective level of alertness and ability to concentrate. The most common adverse events (AEs) reported were headache (19.6%), somnolence (7.5%), and pharyngolaryngeal pain (7.5%), with no differences in number or type of AEs between any active treatment group or placebo.
Conclusions: Using PSG-defined measures, all tested doses of TAK-375 resulted in significant reductions in LPS, and increases in LS mean TST and sleep efficiency. Subjects administered TAK-375 experienced AEs of only mild or moderate intensity, with no residual next-day pharmacologic effects.

0749.L

Vicious Cycles Of Sleeplessness: A New Scale For Insomnia

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Introduction: The mechanisms behind the development of persistent insomnia are complex. Worries about sleep, negative expectations of sleep, and frustration about sleep loss are assumed to play an important role. From an earlier study eight items, designed to measure aspects of vicious cycles of sleeplessness (VCS), were extracted. Insomnia patients and controls have been found to differ significantly on these items and the items were also found to be intercorrelated. The aim of the present study was to investigate the new VCS Scale in the general population with regard to some psychometric properties.
Methods: A sleep questionnaire including the VCS scale was sent to a randomly selected sample of 1400 subjects, aged 20–64 years. Response rate was 78.0%. The scale comprised the following items: (1) The thought of going to bed repels me, since I know how it usually turns out. (2) I become tired and almost on the verge of falling asleep – and just when I am about to fall asleep I become wide awake again. (3) I think about how my sleep will be even before I go to bed. (4) It happens that I get angry with myself if I wake up at night. (5) Even before I go to bed, I can have a feeling of how easy or difficult it will be to fall asleep. (6) When lying awake I get annoyed about being unable to fall asleep. (7) I feel a kind of discomfort about the night as such. (8) When in bed, I think a lot about "having to go to sleep", and "how am I going to manage tomorrow if I don't fall asleep?". Responses were given in a five-choice format (0=never, 1=seldom, 2=sometimes, 3=often, 4=always).
Results: The scale had a one-factor structure, i.e., it measured a unitary concept. Mean ± SD was 6.7 ± 5.6. It had an adequate internal consistency (averaged corrected item-total correlation was 0.65 and Cronbach's alpha was 0.88). Women scored higher than men (7.3 ± 5.8 vs. 5.9 ± 5.2; t=4.1; p<0.0001). There was no age relationship. Scores were significantly higher in a group of 263 subjects that complained of insomnia than in the others (12.7 ± 6.0 vs. 4.6 ± 3.7; t=26.0; p<0.0001). The scores of subjects complaining of insomnia were fairly normally distributed and subjects in the lower quartile had a mean score of 5.2 ± 2.2, not being very different from the mean of subjects without sleep disturbances. Conversely, subjects in the upper quartile had a mean of 20.2 ± 3.2. Thus, subjects with insomnia have a wide range of scores.
Conclusions: The VCS scale showed an adequate reliability and is a possible tool for characterizing patients with insomnia. The next step will be to administer the scale to a clinical sample, and also to let patients fill out the scale before and after treatment.

0750.L

Sleep-Disordered Breathing Status Predicts Outcomes Among Insomnia Patients Receiving Cognitive-Behavioral Therapy

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Introduction: Insomnia chronically affects 9-17% of adult Americans. Yet, no definitive treatment for this condition has been established as a cure. Instead, residual sleep symptoms (RSS) are common outcomes after standard insomnia therapies. Evidence suggests RSS may be associated with Sleep-Disordered Breathing (SDB), which appears to be highly prevalent in insomniacs. To investigate the relationship between SDB and RSS after insomnia treatment, we studied patients who completed cognitive-behavioral therapy (CBT) for insomnia in a pilot occupational health program.
Methods: At baseline, 35 participants were presumptively diagnosed with SDB using AASM research criteria and were classified into four SDB presentation types: No SDB, SDB Type-A (*criterion A only: sleepiness*), SDB Type-B (*criterion B only: insomnia-type*), and SDB Type-AB (*criteria A and B*). After CBT, we re-examined SDB criteria and presentation types to compare with baseline assessments. We also evaluated CBT effects on insomnia based on post-treatment SDB Types. Validated scales to measure insomnia (ISI), daytime impairment related to sleepiness (FOSQ), and quality of life impairment (Q-LES-Q) were analyzed with repeat measures ANOVA and Cohen's d effect sizes. We hypothesized that SDB Types determined at follow-up would predict post-CBT outcomes and RSS.

Results: At baseline, 8 (23%) presented with SDB Type-B, and 27 (77%) presented SDB Type-AB. However, after CBT, 8 (23%) had No SDB, 17 (49%) had SDB Type-B, and 10 (28%) had SDB Type-AB. In examining CBT effects by SDB Types at follow-up, the No SDB group (N=8) reported milder sleep symptoms at baseline coupled with large improvements for all measures [ISI (d=2.5,p<.001); FOSQ (d=1.4,p<.05); QLESQ (d=1.2,p<.01)]; CBT appeared to cure their insomnia. In extreme contrast, SDB Type-AB (N=10) reported severe sleep symptoms at baseline and only medium improvements for insomnia [ISI (d=0.6,ns); FOSQ (d=0); QLESQ (d=0.2,ns)] with moderate-severe RSS. Last, SDB Type-B patients were nearly as severe as SDB Type-AB, but SDB Type-B patients had larger improvement in insomnia [ISI (d=0.9,p<. 01); FOSQ (d=0.2,ns); QLESQ (d=0.5,ns)] with moderate RSS.
Conclusions: This study suggests that SDB Type may predict insomnia treatment outcomes. Changes in SDB presentation types observed between baseline and follow-up are most likely a function of broad SDB research criteria that overlaps with insomnia symptoms. Nonetheless, examining SDB types after CBT provided interesting insight into the composition of this sample. That is, 25% were essentially pure insomniacs without SDB requiring only CBT to cure their insomnia; whereas, a majority (75%) reporting insomnia and SDB showed some improvements but still required additional insomnia or SDB treatment. However, the challenge is determining the proper, subsequent treatment, because RSS could be fueled by persistent insomnia, SDB, or both. In order to tease this apart, investigations are underway to determine the effects of simultaneous and sequential CBT and SDB treatment. In our clinical and research experience, sequential treatment (e.g. adding CPAP) decreases RSS, but we speculate that simultaneous therapy may be more potent.

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0751.L

Screening for Complex Insomnia (Insomnia plus Sleep-Disordered Breathing) in an Occupational Health Setting

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Introduction: Insomnia and sleep-disordered breathing (SDB) are two highly prevalent disorders that appear to have a high rate of comorbidity. The term "complex insomnia" has been used to describe this phenomenon, which comprises both psychological and physiological elements. Making the distinctions between insomnia or complex insomnia can be a difficult task given the overlapping symptomatology. To highlight this clinical conundrum, we examined the frequency of SDB symptoms in a group of treatment seeking sleep maintenance insomnia (SMI) patients in an occupational health setting.
Methods: Ninety-six participants with a mean (SD) age of 50.0 (8.9) and body mass index (BMI) of 27.2 (4.6) completed a two-page screening questionnaire. Screening included demographics, insomnia severity on a five-point scale (0 = none, 4 = very severe), snoring and other disturbed sleep breathing (choking, gasping, or struggling for breath), SDB peripheral symptoms (morning headache, nocturia, dry mouth upon awakening), current and past medication use, and current and past psychiatric and medical history. Participants were divided into an SDB or No SDB group based on relatively stringent criteria. Reports of snoring plus other disturbed sleep breathing, snoring plus two or more SDB peripheral symptoms, or other disturbed sleep breathing plus one or more SDB peripheral symptom once or more per week yielded a presumptive diagnosis for SDB.
Results: Insomnia symptoms, including moderate to severe difficulty staying asleep and waking up too early [Mean (SD)=2.5 (.83)], were present in the entire group, and 48% (N=46) met criteria for a presumptive diagnosis of SDB. No significant differences were found between the SDB and No SDB groups with respect to age, insomnia severity levels, medication usage, and mental health status. BMI averaged (SD) 28.6 (5.0) in the SDB group and 25.9 (3.9) in the No SDB group (p=.004), a small increase of approximately 13 pounds given this overall non-obese sample. The SDB group was predominately male (N=30) (p=.02), while women comprised only 35% (N=16). However, women without SDB were on average 4 years younger compared to the women with SDB (d=.42), suggesting age might account in part for sex differences in the SDB group.
Conclusions: Screening for SDB symptoms in patients presenting with insomnia in an occupational health setting may provide needed insight regarding the presence of complex insomnia. Screening solely for insomnia symptoms may not supply the information needed to differentiate between insomnia and complex insomnia. Complex insomnia has been shown to be highly prevalent among trauma survivors and crime victims. The current study suggests that complex insomnia may also be highly prevalent in non-psychiatric SMI patients seeking treatment in an occupational health setting.

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0752.L

Is Cognitive Over-Activity Epiphenomenal In Insomnia? A Pilot Study

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Introduction: Patients with persistent primary insomnia (PPI) complain of mental over-arousal more than physiological over-arousal and sleep disruption has been associated more strongly with cognitive arousal than physiological arousal. However, conflicting results from studies investigating the relationship between cognitive activity and sleep latency suggest the possibility that cognitive arousal is an epiphenomenon of delayed sleep onset. This study aimed to compare the pre-sleep cognitive activity of insomniacs with that of individuals with delayed sleep phase syndrome (DSPS) and good sleepers (GS). DSPS, a circadian timing disorder that results in delayed sleep onset, but with no presumed cognitive pathway, provided a suitable comparison group for this study. A second aim of this study was to attempt to identify an objective correlate or physiological marker of pre-sleep cognitive over-arousal by establishing which EEG measures are most representative of the mental and physiological inter-relationship associated with PPI.
Methods: Thirteen male and 16 female (mean age = 23.3) campus recruited participants meeting ICSD-R & DSM IV criteria for psychophysiologic/primary insomnia (N=10), DSPS (N=9) and GS (N=10) completed 7 nights sleep diary, 3 diagnostic questionnaires, 6 questionnaires to assess subjective pre-sleep cognitive arousal, 7 nights actigraphy and 2 nights Trackit EEG/BioSleep® (home-based EEG), which recorded and analysed neural EEG activity on a second to second basis.
Results: A combination of inferential and descriptive statistics was applied to the pilot data. Self-report measures of pre-sleep cognitive over-activity revealed that PPI & DSPS groups reported similar cognitive symptoms significantly greater than GS (p>.01). The percentage of pre-sleep thoughts relating to cognitive activity for each group (derived by content analysis of diary responses) was: PPI = 67.5%; DSPS = 77.2%; GS = 56%. Subjective (diary) analysis of sleep onset latency (SOL) revealed that the PPI & DSPS groups reported similar SOL significantly greater that those of GS (p>.001). While objective EEG revealed that DSPS & GS had similar SOL less than PPI (p>.05 & p>.008 respectively)actigraphy did not.
Conclusions: Questionnaire and diary results indicated that PPI and DSPS groups experienced similar levels of pre-sleep cognitive activity greater than GS and that individuals with DSPS were most likely to report thoughts relating to cognitive activity during the pre-sleep period. These preliminary results suggest that cognitive over-arousal is epiphe-

nomenal of pre-sleep wakefulness and have important implications for the study and treatment of PPI. Therefore, a further study with a larger sample of participants is warranted. Results also indicated that, as would be expected, PPI and DSPS groups had similar subjective SOL, greater than the GS group, but that DSPS and GS groups had similar objective EEG SOL, less than the PPI group. The discrepancy between the subjective and objective SOL of the DSPS group requires further exploration. Further work must be carried out in order to determine which EEG measures are most representative of the mental and physiological inter-relationship associated with PPI and DSPS.

0753.L

Effects of Modafinil on Sleep Continuity, Daytime Sleepiness, and Treatment Adherence in Subjects with Primary Insomnia

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Introduction: Last year we presented preliminary data on whether modafinil may be combined with traditional cognitive behavioral therapy (CBT) treatment to augment treatment outcome. The data presented are the results of the final study. The hypotheses were that modafinil would not negatively affect treatment outcome and might potentiate sleep continuity treatment gains, diminish treatment related increases in daytime sleepiness, and/or promote adherence to the behavioral treatment regimen.
Methods: 27 subjects who met ICSD criteria for Primary Insomnia participated in this study. Subjects were screened via a multi-tier process which included: completion of preliminary questionnaire by phone or via the Internet (www.sleeplessinrochester.com), an in-house clinical interview, a physical with a comprehensive blood, and urine chemistries panel, a 7-14 day sleep diary monitoring period, and an in-lab sleep study to rule out intrinsic sleep disorders. Eligible subjects were randomized to one of three treatment conditions: 1) placebo + 8-week CBT Tx for insomnia, 2) 100 mg modafinil + CBT and 3) 100 mg modafinil + a monitor-only condition. Subjects were continuously monitored with sleep diaries from study intake until study end (12 weeks). Subjects were also evaluated on a weekly basis for changes in sleepiness (Epworth Sleepiness Scale). Baseline data were compared to end-of-treatment data for the subjects in the 3 treatment conditions for sleep latency (SL), wake after sleep onset time (WASO), total sleep time (TST), daytime sleepiness, and for treatment adherence using a sleep diary based metric.
Results: The mean age of the group was 41.3 yrs. (13.4) and 70.4% of subjects were female. All three groups exhibited mean sleep latency and wake after sleep onset times that were ³ 40 minutes in duration. The mean pre-treatment sleep continuity profiles did not significantly differ. Modafinil administered alone did not positively or negatively affect sleep continuity (versus baseline), and a trend was evident for improved sleep latency. Modafinil as an adjunct to CBT did not positively or negatively affect sleep continuity gains and was associated with 1) improved daytime wakefulness as measured by the Epworth Sleepiness Scale and 2) enhance compliance with CBT. With respect to the latter, subjects in the CBT+M group more reliably adhered to the prescribed phase delay in bedtime than did the CBT+ placebo group.
Conclusions: These data suggest that modafinil, when administered qam does not interfere with the successful conduct of cognitive behavioral therapy for insomnia. More importantly, it may serve to diminish the negative side effects of CBT (increased daytime sleepiness) and may increase subject compliance with therapy. Whether 1) enhanced daytime function mediates the change in adherence and 2) reduced sleepiness and enhanced compliance translate in to less patient attrition in the clinical setting remain to be evaluated.

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0754.L

Day-to-day Determinants of Sleep Quality - A Longitudinal Diary Study

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Introduction: Several recent studies have shown a relation between stress, in particular uneasiness and tension at bedtime, and subjective sleep quality. The aim of the present study was to investigate the association between stress, sleepiness, health and other behaviors, and insomnia complaints, using a diary approach.
Methods: The sample consisted of 46 subjects (26 females, 20 males; mean age: 42 years, range: 18-69 years) who filled in a sleep/wake diary during 6 weeks. The sleep diary included 4 items that formed a sleep quality index (SQI; “ease falling asleep”, “how did you sleep”, “restless sleep”, “slept throughout”). The score of the SQI varied between 1 (very poor) and 5 (very good). The diary also included the following determinants of the SQI: “mean daily stress” (1 low-9 high), “mean daily sleepiness” (Karolinska Sleep Scale - KSS, 1 alert-9 sleepy), “perception of the next day” (1 difficult-9 pleasant), “weekday” (0-1 weekend), “health” (1 poor-7 excellent), “quality of the day” (1 poor-9 good), “coffee consumption” (no. of cups), “alcohol” (amount), “napping” (0-1 yes), “uneasiness/stress at bedtime” (1 high-5 not at all), “KSS at bedtime” (1 alert-9 sleepy), “bedtime”, “wake-up time” and “previous day SQI (lagged)” (1 poor-5 good). The statistical analysis was based on intraindividual correlations and a stepwise multiple regression analysis. Each individual was dummy coded and forced into the analysis in order to remove the interindividual variance of the data set. The number of data points in the analysis was 1603.
Results: The mean SQI score was 4.12 (sd=0.42) and the mean range, across individuals, was 2.6 (sd=0.72). Thus, there was relatively high variation in sleep quality within the subjects. The variables “uneasiness/stress at bedtime” ($r=0.32$, $p<0.001$), “wake-up time” ($r=0.17$, $p<0.001$), “perception of the next day” ($r=0.15$, $p<0.001$), “KSS at bedtime” ($r=0.14$, $p<0.001$) and “health” ($r=0.10$, $p<0.001$) showed the strongest correlations with the SQI. The remaining variables, except “coffee consumption”, also showed significant but weak ($r<0.10$) correlations with the SQI. All independent variables were entered in a multiple regression analysis and 6 predictors became significant: “uneasiness/stress at bedtime” (R2 change: +7.4%, beta in the last step: 0.28), “KSS at bedtime” (+1.1%, 0.15), “wake-up time” (+0.9%, 0.11), “health” (+0.2%, 0.06), “napping” (+0.2%, -0.05) and “lagged SQI (previous day)” (+0.1%, 0.05). The amount of explained variance was 9.9%. Thus, poor sleep quality was associated with stress at bedtime, alertness at bedtime, early wake-up time, poor health, napping and poor sleep quality previous day.
Conclusions: The results showed that stress and uneasiness at bedtime was the strongest determinant of subjective sleep quality. This result fits with the theories emphasizing arousal at bedtime as a key predictor of sleep disturbances, particularly insomnia. However, also lack of sleepiness at bedtime, early wake-up time, poor health and prior napping were determinants, although weak, of sleep quality.

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0755.L

Insomnia and Obstructive Sleep Apnea (OSA): Evaluation and CPAP Therapy

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Introduction: Patients with insomnia and sleep apnea pose special problems both in the performance of the polysomnogram (PSG) and in CPAP

treatment for OSA.
Methods: We performed a retrospective chart review of 207 consecutive patients who underwent a split night polysomnogram with CPAP titration in the second half of the night. The patients in this series had an apnea-hypopnea index (AHI) of 5/hour or greater. They were able to breathe on CPAP the second half of the PSG and they accepted a prescription for CPAP. All patients had an initial sleep consultation by a sleep specialist. Prior to the study, the patient viewed a video on OSA and CPAP use, CPAP was discussed by the physician and technician and they were fitted with a CPAP mask. A hypnotic was prescribed if the physician felt necessary.
Results: Patients were separated into two groups, OSA with a clinical diagnosis of insomnia (I) and patients with non-insomnia OSA (NI). There were 23/207 (11%) in the I group and 184/207 in the NI group. The mean age in the I group was 58 yrs and the female:male ratio was 10:13 (43%) vs. 54 yrs and 50:134 (27%) in the NI group. The I group demonstrated an average total control sleep time of 155 min and a control AHI of 24 compared with 178 min and 43 for the NI group. During the CPAP portion of the study, the I group had an average total sleep time of 159 min and an AHI of 8 vs. 178 min and 8 for the NI group. The I group had an average optimal CPAP pressure of 7cm H20 vs. 9cm H20 for the NI group. CPAP compliance on a scale of 0-2 (0=non-compliance, 2=good compliance) was 1 in the I group and 2 in the NI group.
Conclusions: Insomnia is uncommonly seen in patients with OSA symptoms presenting for evaluation to a sleep lab. When present, patients tend to be older and insomnia is more common in females. In this group of patients, insomnia did not prevent adequate evaluation by split night PSG. CPAP pressure tends be lower with insomnia. Follow up of this group is in progress, however initial chart review suggests sub optimal CPAP acceptance in patients with insomnia.

0756.L

A Comparison of Two Scales for Sleepiness and Tiredness in Sleep Disordered Patients

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Introduction: Daytime sleepiness is a typical feature of narcolepsy (NAR), hypersomnia (HYP) and sleep apnea syndrome (SAS), while patients with insomnia (INS) frequently complain to be tired but not sleepy. The Epworth Sleepiness Scale (ESS) is a valid instrument to measure sleepiness. However, there is no routinely used item scale to measure tiredness. For this reason our group has developed the Tiredness Symptoms Scale (TSS; Schulz et al., Sleep Res. 1991;20A: 515), a 14-items instrument, measuring physical and mental aspects of tiredness. After an introductory remark ("If I am tired, I notice ..."), 14 symptoms like "heavy eyelids" or "poor concentration" are presented which have to be answered with Yes or No. The TSS score is the sum of Yes answers and varies between 0 and 14. The objective of the present study was to compare the ESS and TSS in patients with either SAS or INS. Patients with NAR or HYP were used as a reference group for excessive daytime sleepiness.
Methods: Patients with a complaint of disturbed sleep or daytime vigilance filled in the ESS and TSS as part of the routine diagnostic procedure. The association between both scales was investigated in 37 INS patients, 87 SAS patients and 15 NAR+HYP patients. Median age was 59 y (range: 29-74 y) for SAS (66 m, 21 f), 54 y (range: 32-72 y) for INS (10 m, 27 f), and 42 y (range: 19-68 y) for NAR+HYP (5 m, 10 f). Non-parametric statistical tests were applied for group comparisons.
Results: The distribution of ESS scores differed significantly between all three patient groups. Mean ESS scores were lowest for INS (6.1 $\pm$ 5.3), significantly higher for SAS (9.2 $\pm$ 5.2; p = .001, Mann-Whitney U test) and highest for NAR+HYP patients (17.4 $\pm$ 3.4). While 100.0% of the NAR+HYP patients scored above the common median (ESS score 8), this was the case for 48.3% of the SAS and 24.3% of the INS patients. Mean TSS scores were lowest for SAS (6.1 $\pm$ 2.9), significantly higher for INS (7.5 $\pm$ 3.0; p = .043, U test) and highest (9.1 $\pm$ 2.0) for NAR+HYP patients. For the TSS, the percentage of patients above the median (TSS score 6) was 93.3% for NAR+HYP, while it was similar for SAS (46.0%) and INS (51.4%).
Conclusions: ESS and TSS scores were both high in NAR+HYP patients while they differed between SAS and INS patients. INS patients scored lower on the ESS but higher on the TSS than SAS patients. The results support the assumption that daytime consequences of disturbed night sleep depend on the pathophysiological mechanism of the sleep disorder. If poor sleep results from hyperarousal, as suggested for insomnia, sleep propensity may be lowered across 24 hours, and tiredness (high TSS) with difficulty to fall asleep (low ESS) will be the consequence. However, if sleep propensity is normal but sleep continuity is low, as e. g. in sleep related breathing disorders, increased daytime sleepiness and high ESS scores may result. The severity of the sleep disorder, as well as the type of daytime activities and demands, may act as additional moderator variables.

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0757.L

A Prospective, Randomized, Study Comparing Cognitive Behaviour Therapy, Pharmacologic Treatment and Combination Therapy in Non-Elderly Patients with Primary Insomnia

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Introduction: Cognitive behaviour therapy (CBT) and Pharmacologic treatment (PT) have both been shown to be effective treatments for Primary Insomnia. There is some evidence that CBT may be more effective than PT in the long-term. We set out to compare the short and long-term effectiveness of CBT, PT and a combination (CT) of the two treatments in a sample of patients referred to a tertiary level specialist sleep disorders centre in London.
Methods: This is a prospective randomised, trial comparing CBT, PT and CT for chronic primary insomnia, in non-elderly (<65 years) patient volunteers. All patients who fulfilled the DSM IV criteria for Primary Insomnia (PI) and who scored > 5 on the Pittsburgh Sleep Quality Index (PSQI) were entered into the study and assigned to one of the three groups i.e. cognitive behavioural therapy (CBT), to Standard outpatient medical treatment (PT) or to a combination (CT) of both treatment modalities. All groups were seen initially on a weekly basis for 6 weeks (3-6 hours of total contact) and then followed up at 6months, 1 year and 18 months post -treatment. All the patients underwent the following assessments: The Beck Depression Inventory (BDI); General Health Questionnaire (GHQ); Hospital Anxiety and Depression Scale (HAD); The Epworth Sleepiness Scale (ESS); Daily Sleep Diary on awakening in the morning for two weeks pre-treatment, the 6 weeks of treatment, and two weeks post treatment.The Primary Efficacy Assessments were daily subjective assessments of total sleep time and sleep latency using a sleep diary. The changes in sleep latency, total sleep time and wake time after sleep onset (WASO) from baseline to week 6, and changes in the GHQ score were also analysed.
Results: This is an ongoing study and our preliminary results are given below. Of the 105 primary care referrals to the Sleep disorders centre (71 Females, 34 Males), 85 were suitable for entry into the study (54 Females, 31 Males) and allocated as follows – CBT group n = 31, PT group n = 33, CT group n -= 21. Our results for the initial 6 session treatment period shows all groups having a similar increase in Total Sleep Time (TST) and in mean reduction in sleep latency (SL). Significant differences were found between the groups in the mean reduction of WASO. The CT group had the greatest reduction in WASO from 83 min-

utes to 37 minutes, followed by the CBT group showing a reduction from 81 minutes to 46 minutes and the PT group from 86 minutes to 65 minutes.
Conclusions: Early indications suggest that CT may be superior to CBT and PT alone in the short term for the treatment of primary insomnia.

0758.L

Daytime Side Effects Associated With Cognitive-Behavioural Treatment For Insomnia

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Introduction: The cognitive-behavioural treatment (CBT) has been proven effective in the management of insomnia. While producing durable sleep improvements, this non-pharmacological alternative is assumed to avoid the potential daytime residual effects associated with sleep medications. However, CBT could also produce some degree of daytime impairment in insomnia sufferers. In clinical practice, increased sleepiness and temporary worsening of daytime symptoms of insomnia are frequently reported. In spite of this, the possible side effects of CBT have not been systematically evaluated. This study attempts to describe the pattern of daytime symptoms during CBT in adult chronic insomnia sufferers.
Methods: The sample included 32 adults suffering of chronic insomnia (20 women, mean age 41.9 years, SD = 9.10) who were involved in a study comparing three CBT modalities (individual, group or phone intervention). All received an 8-week cognitive behavioural intervention including sleep restriction, stimulus control, cognitive therapy and sleep hygiene education. Side effects were assessed by a questionnaire measuring the level of irritability, fatigue, physical tension, difficulty with concentration, anxiety and sleepiness on a 5-point Likert scale (0 = absent, 4 = very severe). The questionnaire was completed on a weekly basis at the beginning of each treatment session.
Results: A repeated measures MANOVA was computed on the side effects data. Results indicate that daytime symptoms did not differ between the three treatment modalities. There was a significant effect of the treatment on the severity of the symptoms, $F(42,1302) = 2.908$, $p = .0001$. A trend analysis was performed to describe the variation of the symptoms during the treatment. Physical tension and difficulty with concentration appeared to decrease linearly as the treatment progresses. In contrast, variations in the severity of irritability, fatigue and anxiety involved both linear and higher order components. Visual inspection of the curves suggests that irritability and fatigue first increased around week 3 and then decreased until treatment was completed. Anxiety was stable during most of the treatment except for a peak at week 2 and a decrease in the last two weeks. The variation of sleepiness during treatment was described by a quadratic and a higher order component. The level of sleepiness appeared to remain elevated from week 3 to week 6 but returned to baseline level at week 8. Overall, the severity of the symptoms remained in the mild to moderate range, except for fatigue and sleepiness which reached moderate to severe intensity in the early stages of treatment.
Conclusions: The results confirm the clinical observation of daytime side effects associated with CBT. During the first weeks of treatment, CBT appears to exacerbate some of the symptoms associated with insomnia such as irritability, fatigue and sleepiness. However, the worsening of symptoms seems to be of limited magnitude and duration. The increased daytime impairment coincides with the introduction of the sleep restriction component and could therefore result from a mild sleep deprivation.

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0759.L

Neuropsychological Functioning of Patients with Primary Insomnia as Compared to Good Sleeper Controls

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Introduction: Its stands to reason that the chronic sleep loss that occurs with Primary Insomnia (PI) should be associated with impaired cognitive performance. Studies investigating cognitive deficits in these patients have found slower reaction times, deficient semantic memory processing and divided attention deficits. A preliminary analysis by our group (2002) found that PI's performance on a semantic memory task was deficient when compared to normative data, indicating deficits in long-term memory processing and on-line problem solving. The present investigation included a larger sample of PIs and compared their performance on a brief neuropsychological battery to good sleeper controls. Both groups were assessed in-lab and under common conditions.
Methods: 49 subjects participated in this study. 32 were diagnosed with Primary Insomnia (PI) and were enrolled in a treatment outcome study. Seventeen were healthy sleeper controls who were locally recruited. Neuropsychological tests were administered prior to treatment on the first evening of an in-lab study. The test battery consisted of the Hopkins Verbal Learning Test (HVLT), Trailmaking Test, Controlled Oral Word Association Test (COWAT: FAS), Digit Span Test, Letter-Number Sequencing and Digit–Symbol Tests (WAIS-III), Brief Test of Attention (BTA: Numbers, Letters), the Stroop Test (Golden version) and a modified version of the Psychomotor Vigilance Task (PVT). PI performance was compared to that of healthy sleepers using t-tests.
Results: PI and Control subjects did not significantly differ on demographic measures including, age, sex, race, BMI, education, handedness, and menopausal status. As with our prior study, it was found that the PIs did better on some tasks (sustained attention and verbal fluency) and worse on others (verbal long term memory and visual motor performance). It should be noted however, that significant differences in performance emerged only on ancillary measures, such as HVLT perseveration ($p<.01$) and Trailmaking Test errors ($p<.05$). Similar trends were observed for COWAT intrusions ($p < 0.06$) and for PVT lapses ($p < 0.13$).
Conclusions: The present findings suggest that "on-task" performance (performance that requires higher order processing of new information) is compromised in patients with Primary Insomnia. In addition it appears that patients with insomnia have difficulty inhibiting inappropriate responses and this leads to increased error rates, which is, in turn, indicative of deficiencies in higher order reasoning.

0760.L

Do Patients with Primary Insomnia Have a Preferred Medication Use Schedule?

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Introduction: No research has been conducted on whether patients have a preferred dosing strategy when taking medication ad libitum. The present study uses local archival data from a multi-site study on long term efficacy of zolpidem to assess this issue.
Methods: 23 subjects who met ICSD criteria for Primary Insomnia participated in the parent study. Eligible subjects were randomized to one of two treatment conditions (zolpidem 10 mg [ZOLP] or placebo [PLA]). Subjects were instructed to take no less than 3 and no more than 5 pills per week for a period of 12 weeks. Ten pills were provided in foil packs on an bi-weekly basis, and all subjects were continuously monitored with sleep diaries. Pill use was recorded in sleep diaries. Each week's pill use pattern was coded by assigning a "P" to the night when a pill was

taken and an "N" to the night when subjects did not take a pill. Each week was represented by a series of 7 characters. All 276 subject weeks (23 subjects * 12 weeks) were coded. 110 sequences were observed. To reduce the variability of the sequence data, the patterns were further typed into one of three categories: 1) an intermittent pattern ([I] at least one med-free night between med nights), 2) a continuous pattern ([C] at least two consecutive nights where meds were used) or 3) a mixed pattern [M]. In addition, the number of consecutive and total doses were coded. For example, "PPPPPNN" would be designated a "C5" to represent a continuous pattern where 5 pills were taken consecutively. For the present analysis, the two conditions were compared for 1) number of doses consumed/week and 2) differences in the frequency of preferred schedules. Serial t-tests were used to maximally power the analysis.

Results: The mean age of the group was 44.6 yrs. and 93% of subjects were female. The two groups (PLA n = 11 and ZOLP n = 12) did not significantly differ with respect to age or gender, nor did they differ for the number of pills taken or for preferred sequences. 17 patterns were observed. The average number of pills taken was 3.4 pills per week. 61% of weekly dosing strategies were of one of 4 types: CI23 (22.1%), I3 (14.5%), CI24 (12.7%) and CI34 (12%).

Conclusions: These data suggest that patients do not escalate the number of doses taken per week and that the pattern of dosing with active medication is similar to placebo. The present data should enhance our confidence that, within an intermittent dosing scheme, patients adopt dosing strategies which are conservative – they take fewer pills than allowed and for 60% of the time do not use more than 3 doses in succession.

The parent study was conducted by Lorex

0761.L

A Randomized Controlled Trial of Nasal Dilator Strip Therapy for Sleep Maintenance Insomnia

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Introduction: Chronic sleep maintenance insomnia (SMI) is frequently caused by sleep-disordered breathing (SDB). However, SDB is often absent from the differential diagnosis of insomnia work-ups conducted by healthcare providers, resulting in few referrals to sleep centers for polysomnography and evidence-based SDB treatments. This salient clinical disconnect suggests it may be necessary to establish transitional pathways to encourage those outside the field of sleep medicine to recognize and treat SDB in SMI patients. In our preliminary efforts, we explored Breathe Right® nasal dilator strip (NDS) therapy; in several cases, NDS markedly improved insomnia and motivated patients to pursue definitive care at sleep disorders centers. Thus, we developed an RCT to study NDS therapy in patients with co-morbid SMI and SDB.

Methods: Fourteen adult men (n=10) and women (n=4) were randomized into Treatment (T) (n=8) and Control (C) (n=6) groups for a 4-week protocol. T-patients individually received a(n): (a) Socratic, motivational interviewing, educational session in which SDB impact on sleep fragmentation was discussed in the context of an extensive review of completed sleep questionnaires; (b) physical exam of the upper airway; (c) acoustic rhinometry; and (d) NDS fitting. C-patients individually received physical exam, rhinometry, and a Socratic session without motivational interviewing, using a theme encouraging verbalization of perceptions and understanding of sleep problems based on review of questionnaires. The objective was to covertly stimulate C-patients to self-monitor their sleep problems, which has been shown to produce non-specific therapeutic effects for insomnia. Both groups prospectively monitored sleep symptoms daily. For this report, data included Insomnia Severity Index (ISI, range 0-28, non-clinical cut-off < 11), Pittsburgh Sleep Quality Index (PSQI), and two prospective symptom reports, difficulty staying asleep (DSA) and wake time after sleep onset (WASO), each rated on a 0-4 scale. Cohen's d effect sizes were calculated.

Results: Among 8 T-patients, 4 decreased ISI below clinical insomnia, and mean scores dropped from 16.38 to 10.88 (change = -5.5, d=1.33); whereas, each of the 6 C-patients remained above the clinical cut-off while still showing improvement in mean scores from 17.33 to 14.83 (mean ISI change = -2.5, d=0.87). T showed large effects for sleep quality (mean PSQI change = -2.00, d=0.81) with no change in C (d=0.06). DSA improved in T-patients (d=0.45) and worsened in C-patients (d=-0.47). WASO improved in both T (d=0.38) and C (d=0.32). Among 6 C-patients, 5 crossed over and completed treatment of which 4 decreased ISI below the clinical cut-off (mean change = -5.8, d=1.40). These 5 patients showed large improvements in PSQI (d=0.72), DSA (d=1.45), and WASO (d=1.16) compared to post-control follow-up.

Conclusions: NDS therapy produced larger treatment effects than a non-specific, sleep educational control group. Only those patients using NDS were among the ones to decrease insomnia into a non-clinical range. This RCT will comprise a larger sample with a longer post-treatment follow-up period, which will be analyzed after study completion.

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0762.L

Maternal/Paternal Conditioned Insomnia - A New Concept of Adult Insomnia Induced by Infant/Child Night-Crying

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Introduction: Chronic insomnia in adults is known to result from the conjunction of precipitating and maintaining factors. Among these factors, night crying in infants or young children has never been documented as a possible and important cause of precipitating and/or maintaining insomnia in young healthy women (men) with no previous history of sleep disorders. Sleep-onset association disorder (SOAD) is one of the most frequent sleep disorders in children affecting up to 20% of the children before the age of three years (ICSD, 1997). Children with SOAD require specific interaction with a parent to fall asleep at bedtime or during night-awakenings. Mothers (fathers) of infants/children with SOAD often complain of disturbed sleep and daytime somnolence. Recurrent induced night awakenings could lead to spontaneous awakenings (prone to occur in the absence of the causal stimulus) in some parents, developing to maternal/paternal conditioned insomnia (M/PCI).

Methods: 25 SOAD children (ICSD, 1997), 11 boys and 14 girls, mean age 17 ± 12 months, and their parents have so far participated in the study. History of SOAD (age of onset, duration of symptoms, mean number of night awakenings during the passed two months) was assessed using parental reports. Both parents (n=14) or mother only (n=11) have been assessed for nocturnal sleep complaints using sleep logs, previous history of sleep disorders, adapted questionnaire measuring cognitive anticipation to sleep disruption. Mean age of parents was 24 ± 5 years in women and 28 ± 7 years in men.

Results: Diagnosis of M/PCI was accepted when a sleep complaint was reported for more than 2 months and when at least 4 of the following items were present: ·Anticipates child awakenings during the night ·Spontaneously wakes up before the child wakes up ·Stays awake and alert until the child signals his awakening ·Shows over concern for not hearing the child if it cries in the night ·Excessively worries or checks the child if it doesn't wake up during the night ·Has trouble going back to sleep after provoked or spontaneous awakening ·Spontaneously awakes during the night even in the absence of the child ·Anticipates night awakening before going to bedMean duration of SOAD was 11 ± 6 months in our sample. None of the mothers or fathers had previous sleep disorder complaints. 56% (n=14) of the mothers and 28% (n=4) of

the available fathers met defined criteria for M/PCI. 75% of the MCI mothers complained of altered daytime functioning, impaired relation with their offspring and excessive daytime sleepiness as measured by Epworth sleepiness scale (mean score 14 ± 4).
Conclusions: Repetitive night crying in infants/children is responsible for provoked and spontaneous conditioned awakenings in more than half of the mothers of our sample. Mothers (fathers) submitted to provoked awakenings may develop after sometime spontaneous awakenings possibly responsible for chronic insomnia. This ongoing study should help determinate if M/PCI is a relevant disorder and an important and underestimated cause of chronic insomnia in adults.

0763.L

Reported Mental Activity During Sleep For Insomniacs And Good Sleepers

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Introduction: Insomniacs are more likely than good sleepers to misperceive prior sleep as being wakefulness following overnight awakenings. This difference could potentially be explained by higher levels of mental activity persisting during sleep for insomniacs.
Methods: Twenty four insomniacs (15F, 9M) who reported SOL>30min, WASO>40min, and SEF<80% on a 7-day sleep/wake diary underwent 4 weekly laboratory PSG recordings and were compared to 10 good sleepers (6F, 4M, diary SOL<20min, WASO<20min, SEF>90%). Across the night subjects were delivered a tone through a speaker at the bed head. After verbal acknowledgment of hearing the tone, the following recorded questions were presented; "What was going through your mind just before hearing the tone?" and "Can you give me any more detail about what you've told me?" The tone and questions were presented under four different conditions; Wake- after 5 minutes of wake without movement, Early Non-REM- 5 minutes after the first sleep spindle/K complex following sleep onset, Late Non-REM- 5 minutes after the return to Stage 2 following SWS, or 20 minutes of continuous Stage 2, REM- 5 minutes after REM onset. The schedule cycled through these four conditions to maintain sleep architecture and provide samples of each sleep/wake probe distributed evenly across the night. Responses to both questions were recorded and later transcribed and coded by a judge blind to subject condition. A Word Count (WC) score was calculated for each probe by adding the number of words in the responses to both questions, excluding verbal intrusions, corrections and repetitions. A Thought Unit (TU) measure was calculated for each probe, which reflected the number of distinct, thematically homogenous thought sequences in each report.
Results: Contrary to our predictions, Controls' mentation reports contained more words and more Thought Units than those for Insomniacs with respect to all probe types, although none of these differences achieved statistical significance when compared using one-way ANOVAs. In order to account for subjects' differences in verbosity or reporting style, ratios of wake to sleep WC and TU were calculated for each type of sleep probe. The lower the ratio, the less WC or TU were elicited from sleep compared to the amount elicited from wake. Mean WC wake/sleep ratio showed no significant group difference for Early Non-REM [Insomniacs Mean (sd) .764 (.307), Controls .840 (.309)], Late Non-REM [I .790 (.472), C .732 (.318)] nor for REM [I .956 (.531), C .908 (.286)]. Insomniacs demonstrated lower (n/s) mean wake/sleep TU ratios for Early Non-REM probes [I .660 (.355), C .874 (.468)], Late Non-REM probes [I .642 (.481), C .730 (.548)] and REM probes [I .897 (.547), I 1.30 (1.31)].
Conclusions: Insomniacs do not report more mental activity during sleep than good sleepers. Insomniacs' sleep misperception does not appear to be explained by increased nocturnal mentation.

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0764.L

Family Studies In Insomnia

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Introduction: Several predisposing factors to insomnia have been hypothesized, including a familial component. A recent study found that more than one third of insomniacs had a familial history. However, the absence of a control group and validation assessment of the probands limited the conclusion of that study. Here, we evaluated the incidence of insomnia among first-degree relatives of patients with insomnia of different etiologies.
Methods: 256 consecutive patients (142 women, 114 men; mean age = 47.88 ± 13.29; mean age of onset = 35.14 ± 14.32) with a primary complaint of insomnia completed a clinical interview, several questionnaires (Insomnia severity index, Beck depression, Spielberger anxiety, Fatigue and Epworth scales) and, when indicated (n = 92), polysomnography. Patients were diagnosed with either primary (n=77) or secondary insomnia (n=179), with the later including psychiatric (n=104), drug/alcohol abuse (n=14), sleep apnea syndrome (SAS; n=26), restless leg syndrome-periodic leg movement (RLS-PLM; n=19), pain condition (n=6), and other causes (n=10). All patients completed a questionnaire in order to estimate the incidence of a family history of insomnia among first-degree relatives (parents and siblings). In addition, 74 relatives (from 27 consecutive families) completed the same questionnaire to verify the accuracy of the proband assessment. Finally, 90 spouses were interviewed and completed the same questionnaire in order to estimate a base-rate incidence of insomnia in their families.
Results: Among 256 insomnia patients, 125 (48.83%) reported that at least one first-degree relative was affected compared to a rate of 23.5% in the non-insomnia control group. Of those with primary insomnia, 72.7% reported familial insomnia with 32% of the relatives affected. Among patients with secondary insomnia, 43.3% of those with a psychiatric disorder, 26.9% with SAS, and 42.1% with RLS-PLM reported a positive familial history of insomnia. Comparisons between the family incidence rates of insomnia assessed by the probands and by the 74 first-degree relatives yielded discrepancies in only 10 cases (13.5%). In addition, sleep-onset insomnia and a younger age at onset were significantly associated with familial insomnia. The mother was the relative most frequently affected (56 %) in familial cases.
Conclusions: This study reports a dramatic increase of familial aggregation of insomnia, warranting further genetic studies in primary insomnia with early age at onset.

0765.L

Variability in Sleep Patterns of Chronic Insomniacs

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Introduction: The sleep of chronic insomniacs is often characterized by extensive night-to-night variability. Some patients complain that their sleep is totally unpredictable and, even when insomnia is persistent, it is common to have an occasional good night's sleep intertwined with several nights of poor sleep. Some individuals complain of insomnia primarily on Sunday nights and, still others, report that they sleep poorly on weeknights but can recover on weekends. This study examined whether sleep variability observed in insomnia follows specific/predictable patterns.

Methods: The sample included 106 participants (57.6% women, mean age = 45.5). Participants met diagnostic criteria for persistent primary insomnia. Mean insomnia duration was 12.8 years. Participants completed daily sleep diaries for an average of 31 days (SD = 12) before receiving insomnia treatment. Standard sleep parameters were derived from the sleep diary: Sleep efficiency (SE), sleep onset latency (SOL), and wake after sleep onset (WASO). For the purpose of the present study, an insomnia night was defined as a SOL and/or WASO equal or greater than 60 minutes, with a SE equal or smaller than 80%.
Results: Conditional probabilities to have a good night after 1, 2, or 3 consecutive insomnia nights were computed from time-series diary data for each participant. As a group, these results suggested that sleep was unpredictable, with probabilities to have a good night's sleep varying from 0.50 to 0.52, after 1, 2, or 3 nights of insomnia. Conditional probabilities were submitted to a cluster analysis in order to identify subgroups of participants exhibiting similar levels of conditional probabilities. A three-cluster solution was retained based on the parsimony of the solution and the largest variance explained. The first cluster comprised participants (40 to 60% of the sample) exhibiting an unpredictable insomnia pattern, with probabilities to have a good night after 1, 2, or 3 insomnia nights of 0.49 to 0.50, respectively. The second cluster (21 to 32% of the sample) included participants with a low probability to have a good night following insomnia nights (0.17 to 0.15). The third cluster (21 to 26% of the sample) comprised participants exhibiting a high probability to have a good night following insomnia nights (0.86 to 0.99). For this group, the probability of having a good night increased linearly with the number of previous insomnia nights.
Conclusions: These findings confirm the presence of extensive variability in the sleep of about half of individuals with chronic insomnia. The other half is divided equally in two subgroups, including one for whom sleep is invariably disrupted from night to night, whereas the other group shows a higher probability of experiencing a good night's sleep as a function of the number of preceding poor nights' sleep. These data suggest that sleep is not unpredictable for everyone with insomnia and that some forms of insomnia may be more subject to a homeostatic effect. Additional research is needed to characterize those subtypes of insomnia in terms of diagnosis, clinical features, or temporal course of insomnia.

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0766.L

Accelerated Sleep Onset Training for the Treatment of Sleep Onset Insomnia

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Introduction: Stimulus control therapy is considered the most effective long term behavioral treatment for sleep onset insomnia. By following its instructions a patient would obtain a single rapid sleep onset each night. This rapid sleep onset usually follows several unsuccessful sleep onset attempts each night, particularly in the early weeks of therapy. In practice, compliance to instructions can be a problem since it usually produces increased daytime sleepiness over many weeks of therapy. The question is, could the goals of stimulus control therapy be achieved in a more intensive, short duration therapy? Such a therapy may be administered by facilitating a large number of rapid sleep onsets during acute sleep deprivation.
Methods: In a pilot study 10 healthy sleep onset insomniacs (mean age of 33.5 years) were obtained by advertisement in local newspapers. All had subjective (two weeks sleep diary) and objective (wrist activity monitors) sleep onset latencies > 30 minutes with a mean subjective TST of 5.2 hours and sleep efficiency of 62%. Participants were involved in a wakeful bedrest routine of at least 26 hours starting at 2000 hours or earlier and which included half-hourly multiple sleep latency tests (MSLTs). The MSLTs allowed a possible 25 minutes in which to initiate sleep which was defined as the first of three consecutive 30 second epochs of sleep. At each sleep onset the subject was aroused to ensure the continuation of acute sleep deprivation. Over the 26 hour period this provided at least 50 sleep onsets in all subjects. Two weeks of sleep diary and activity monitor data were collected at home after a night of recovery sleep and for another two weeks at eight weeks follow-up.
Results: Over the 50+ MSLTs sleep latency decreased from a mean of about 16 minutes to less than three minutes from the middle of the first night of sleep deprivation to the end of the wakeful bedrest routine at about 2200 hr the following night. Subjects were pleased at how well they tolerated the procedure and with the experience of so many (>40) short sleep latencies. The two week pre-treatment period was compared with the immediate two week post-treatment and follow-up two week period. Mean subjective sleep latency decreased significantly from 75 min in pre-treatment to 32 min at short term ($t(9) = 5.1$, $p<0.001$) and 45 min at longer term follow up ($p<0.01$). Subjective TST increased from 312 min to 397 min ($p<0.001$) and 372 min ($p<0.01$) at follow up. Mean sleep efficiency increased 15% to 78% ($p<0.01$). Activity monitor data showed similarly significant yet less dramatic changes.
Conclusions: It appears that this procedure promises to be an effective treatment for sleep onset insomnia. In a concentrated period of 26 hours of sleep deprivation, it provides rapid improvement in sleep that would normally take 4-6 weeks of stimulus control therapy to yield comparable improvements.

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0767.L

The Effects of Rumination About Work Issues During Leisure Time on Sleep: A Two Day Diary Study

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Introduction: School teachers commonly complain that they are unable to get to sleep at night, and report poor sleep maintenance due to unwanted, ruminative thoughts and concerns about work-related issues. The present study investigated the effects of ruminative thinking on sleep, using self reported diaries.
Methods: One-hundred and forty five school teachers were asked to keep a diary record of their thoughts about work over a workday evening over two consecutive nights and were monitored hourly from 17.00 hrs until bedtime. Each individual also completed a self-report assessment of their sleep patterns over the same night. Using information obtained from the diaries the sample was divided into high ruminators (thought about work issues a lot during the evening) and low ruminators (thought about work issues little during the evening) using tertile splits.
Results: After adjusting for age and gender, high ruminators over the first night reported: 'difficulty falling asleep' [odds ratio (OR) = 3.2], 'difficulty waking up' (OR = 4.0), 'difficulty getting back to sleep if awoken during the night' (OR = 5.1), and 'feeling unrefreshed after awaking' (OR = 5.9). On the second night, high ruminators reported difficulty waking up' (OR = 4.2), and 'feeling unrefreshed after awaking' (OR = 6.1). When controlling for evening working patterns 'difficulty waking up' for the first night, was no longer significant. Thus, for the most part, the results could not be explained by working practices during the evening.
Conclusions: Ruminating about work-related issues appears to be associated with self reported sleep disturbance. It is important therefore that individuals learn to 'switch-off' from work during the evening in order to obtain good quality sleep.

0768.L

Dose Response Effects Of Behavioral Insomnia Therapy: Clinical Trial Update

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Introduction: Previous reports suggest that two, four, six, and eight sessions of cognitive-behavioral insomnia therapy (CBT) are all effective, but the relative efficacy of such varied treatment doses remains to be determined. Given market pressures such as managed care and capitation models of health care delivery, this study was undertaken to determine the optimal dose of CBT.
Methods: Study enrollees were first screened via structured interviews, medical examinations, TSH testing, and polysomnography. Individuals 40 to 75 year old who met DSM-IV criteria for Primary Insomnia and had an average wake time after sleep onset (WASO) > 60 min. were enrolled. Participants completed baseline assessment including sleep logs (2 weeks), actigraphy (one week), and multiple questionnaires. They were then randomized to a waiting list control or to one (week 1 only), two (weeks 1 and 5), four (weeks 1, 3, 5 & 7), or eight (weekly) therapist-guided CBT sessions. Outcome data for the current report were derived from measures completed before, during, and 6-months after treatment.
Results: To date, 82 (39 men) study patients (M_Age = 55.7 yrs.; SD = 9.6 yrs.) with significant sleep maintenance insomnia (M_baseline WASO = 94.1 min./night; SD = 45.0 min./night) provided sufficient outcome data for analyses. A 5 (treatment dose) x 2 (baseline vs. week 8) x 4 (sleep log measures: TST, TWT, WASO & SE%) MANOVA yielded a significant treatment dose x time ($F [4, 77] = 2.70$, $p = .04$) interaction. A univariate ANOVA of the primary outcome measure, WASO, also showed a significant ($F [4, 77] = 2.96$, $p = .03$) treatment dose x time interaction. Only the groups receiving the one-session and four-session protocols achieved significant reductions in WASO. However, 61% of those patients receiving 4 CBT sessions achieved at least a 50% baseline-to-treatment-end reduction in WASO, whereas only 37.5% of those in the one-session protocol achieved this level of WASO decline. About 64% of those receiving 4 CBT sessions versus 44% of those receiving one-session achieved normal insomnia symptom questionnaire scores (ISQ) by the end of treatment. Those receiving eight CBT sessions averaged a 26.4% reduction in WASO. Only 1/3 in this group achieved a 50% decline in WASO and normal ISQ scores by treatment end. Analyses of available follow-up data showed a persistence of these trends six months after treatment.
Conclusions: Results suggest a moderate CBT dose (four sessions) may represent optimal treatment. This dose, with sessions scheduled two weeks apart, may afford patients sufficient therapist contact, yet provide ample opportunity to independently practice sleep-improving strategies. One or two CBT sessions may not provide patients sufficient therapist contact to assure improvements, whereas high dose (8 weekly sessions) CBT may not foster proper independence for patients to implement treatment strategies on their own.

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0769.L

Trait Vulnerability to Stress-related Sleep Disturbance and Hyperarousal

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Introduction: Multiple stressors including caffeine, circadian phase shifts, and laboratory adaptation have been shown to produce sleep disturbance in some, but not all individuals. However, studies have not identified specific trait characteristics consistent with a vulnerability to sleep disturbance. This report describes the use of a self-report scale for predicting vulnerability to a first night effect.
Methods: One-hundred sixteen participants from a population-based sample (46% M, mean age = 41.1 $\pm$ 13.0) completed a 27-item questionnaire regarding sleep disturbance in response to commonly experienced stressful situations. Reliability of the scale was determined by factor analyzing the items (principal components with Promax rotation) and computing internal consistency using Chronbach's alpha. Nine items were used in the final scale (Ford Insomnia Response to Stress Test, FIRST). Individuals scoring high and low (median split) on the scale were compared regarding sleep during a first night in the laboratory (8.5 hour PSG) and alertness in the 2 groups was compared using the Multiple Sleep Latency Test (MSLT).
Results: One factor accounted for 29.2% of the total variance with 9 items loading above .4 on this factor. Chronbach's alpha = .85 for the 9-item FIRST scale with a mean = 20.0 $\pm$ 5.9 and a range = 9-36. Individuals with high scores on the FIRST had lower sleep efficiency (82.2% $\pm$ 13.5 vs. 87.8% $\pm$ 12.0), $t(105) = 2.2$ $p = .03$, increased latency to persistent sleep (32.8 min $\pm$ 40.0 vs. 17.5 min $\pm$ 17.4), $t(105) = -2.4$, $p = .02$, and elevated MSLT scores (12.8 min $\pm$ 4.7 vs. 10.4 min $\pm$ 4.2), $t(99) = -2.7$, $p = .009$, on the first night/day in the laboratory as compared to individuals with low scores. Frequent and persistent insomnia symptoms were reported in 28% of individuals with high FIRST scores whereas only 12% of individuals with low FIRST scores reported such symptoms. Importantly, after eliminating individuals with any history of insomnia the above comparisons remained significant (SE = 78% vs. 86%; LPS = 44.4 min vs. 17.4 min; MSLT = 13.2 min vs. 10.2 min). In addition, for individuals with no history of insomnia, correlations between measures of sleep disturbance and FIRST scores were significant for sleep efficiency ($r = -.52$, $p < .001$), latency to persistent sleep ($r = .50$, $p = .01$), and MSLT ($r = .31$, $p = .03$) indicating that higher scores on the FIRST were associated with a robust first night effect and hyperarousal even in individuals without insomnia.
Conclusions: These differences in sleep as a function of FIRST scores support the hypothesis that there are individual differences in vulnerability to stress-related transient insomnia. Furthermore, the elevated MSLT scores in these individuals, despite significantly disturbed sleep, supports the notion that these individuals exhibit physiological hyperarousal and may be vulnerable to developing chronic primary insomnia.

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0770.L

Sleep and Daytime Consequences in Partners of Patients with Obstructive Sleep Apnea

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Introduction: Partners of patients with sleep apnea/hypopnea obstructive syndrome (SAHOS) frequently complain of tiredness, pain and marital difficulties related to snoring and restless sleep of their spouses. The objective of this study was to evaluate the interference of SAHOS in the partner's sleep, pain manifestations and marital relationship.
Methods: Wives of 16 consecutive untreated patients with severe SAHOS confirmed by polysomnography (WP, aged 47.4 (6.3 yr.) and 12 matched controls married to healthy men (CTRL, aged 45.8 (4.7 yr.) were included in this study. Musculoskeletal symptoms, sleep complains and relationship difficulties with the husbands were assessed by questionnaire. All participants underwent tender point examination for the investigation of fibromyalgia and all-night polysomnography (Harmonie, Stellate TM).
Results: The bedroom was considered as an unpleasant place by 10 (62.5%) of WP patients, vs. 1(3.3%) of CTRL (p=001). Among the WP,

13 (81%) reported husband snoring for more than 5 yr., and 12 (75%) complained of deterioration of the sleep. Thirteen (81%) of the WP adopted strategies to overcome these condition, such as sleeping during the day (12.5%), changing bed during the night (18.5%), using ear plugs (12.5%), awakening the husband (18.5%), going to bed later (6.2%), and many strategies (12.5%). Non-refreshing sleep was a complaint of 8 (50%) of the WP, and 11 (68.7%) reported more than three awakenings during the night in the previous week. Fatigue was also more frequently reported by WP, comparing to CTRL: 56.2% vs. 16.7%, p=0.03. Musculoskeletal pain was present in 13 (81.2%) of WP vs. 3 (25%) of CTRL (p=0.01) and was a recent complain (< 2 yr.) in 9 (69.6%) out of the 13 painful WP. Eight (50%) of WP fulfilled criteria for fibromyalgia, and none of CTRL. Difficulties in marital relationship was more frequent among WP than in CTRL, 9 (56.2%) vs. 2 (16.7%), p = 0.03. Regarding polysomnography data, evidences of sleep disturbance in WP comparing to CTRL were supported by decrease in sleep efficiency (81.9 (6.3% vs. 94.0 (4.7% , p < 0.001) and in delta sleep % (20.3 (9.6 vs. 28.0 (2.7 , p =0.01), increase in sleep latency (12.0 (5.8 min. vs. 4.2 (1.1 min., p < 0.001), stage 1% (5.8 (2.8 vs. 3.6 (1.6 , p = 0.03), and arousal / hr (11.5 (8.3 vs. 4.9 (2.5 , p = 0.03). Alpha-delta sleep assessed by the ratio of alpha activity in delta sleep / stage 2 >1 was detected in 6 (37.5%) of WP, all of them with diagnosed as fibromyalgic.
Conclusions: Sleep disturbances, pain complains and marital difficulties are frequent complaints of partners of patients with severe SAHOS.

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0771.L

Past-Year Opiate Use and its Correlates in an Age- and Sex-Matched Sample from the General Population
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Introduction: Previous studies have indicated an association between opiate use and sleep disturbance in both healthy normal and addicted populations. This report evaluated the association of opiate use with sleep problems, and the extent to which this association is mediated by pain and psychological factors in a population-based sample.
Methods: In a population-based sample, 30% (n=770) endorsed the use of Vicodin, Darvon, Demerol, Dilaudid, methadone, Talwin, morphine, Percodan, or Tylenol with codeine in the past year. A subset of this sample (n = 381) was selected for standard NPSG and MSLT study. Of the 381, 137 (36%) reported past year use of the above-listed opiates. Given that age and female sex are associated with increases in sleep problems, an age- and sex-matched sample (n = 137) was drawn from the total PSG sample, excluding opiate users, for comparison purposes.
Results: The subsample of age- and sex-matched opiate- and non-opiate users did not differ on race, marital status, or education. Opiate users were more likely to have difficulty falling asleep, waking more than 3 times during the night, and waking up too early in the morning. In terms of objective PSG findings, opiate users had significantly less time in stage 3-4 sleep than non-opiate users, but no differences were found in sleep induction or maintenance parameters. When comparing level of daytime sleepiness between opiate and non-opiate users, no differences were found for mean latency to sleep on MSLT. Opiate users were more likely to use alcohol and medications to help them sleep. Interestingly, opiate users were also were more likely to take medications to help them stay awake. Because opiate users had higher rates of arthritis, migraines, neurological problems, and menstrual or gynecological problems and endorsed higher rates of depressive symptomatology than non-opiate users, we next controlled for depression (BDI-II) and reported pain level (SF-36: Bodily Pain subscale). After controlling for pain and depression, opiate users were still significantly more likely to have difficulty falling asleep and more likely to awaken more than 3 times during the night. However, no significant differences remained for any PSG parameters.
Conclusions: In this age- and sex-matched sample, opiate users reported higher levels of sleep disturbance and more use of substances to help with problems of both sleep and daytime alertness. Unlike previous studies, the current sample demonstrated that opiate use negatively impacted sleep quality even after controlling for pain and depression.

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0772.L

Insomnia as a Path to Alcoholism: Dose Escalation
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Introduction: Our previous studies showed that ethanol at a low dose improved the sleep of insomniacs and that insomniacs self administered low ethanol doses at bedtime (i.e. as a hypnotic) to a greater extent than non insomniacs with similar social drinking histories. Also in surveys, 22% of insomniacs report use of alcohol for sleep, which is a concern in that, what may initially be sleep medicating behavior could subsequently evolve into drug seeking behavior as tolerance to the sleep effects develops and other effects of ethanol become reinforcing. This study assessed whether or not the dose self administered by insomniacs before sleep is increased after one week of nightly ethanol use.
Methods: Twelve healthy, 21-55 yrs old, insomniacs in good medical and psychiatric health with no history of alcoholism or drug abuse participated. All had complaints of insomnia and sleep efficiencies <85% on a screening 8 hr NPSG with no evidence of primary sleep disorders. They were randomized to an ethanol or placebo pretreatment group and on 7 nights received ethanol (0.45 g/kg, the dose shown to improve sleep) or placebo, presented in color coded cups, 60 min before bedtime with 30 min for beverage consumption. On night 8 they received the opposite beverage (color coded cup). On 7 subsequent nights they choose their preferred beverage by the color code and had the opportunity to request 3 refills of their chosen beverage (0.2 g/kg per refill or placebo refills) with a 0.8 g/kg total possible ethanol dose.
Results: The ethanol pre treated insomniacs choose ethanol on 53% of nights in comparison to 37% of nights for the placebo pre treated insomniacs (p<.09). On these ethanol selected nights, the ethanol pre treated insomniacs choose on average 7.0 $\pm$ 1.91 (sd) ethanol refills compared to the 3.57 $\pm$ 2.15 ethanol refills of the placebo pre treated insomniacs (t=2.46, p<.03). On placebo chosen nights, ethanol pre treated insomniacs choose 4.71 $\pm$ 1.70 placebo refills and placebo pre treated insomniacs choose 4.01 $\pm$ 1.29 placebo refills (NS).
Conclusions: The results of this study indicate that 7 consecutive nights of ethanol pretreatment with a nightly "hypnotic" dose of 0.45 g/kg leads to a significantly greater number of ethanol refills (yielding a 0.69 g/kg dose), but not placebo refills. This suggests tolerance development during the pretreatment and dose escalation for the reinforcing effects of pre sleep ethanol in insomniacs.

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0773.L

How Do Individuals Sleep In The World? Results From The SLEEP (Sleep Epidemiological) Survey
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Introduction: Among several countries from different continents, to describe the rate of individuals having sleep troubles, to detail the troubles and the way people solve them out, to detect the rate of individuals likely having sleep disorders but who are unaware of and among individuals aware of their sleep disorders, to document the use of sleep med-

ication and the degree of satisfaction

Methods: Cross sectional survey conducted in ten countries with the same case report form translated in local language, based on a sleep outcomes evaluation short form and two reference evaluation scales (Athens Insomnia scale AIS and the Epworth Sleepiness Scale ESS), data managed in a single statistical centre, and analysed according to a single statistical plan. Data have been collected on the International Sleep Well Day (March the 21st, 2002) from a general population attending booth in different public places such as street, railway stations, …. and from phone and Internet calls.

Results: 35 327 individuals from 10 countries (Austria, Belgium, Brazil, China, Germany, Japan, Portugal, Slovakia, South Africa, Spain) from 4 continents have been enrolled in the survey. In the 10 studied countries, an average of 24.7% of individuals is aware of having sleep disorders: the percentage significantly varies between countries (from 10.4% in Austria to 32.2 % in Belgium). Among individuals aware of their sleep disorders, less than a half (46.6%) undertake action to solve their troubles and the solution widely differs from country to country . Only 32.0% take sleep medication (from 9.8% in Austria to 51% in South Africa, $p<0.001$) while 19.4% drink alcohol in order to fall asleep more easily (from 9.8% in Austria to 30% in Japan, $p<0.001$). One sleep medication in four is initiated without any medical advice. This may explain that only one half of these individuals (51.8%) is satisfied with the medication (from 34.6% in Japan to 100% in Austria, $p<0.001$). Only 42% of individuals with sleep medication take it every night while 25.2% take it once a week and 33.2% less than once a week with a similar level of satisfaction. Once again there are significant variations in the frequency of intakes per week from a country to another one. Among individuals who do not complain of sleep disorders in the sleep outcomes evaluation, 35.8% of them have an AIS score > 4 (from 32% in Austria to 93.6% in Brazil, $p<0.001$) which means that they are unaware of their sleep disorders even if 33.5% are really sleepy or very sleepy during the day according to the ESS (from 7.5% in Germany to 34% in Belgium) . They represent 27.0% of the global population which means than taking into account people aware and not aware, a person in two has sleep disorders.. Among these individuals who are not aware of their sleep disorders according to the AIS, 48.1% are clearly rated insomniac and 44.1% have daytime sleepiness. Paradoxically, their troubles have an important impact on their daily life, they are aware of this impact but they do not link them to their sleep disorders for which a medical advice should be required

Conclusions: although there are huge variations in the incidence of insomnia and its management among the 10 studied countries, this survey concludes that one individual in two has more or less sleep disorders whatever the country and only one in four is aware of his sleep troubles. Only one third of those who are aware of their sleep disorders take sleep medication and often without medical advice. These results show that a better communication on sleep disorders and their management should be widely spread out.

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0774.L

Effects Of A Structured Problem-Solving Procedure On Pre-sleep Cognitive Arousal In College Students With Insomnia

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Introduction: The pre-sleep cognitive activity of those with insomnia is more focused on worries, environmental stimuli like noise, and the consequences of not sleeping, whereas good sleepers focus on "nothing in particular" (Harvey, 2000). Results from correlational and regression analyses suggest worry/problem-solving and thinking about sleep and the consequences of sleep loss, are the strongest cognitive predictors of delayed sleep onset latency (Wicklow & Espie, 2000). The purpose of the study was to reduce the subjective complaint of pre-sleep cognitive arousal via an early evening problem-solving procedure.

Methods: Thirty-three undergraduate students who reported insomnia, were screened to exclude those with (1) Anxiety or Mood disorders, or substance abuse; (2) self-reported signs of sleep disorders other than insomnia; (3) extremes in circadian tendency using the Morningness/Eveningness Questionnaire, and; (4) current psychoactive medication use. On baseline nights, participants wore actigraphs, and completed a worry monitoring form between 6-8 PM; a Pre-Sleep Arousal Scale (PSAS) and State-Trait Anxiety Inventory-State Anxiety subscale (STAI-S) before bed; and a Sleep Diary (SD) the next morning. Participants were then trained on either a procedure that generated possible solutions to their worries (Constructive Worry; CW group), or they were trained how to fill out the Worry Domains Questionnaire – WDQ, and Penn State Worry Questionnaire - PSWQ (Worry control group). On the five subsequent nights, the groups engaged in their respective procedures for 15 minutes sometime between 6-8 PM, and completed the same measures as baseline.

Results: There was a statistically significant interaction on a repeated measures MANOVA (PSAS, PSAS Cognitive subscale, PSAS Somatic subscale, and STAI-S subscale), Wilks' = 0.592, $F(4, 27) = 4.659$, $p = 0.005$. Follow-up ANOVAs for PSAS [$F(1,30) = 10.285$, $p = 0.003$], and PSAS Cognitive subscale [$F(1,30) = 18.249$, $p = 0.001$] were significant. Follow-up tests on CW scores found that post-intervention PSAS was significantly lower than baseline PSAS, $t(15) = 6.97$, $p < 0.001$, and the CW scores on the post-intervention PSAS Cognitive subscale were significantly lower than baseline PSAS Cognitive subscale, $t(15) = 7.22$, $p < 0.001$. In contrast, the Worry group's scores did not significantly change from baseline to post-intervention, on either the PSAS, $t(16) = 2.62$, $p = 0.07$, or the PSAS Cognitive, $t(16) = 2.55$, $p = 0.07$. There were no significant results for any other sleep or arousal variables.

Conclusions: Although the CW group reported decreased cognitive arousal, there were no significant effects on somatic arousal, anxiety, Sleep Diary or actigraphy sleep variables. One possible explanation for the inconsistent relationship between pre-sleep cognitive arousal and sleep is low statisitcal power; however, another explanation is that cognitive and/or somatic arousal in patients may be experienced differently across individuals, and this may have differential effects on their sleep (Spielman, 1986). One rationale for treating pre-sleep arousal is the complaint that excessive mentation and worry before bed is troubling to those with insomnia (Broman & Hetta, 1994; Lichstein & Rosenthal, 1980), and in this study, adding a cognitive treatment for these patients helped with this specific complaint. Future investigations could test a CBT plus Constructive Worry treatment package to see whether CBT + CW produces superior improvements to CBT only.

0775.L

Benzodiazepine Discontinuation in Chronic Insomnia: A Survival Analysis Over a 24-Month Follow-up

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Introduction: Discontinuation of benzodiazepine (BZD) treatment for insomnia can be difficult. Relapse rate after discontinuation is high. Supervised medication withdrawal with cognitive-behavior therapy (CBT) for insomnia has been shown efficacious to facilitate discontinuation, with global abstinence rates reaching 70%. In a previous report, significantly more participants who had received this intervention were drug-free by the end of the treatment compared to those who had not received it. In this report, we examined survival time and relapse after BZD discontinuation.

Methods: Seventy-six older adults (mean age 63.2 years; 50% women) with persistent insomnia and prolonged BZD hypnotic usage participat-

ed in this study. Two groups underwent a 10-week physician-supervised medication tapering, of which one received CBT for insomnia during taper while the other did not. A third group received CBT alone without the supervised taper program; participants were encouraged to consult their family physician if they wished to stop BZDs during the course of the study. Follow-up was of 24 months post-treatment. All drug-free participants at post-treatment were entered in the analysis. Survival time was calculated using Kaplan-Meier survival analysis. Event to predict was relapse, defined as resumption of regular use of any sleep promoting medication. Lapses, defined as circumstantial and isolated use of any hypnotic medication, were documented but not entered in these analyses.

Results: At post-treatment, 67% of the sample was drug-free, 56.5% in the CBT group, 50% in the taper group and 92% in the combined group. At the end of the follow-up period, 46% had relapsed, 69% in the CBT, 35.7% in the taper and 39% in the combined groups. Survival at 3 months for the 3 groups respectively was of 53.8%, 100% and 78.3%. At 12 months, survival was of 38.5%, 84.6% and 64.5% respectively. At 24 months, survival was of 28.9%, 59.2% and 59% respectively. Mean survival times were 8.5 months (SE = 1.8), 19.9 months (SE = 2.1) and 11.8 months (SE = 1.4) respectively and Post-hoc Log-rank test reveals a significant difference between the CBT alone and taper alone groups (p = 0.03). Participants in the taper alone group fared better than their counterparts from the CBT alone group.

Conclusions: Results confirm that relapse after discontinuation is frequent, regardless of the intervention received. However, time to relapse varies considerably between treatment groups. Although most participants in the CBT group achieved drug-free status by the end of treatment 21.7% relapsed within 3 months. Participants in the taper alone group showed a better survival time. These participants may fare better because of baseline personal and psychological characteristics, which might have helped them cease hypnotic medication without formal psychological help. Other predictors remain to be explored. Adding booster sessions to withdrawal programs at critical time-points may help prevent relapse.

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0776.L

Hamilton Depression Inventory (HDI): A Quality Of Life Measure For People With Insomnia?

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Introduction: With increasing evidence of the importance of quality sleep for optimal functioning, it is of concern that 10-15% of people in general population report severe chronic insomnia. In fact, it can become the nucleus of generalized psychological distress, manifesting itself as a host of symptoms and interpersonal difficulties which adversely affecting the quality of life. We routinely use the Hamilton Depression Inventory (HDI), a self-report version of the Hamilton Rating Scale for Depression in our clinic as an outcome measure. We have noted a tendency that patients with primary insomnia in their initial clinic visit have scores above the clinical cutoff on this instrument. After CBT treatment for insomnia the HDI scores drop significantly. We believe that the HDI, when used with insomniacs, is functioning more as an indicator of quality of life tapping generalized subjective distress than an assessment of depression severity.

Methods: Pre- and Post-treatment HDI data were collected from 30 patients (16 females, 14 males; mean age of 47) referred for treatment of chronic insomnia after evaluation by a sleep specialist. One patient was diagnosed with Major Depressive Disorder (MDD) prior to treatment. To determine if the drop in scores were due to the improvement in the quality of sleep, we analyzed the HDI without the sleep and fatigue questions. The original scores on the HDI were adjusted by removing five questions, which measured insomnia (questions 4-6), fatigue (question 13), and hypersomnia (question 18). Paired T-Test (pre vs post-treatment) was conducted using SPSS 10.

Results: On average 8 sessions were utilized for assessment and treatment. As a group, the original HDI scores showed a significant drop of 10 points from Pre- (mean=19) to Post-treatment (mean=9) (p=.001). The new HDI score maintained the trend with Pre-treatment score of 14 and 6 for Post-treatment (p=.001). There was no significant influence of gender or age on the number of sessions required for treatment or on the post-treatment score on the HDI. Only one patient's original post-treatment score (28.5) on the HDI was higher than the pre-treatment score (21.5). The removal of the sleep and fatigue related questions did not significantly change the new pre-treatment (19.5) or post-treatment (27) HDI scores for the patient with MDD.

Conclusions: Our results indicate that primary insomniacs, as a group, have elevated scores on the HDI despite no clinical evidence of MDD. This suggests that the elevated HDI scores in insomniacs is due to a global reduction in quality of life. The five-point difference between the original HDI Post-treatment score (9) and the adjusted Pre-treatment score (14) suggests that improvements were made in other areas besides sleep and fatigue. Thus, as the HDI data suggests, outcome data should include the gains made inside and outside of the bedroom.

0777.L

Treating Insomnia with Mindfulness-Based Stress Reduction

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Introduction: A pilot study was designed to explore the effects of Mindfulness-Based Stress Reduction (MBSR for insomnia. We examined the impact of MBSR on two sleep variables from daily diaries, sleep onset latency and wake after sleep onset and on two questionnaire measures of distress, depression and worry. Prior research has found substantial effects of mindfulness-based interventions on decreases in anxiety and depression (Miller, Fletcher, Kabat-Zinn, 1995, Shapiro, Schwartz, & Bonner, 1998) and decreases in general medical symptoms (Kabat-Zinn 1993). Mindfulness interventions are also effective for the prevention of relapse of major depression (Teasdale, Segal, Williams et al., 2000, Teasdale, Segal, Williams, 1995). In the present study, we hypothesized that MBSR would be an effective intervention for decreasing stress and reducing anxious worry as well as enhancing sleep.

Methods: Seven women with insomnia (average age of 33.5 years and sd = 6.4) who had participated in other sleep research in our lab were recruited to receive a six-week group MBSR intervention for insomnia. Each session lasted one and a half hours. Participants kept daily sleep diaries and filled out questionnaires at baseline and post-therapy. The intervention was modeled after a well-established cost-effective stress reduction program, mindfulness-based stress reduction (MBSR), developed by Kabat-Zinn and colleagues at the University of Massachusetts Medical Center (Kabat-Zinn, 1982). MBSR is an educationally-based program focusing on training in mindfulness meditation. It is designed to teach participants to become more aware of, and to relate differently to, thoughts, feelings, and body sensations. MBSR helps participants cultivate a non-judging yet discerning observation of all the stimuli that enter their field of awareness moment by moment. Mindfulness practice helps bring greater awareness to the "here and now," as the practitioner learns to let go of ruminations about the past and fears regarding the future.

Results: Participants improved significantly on the Penn State Worry Questionnaire (pretest and posttest means of 57.71 and 46.71, p<.01) and on the Beck Depression Inventory (pretest and post-test means of

15.83 and 6.83, p<.01). Participants demonstrated a reduction in the amount of wakefulness experienced during the night (WASO pretest and post-test means of 68.29 and 31.16 minutes, p=.07) but did not improve on sleep onset latency (pretest and posttest means of 31.16 and 37.38 minutes).
Conclusions: Even with this small sample, the results of the pilot study are encouraging. MBSR was particularly effective at producing reductions in worry and depression. It was less effective in producing changes in sleep variables although the decrease in wake-after-sleep onset indicated that sleep maintenance problems may decrease as distress lessens. Controlled research is needed to confirm these preliminary results. This study suggests that there is potential for integrating mindfulness meditation interventions into cognitive-behavioral treatment of insomnia.

0778.L

Epidemiology of Insomnia in 13,869 Workers in One City Transportation Company

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Introduction: In occupational medicine, sleep disorders are often considered as an early sign of work disadaptation. A big transportation company in the Paris area (France) has decided to conduct a study on sleep disorders in all it staff (41229 persons) to observe the link between several work conditions and sleep disorders.The goal was to describe sleep disorders in the whole company and in several occupational groups: train drivers, bus drivers, white collars, security and station keepers.
Methods: We sent a questionnaire based on the DSM-IV and ICSD minimum criteria of insomnia, previously used in epidemiological studies (Leger et al 2000) to the whole staff of the company (41229 persons). The questionnaire also included a short description of working conditions. We got 14 332 answers, in which 13 869 were fully completed. Statistical analyses were completed to describe insomnia in the whole group and to compare it in the different working categories using the SAS epidemiological program. We also secondly interviewed a group of 145 non respondents to the questionnaire to compare the results to those of the first group.
Results: The workers interviewed were statistically representative of the company (no statistical difference for age, sex and working categories). 31.8% complained of difficulties in initiating sleep, 41.2% of awakenings during the night, 35% of early awakening and 35.5% of a poor sleep quality. According to the DSM-IV minimum criteria 26% had insomnia. Insomnia was more prevalent in station keepers and control employees (31.7%), train drivers (31.4%), white collars (29.4%) than in technicians (19.1%), blue collars (19.6%) or engineers (204%) (p <0.0001). Insomnia is more frequent in workers with irregular schedules (26.9% vs 21.7%, p = 0.001), and in shift workers: 29.8% vs 24%; p = 00001). However only 7% of the group takes medications to sleep.
Conclusions: The prevalence of insomnia in this transportation company was higher than in the general population. Several working conditions had a statistical impact on the prevalence of insomnia. Debates and studies including several groups of the company have been engaged to give education and information about sleep to all the workers. Ref: Leger D et al. Prevalence of insomnia in a survey of 12 778 adults in France. J. Sleep Res 2000;9:35-42.

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0779.L

The Sustained Efficacy and Safety of Eszopiclone Over Six Months of Nightly Treatment: A Placebo-Controlled Study in Patients with Chronic Insomnia

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Introduction: To date, placebo (PBO)-controlled data on long-term efficacy and safety of nonbenzodiazepine anti-insomnia agents have been non-existent. This study determined the efficacy and safety of nightly administration of eszopiclone (ESZ) – a novel, cyclopyrrolone, non-benzodiazepine – over six months of treatment in patients with chronic insomnia.
Methods: In this randomized, double-blind, multicenter study, chronic insomniacs aged 21-69 years received nightly treatment with either PBO (n=195) or ESZ 3 mg (n=593) for six months. Entry criteria included DSM-IV insomnia, with a history of sleep less than 6.5 hrs per night and sleep onset of greater than 30 min. The population was not enriched for wake time after sleep onset (WASO) problems, a key measure for evaluating sleep maintenance. Subjective sleep maintenance, sleep latency, total sleep time (TST), and sleep quality were assessed weekly via telephone using an interactive voice response system, and efficacy results were calculated for Week 1 and each individual month. An ANOVA on rank-transformed data was employed using a last observation carried forward (LOCF) approach. Safety was assessed monthly.
Results: Completion of six-month treatment was similar in both groups (PBO, 56.6%; ESZ, 60.5%). At Week 1 and at every month, ESZ improved sleep maintenance (WASO, number of awakenings, and number of nights awakened; p<0.01), sleep latency (p<0.0001), TST (p<0.0001), and sleep quality (p<0.0001) relative to PBO. Pharmacologic tolerance was not observed. Post-hoc results using data from patients remaining at each time point were consistent with the LOCF findings. There was no evidence of abuse as evidenced by similar rates of tablet usage (approx. 6.4 doses per week in each group). The most common AE in the ESZ group was unpleasant taste (PBO, 5.6%; ESZ, 26.1%). There were no safety issues regarding vital signs, laboratory results, ECGs, or physical or neurological examinations.
Conclusions: For the 471 patients who completed six months of double-blind treatment, nightly use of ESZ produced consistent and sustained improvements in sleep maintenance, sleep latency, sleep time, and sleep quality, and was well tolerated with no pharmacologic tolerance.

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0780.L

Measurement of Sleep in Young Insomniacs: A Multi-Trait, Multi-Method Approach

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Introduction: There has long been in interest in determining how best to measure sleep. Polysomnography (PSG) has traditionally been considered to be the gold standard, but is cumbersome on the part of both the investigator and subject. There are also questions regarding the generalizability of measurements taken in the artificial sleep laboratory environment. Sleep logs can be kept for several weeks with ease but are highly subjective. A third alternative is actigraphy, which is relatively simple to use across many days and is less subjective than sleep logs. The choice of which assessment strategy to use is further compounded by the large discrepancies that are often found across techniques. Further difficulties arise with insomniacs because of the often inaccurate self-

report and failure to find objective evidence of sleep disturbance in this population. This study examined the relationships among sleep measurements strategies using a multi-trait, multi-method approach.
Methods: These data are from 11 young insomniacs (mean age 26.8 (4.1)) and 10 healthy controls (mean age 31.9 (4.1)). Each subject was studied for three consecutive nights at home using ambulatory sleep recording equipment (Medilog system), actigraphy (Actiwatch-L), and morning sleep logs. All records were scored using standard practices and the following variables were computed: total sleep time (TST), sleep onset latency (SOL), sleep efficiency (SE), and wake after sleep onset (WASO). The data were averaged across the three nights and then correlations were computed among variables within a single measurement technique (multi-trait, mono-method) and across techniques within a single variable (mono-trait, multi-method).
Results: For control subjects, the sleep variables within a measurement approach had a higher average correlation in sleep logs (r=.84) and actigraphy (r=.72) than in PSG (r=.48). There was greater consistency in insomniacs correlations, such that there was not a large difference among measurement approaches (all r from .48 to .59). Across measures for a single trait, control subjects had the following average correlations: PSG vs. logs r=.63; PSG vs. actigraphy r=.48; logs vs. actigraphy r=.18). Insomniacs had the following average correlations: PSG vs. logs r=.49; PSG vs. actigraphy r=.67; logs vs. actigraphy r=.53).
Conclusions: Results suggest normal sleepers have relative consistency in their sleep appraisals and activity patterns. This is not the case for insomnia sufferers. When comparing measurement techniques, sleep logs were more closely related to PSG than actigraphy among normal sleepers, but this pattern was reversed in insomniacs. These results suggest that sleep logs may provide more accurate information about sleep in healthy subjects, but that actigraphy is a better approach to use for insomniacs. Investigations of sleep should therefore not rely on any single measurement strategy when sampling from both populations.

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0781.L

Withdrawn

0782.L

Sleep and Endocrine Responses to Psychological Stress in Primary Insomnia

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Introduction: Patients with primary insomnia (PI) exhibit increased autonomic arousal on multiple physiological measures. Recently, these findings were extended to include evidence of sustained hyperactivity of the hypothalamic pituitary adrenal axis, suggesting an abnormality of the integrative physiologic stress response. We elected to test this hypothesis by examining the endocrine and sleep/wake responses of patients with insomnia to psychological stress.
Methods: Twelve patients with a complaint of insomnia lasting at least one year (mean age = 40.1y; 6f) were compared to seven controls (mean age = 37.7y; 5f) in a 3-day "background" laboratory protocol examining nocturnal sleep, daytime alertness (MSLT), and hormonal measures. On the final evening, subjects were approached about a second protocol in which a public speaking task would be required the following morning. For those who consented (10 of 12 with insomnia; 7 of 7 with normal sleep), time was provided for topic selection and speech preparation that evening. The following morning, subjects spoke before an audience of research assistants and psychology interns. After completion of the task, the background protocol resumed with MSLT and hormonal measures. Urine was collected throughout the study in 8-hour aliquots for measurement of cortisol and catecholamines. Saliva was collected for cortisol assessment during the public speaking task.
Results: At baseline, patients with insomnia and controls had identical urinary free cortisol levels (44.5 mcg/day), but higher levels of norepinephrine (59.0 vs 46.5 mcg/day) and epinephrine (15.9 vs 14.0 mcg/day). The 24-hour period encompassing speech preparation, the sleep period, and presentation was associated with substantial increases in all three hormonal measures in patients with insomnia [cortisol 12%, norepinephine 10%, and epinephrine 24% ($p<.05$)]. Smaller increases were seen in the controls, and group x treatment comparisons were not significant. When hormonal data were analyzed for each 8-hour aliquot, the largest increases were seen in the evening before the test (during consent and preparation) in patients with insomnia, while normal subjects showed larger changes the following morning, i.e. during the speech itself, resulting in a significant group x time interaction ($p< .05$) for norepinephrine, and similar trends for the other two variables. Preliminary analysis of sleep measures shows substantial deterioration on the night before the speech for both groups.
Conclusions: Modification of the Trier public speaking paradigm to include an intervening night of sleep provides a useful laboratory model of stress-induced insomnia that adversely affects sleep in both normal subjects and those with insomnia. Despite comparable levels of cortisol and catecholamines at baseline, patients with insomnia showed greater stress-related increases in these parameters, supporting the hypothesis that insomnia is associated with increased reactivity of integrative stress response systems.

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0783.L

First-Night Effect In Severe Psychophysiological Insomnia

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Introduction: Several studies have investigated the first-night effect in normal subjects of different age groups. The aim of the study was to measure the first-night effect in a clinical population of patients with severe insomnia and to assess the contribution of various factors including depression and anxiety scores.
Methods: 31 patients with psychophysiological insomnia (mean age: 47.0 $\pm$ 11.4 years) were studied for two consecutive nights in the sleep laboratory. None of the patients had any associated medical or sleep disorders or were taking any medication known to influence sleep. None of the patients met the DSM-IV criteria for any psychiatric disorder. Results obtained in insomniac patients were compared to those of 27 normal controls matched for age and gender (mean age: 46.6 $\pm$ 11.0 years). Exclusion criteria were the same as for patients with insomnia. Values obtained for insomniacs and normal controls were compared by a two-way ANOVA with one independent factor (group) and one repeated measure (night). Pearson's correlation coefficients were also calculated between the Beck Anxiety and Depression Scores and the between-night difference on each polysomnographic variable.
Results: Significant interaction were found for sleep latency ($p = 0.04$), total sleep time ($p = 0.002$), sleep efficiency (0.002) and index of micro-arousals ($p = 0.02$). For all these variables, simple effect analysis revealed a much larger first-night effect in patients with insomnia compared to normal controls. Night effects were seen for percentage of stage 1 sleep ($p = 0.0002$), and for percentage of REM sleep ($p = 0.0001$). For these two variables, both groups showed a significant decrease in stage 1 and a significant increase in REM sleep. For REM sleep latency, a significant interaction was found ($p = 0.004$); simple effects revealed a much larger increase in the control group ($p = 0.002$). There was no cor-

relation between depression or anxiety scales and any of the PSG change listed above. The presence of relationships with other demographic or clinical characteristics will be further investigated.
Conclusions: The present study showed a major first-night effect for patients with insomnia. This effect is greater than what was found in previous studies. Some of these studies were performed either with ambulatory monitoring, without a control group or with controls who were not properly matched for age and gender. Future studies should also look at differences in sleep architecture in insomniacs consulting at a sleep clinic compared to insomniacs recruited for research purposes.

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0784.L

Differential Levels of Subjective Sleepiness among Psychophysiological Insomnia Patients

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Introduction: Insomniacs report daytime symptoms (i.e. excessive daytime sleepiness (EDS) and fatigue) secondary to their sleep difficulties. However, limited data are available on the actual significance of EDS. Day et al. (2001), using the EDS scale of the Sleep Wake Activity Inventory (SWAI), reported a wide range of sleepiness/alertness scores (SAS) among subjects with psychophysiological insomnia (PPI). These scores were found to predict polysomnographicaly determined nocturnal sleep latencies. Interestingly, 22% of the patients had EDS scores indicative of excessive daytime sleepiness. The purpose of this study was to corroborate these findings utilizing the Epworth Sleepiness Scale (ESS) and to further characterize the SAS at different times of the day (am, noon, and evening) using the modified ESS (mESS).
Methods: Fifty-seven consecutive patients evaluated for chronic insomnia completed the ESS and mESS. Of these, twenty-five had PPI as their primary diagnosis (10 males: 15 females; age= 35.8 ± 9.8, range 19-55 years). A Board Certified Physician in Sleep Medicine established the diagnosis of psychophysiological insomnia. Patients were required to be in stable medical/psychiatric condition, have no evidence of other concurrent sleep disorders (RLS, PLMD, SDB, narcolepsy, etc), and report no use of antidepressants and/or anti-seizure medications. Patients using hypnotics were included in the study. Patients were split into three groups according to their ESS scores: ESS £4 suggestive of hyperalertness, n= 10, GRP 1 ESS score= 1.9 ± 1.2; ESS >4 £9 "normal"/ intermediate alertness, n=8, GRP 2 ESS score = 6.8 ±1.3; ESS >10, clinically suggestive of EDS, n=7,GRP 3 ESS score = 13.6 ±2.0.
Results: Twenty-eight percent of participants were found to have significant EDS. Prescribed medications did not account for these differential levels of sleepiness. There were no significant differences in subjective sleep onset latency between the groups (67.8 ±68.7, 51.9 ±59.8, and 75.7 ±53.2 min, GRPs 1, 2, and 3 respectively) or sleep time (298.5 ±77.0, 318.8 ±90.6, and 295.7 ±58.6 min respectively). Reported time in bed was significantly longer in GRP 1(508.5 ±71.6 min; $p<0.03$) when compared to GRP 3 (407.1 ±69.0 min). GRP 2 (453.8 ±74.2 min) was intermediate and not significantly different from the other two groups. On the mESS, there was a main effect of grouping ($p<0.001$). GRP 3 had significantly higher scores on each of the AM, NOON, and EVENING subscales (13.0 ±7.2, 12.9 ±3.2, 10.7 ±6.5) compared to GRP 1 (0.2 ±0.4, 1.9 ±2.5, 2.1 ±2.1, $p <0.05$) and significantly higher scores than GRP 2 on the AM (2.1 ±2.3) and NOON (4.4 ±3.2) subscales ($p <0.05$, EVENING 6.1 ±3.4, ns). GRP 1 and 2 were comparable and revealed no significant differences on the mESS.
Conclusions: The results of this study confirm that patients with PPI present a wide spectrum of SAS scores. The study corroborates significant EDS among some PPI patients (28% in this study). Future studies will be required to further identify the determining factors of EDS among PPI patients.

0785.L

Treatment Of Delayed Sleep Phase Syndrome With Melatonin: A Practical Approach

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Introduction: Delayed Sleep Phase Syndrome (DSPS) is a common circadian rhythm disorder characterized by a chronic phase delay of sleep relative to the desired sleep wake cycle. Although several studies have used melatonin as a treatment for DSPS, there is no consensus regarding the timing or dosage of melatonin administration. Based on the phase response curve to oral melatonin, maximum phase advances occur 3-5 hours prior to dim light melatonin onset (DLMO). However, assessment of DLMO is not feasible for most clinicians. As DLMO typically precedes habitual sleep onset by 2-3 hours, we studied the role of habitual sleep onset as a phase marker. The goal of this study is to demonstrate the efficacy of utilizing habitual sleep time to determine the optimal time of administration of oral melatonin.
Methods: This is an ongoing clinic based, prospective study, and 1month follow-up data is available for 5 patients. Following clinical diagnosis in the Northwestern Sleep Disorders Clinic, baseline data were collected. This consisted of actigraphic monitoring and maintenance of sleep diary for 7-14 days to calculate habitual sleep times. In addition, core body temperature was monitored for 48 hours to determine the circadian nadir, and saliva was collected on one evening for measurement of DLMO. Patients were instructed to take 3mg of melatonin (Twin Labs) 5-7 hours prior to the average sleep onset. Following 1 month of treatment, actigraphic monitoring and sleep diaries were collected for a 1week period. The sleep parameters were compared for differences between baseline and post-treatment measurements.
Results: When analyzed over the entire week, the baseline mean sleep onset was 2:00AM(±1:07) and sleep offset was 9:52AM(±2:30). The mean baseline sleep duration was 7:54h(±2:08). When divided by days of the week, habitual sleep onset occurred at 1:38AM(±0:44) on weekdays (Mon-Thu), and at 2:40AM(±1:41) on weekends (Fri-Sun). The total sleep time was 7:36h(±2:50) on weekdays and 8:16h(±1:21) on weekends. Following 1 month of treatment with melatonin, sleep onset advanced by 58min on weekdays ($p=0.004$). Although a similar trend was observed for the weekends, it did not reach statistical significance. Sleep offset on weekdays did not change, but the weekend sleep offset advanced by 2:40h ($p=.120$). Thus, sleep duration increased by 51min on weekdays, but decreased by 1:21h on the weekends.
Conclusions: Melatonin administered 5-7 hours before sleep onset advances the sleep wake cycle in patients with DSPS. These results indicate that using habitual sleep onset to determine the time of melatonin administration is a practical and effective approach for the management of patients with DSPS. In addition, varying social schedules between weekdays and weekends differentially influence the effect of melatonin on measured sleep parameters. The phase advance resulted in increased sleep duration on weekdays. This apparently diminished the need for recovery sleep on weekends as reflected by decrease in weekend sleep duration.

0786.L

Gender Effects on Treatment Outcome in Patients with Primary Insomnia

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Introduction: "Is it possible that women have better treatment outcomes when receiving cognitive behavioral therapy for insomnia?" This seems

plausible given that women appear to seek treatment more often than men. While this may simply reflect that women more frequently experience insomnia (esp. after the 4th decade of life), this may also correspond to factors that might moderate treatment outcome. One possibility is that women seek treatment more often because their insomnia is more severe (intense and/or frequent and/or chronic). Worse initial complaints may allow for more robust clinical gains. Another possibility is that women are 1) more ready to acknowledge that sleep problems are significant and/or 2) more comfortable seeking treatment. In either case, such factors may affect adherence such that women are more compliant with treatment and as a result experience better outcomes. For these reasons, we evaluated the effects of gender on treatment outcome in patients with Primary Insomnia.

Methods: Archival data were evaluated from a clinical case series data set (2000) which included pre/post sleep diary data for 64 consecutive patients with Primary Insomnia who were treated in our Behavioral Sleep Medicine Service (1998-1999). All subjects were medically and psychiatrically stable. Patients with Primary Insomnia were seen on a weekly basis for a minimum of 4 sessions and were treated with sleep restriction, stimulus control, sleep hygiene and cognitive therapy. For the purposes of the present analysis, treatment outcome data for percent change of sleep latency (SL) and wake after sleep onset (WASO) were evaluated using t-tests.

Results: 57% of the sample were women (41.8 yrs. $\pm$ 5.3). The mean age for men was 40.8 years (SD=17.7). The groups did not significantly differ for age, initial severity of SL or WASO problems, for average number of sessions, or for the percentage of subjects that discontinued treatment. The analyses of the pre-post Tx change by gender did not reveal significant differences. We calculated effect sizes and undertook a power analysis to rule out the possibility that the failure to detect differences was due to the sample size. The effect sizes for SL and WASO were 0.29 and 0.25. These values suggest that the gender differences observed are of a small magnitude.

Conclusions: These results suggest that gender factors do not moderate clinical outcomes for cognitive behavioral therapy for insomnia. Given the absence of "real" differences, it is still possible that gender differences exist. It is entirely plausible that the men in the present sample share one or more characteristics with the women who sought therapy, and thus are not representative of the general male population. Exactly what these factors represent may lead to a more interesting analysis than one based simply on gender. For example: "What factors prompt patients to seek out and eventually benefit from treatment?"

0787.L

Sleep Latency, REM Latency and Slow Wave Sleep Latency in Patients with Primary and Secondary Insomnia and in Good Sleeper Controls

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Introduction: Central to the PSG evaluation of sleep is that summary values be calculated for the epoch data. Traditionally this includes a tally of time spent in each stage of sleep (minutes & percents) and the calculation of two latency values: Sleep Latency and REM latency. Given the ease with which these variables are calculated, it is surprising that a latency variable is not routinely calculated for slow wave sleep. Such a measure might yield information that bears on the homeostatic regulation of sleep and provide a measure of "SWS pressure." Last year we undertook a preliminary analysis using this "new" variable to determine if it might discriminate between patients with Primary Insomnia and Good Sleepers. Contrary to expectation, the two groups did not exhibit significantly different Slow Wave Sleep Latencies (SWS-L). The present analysis extends the prior work by evaluating the SWS-L measure in depressed patients.

Methods: Three groups were evaluated: Primary Insomnia (PI: n=17), Major Depression (MD: n=19), Good Sleeper Controls (GS: n=20). The groups did not significantly differ for age, sex, and body mass. The sample was 63% female and the mean age was 37.5 ($\pm$ 10.7). All records were scored in 30-second epochs according to Rechtschaffen and Kales criteria. In addition to the normal sleep continuity and architectural variables, we calculated a SWS-L variable (minutes elapsed from sleep onset [8 of 10 minutes any stage sleep] to the first epoch of stage 3 sleep). The three groups were compared on the latency variables using one-way ANOVAs.

Results: The groups significantly differed on the traditional latency measures. Sleep latencies for the three groups were as follows: PI: 31.2 (34.7), MD: 17.8, (12.7), GS: 9.4 (8.9) [$p < 0.02$]. REM latencies for the three groups were as follows: PI: 124.4 (67.1), MD: 78.6 (34.9), GS: 92.9 (49.8) [$p < 0.03$]). These data serve to confirm that, on latency measures, our groups exhibit the expected profiles; the PIs have the longest sleep latencies and the MDs have the shortest REM latencies. The ANOVA for the SWS-L also revealed significant differences. The SWS-L for the three groups were as follows: PI: 62.7 (85.7), MDD: 21.0 (15.6), GS: 22.4 (24.2) [$p < 0.03$]).

Conclusions: These results suggest that SWS-L can distinguish between clinical groups. Ironically, the information provided by such a variable (at least when paired with the other latency data) speaks more to circadian than homeostatic issues. The data suggest that PI subjects take longer to fall asleep, and that both SWS and REM sleep are subsequently delayed. Such a pattern is consistent with phase delay syndrome. One or more subjects in our PI sample may be sub-clinically phase delayed or that (as argued by Lacks et. al) phase disturbance is a normal component of primary insomnia.

0788.L

Sleep Disorders and Daytime Somnolence in Adults in Mexico City

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Introduction: There is a known relationship between sleep disorders and social factors sucha as gender, age, sociodemographic factors, lifestyle and coexistent diseases. The aim of our study was to investigate which sociodemographic factors are associated with the perception of poor sleep, sleep disordered breathing, and if there is a correlation with daytime hypersomnia.

Methods: Mexico among other countries celebrated the International Sleep Day on March 21st. In the aftermath of this celebration people were invited via massive comunication media, to attend a full day conference on sleep disorders. A questionnaire on sleep habits, snoring, and daytime somnolence including the Epworth Scale was given to all participants. In order to better assess insomnia, napping, and daytime somnolence, a survey was conducted by telephone in a subgroup of 250 subjects randomly selected.

Results: 1088 adults answered the questionnaire, but 433 (39.9%) were discarded because were very incomplete. Data was analyzed in 797 questionnaires. 562 (70.5%) were females. The mean age was 47.7 /pm 13 years (range 20-82). A bad sleep quality was admitted in 60%, from which 55% were women. 47% admitted taking more than 30 minutes to fall sleep at night. Average Epworth Scale was 8.47 /pm 5.6 points, and 46.8% admitted being sleepy during daytime. When asked if they had visited a physician because of insomnia, 25% admitted at least one visit in the last 6 months. 17% take a prescribed medication to sleep, and 8% take OTC or herbal remedies to improve sleep. 28% referred habitual snoring, and 10.3% were frequently (>2 per week) told they had apneas while sleeping. From the 250 subjects chosen to answer the second questionnaire, 41 declined. Results are presented for 209 subjects. Mean age was 44.6/pm 14.8 years. 58% were married. 17% were students or unemployed, 24% were housewives without other job. The mean sleep time on weekdays was 6.4 /pm 1.37 hours, and during weekends 7.16 /pm

1.83 hours. The mean time to go to bed was 22:47 /pm 1:30 hours. The mean waking time was 6:40 /pm 0:23. 78% of this subgroup said they did not nap, but those who did, took only short naps, on average less than 30 minutes per day. When analyzing factors associated with referred daytime sleepiness we found significance (ANOVA) with age >50 years old, female gender, napping and frequent awakenings during the night. Considering more than 12 points as an abnormal result in the Epworth Scale, the association was significant for female gender and a long latency to sleep.
Conclusions: A high proportion of a sleep concerned population have a perception of having a poor sleep quality, and feel tired and sleepy during daytime. The main factors associated were age > 50 years old and female gender. In Mexico City many people sleep only 6-7 hours per night. Snoring prevalence is similar to the reported in other series.

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0789.L

Stress-Related Insomnia In Caregivers - Taking A Deeper Look
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Introduction: We have previously reported that the chronic stress of caregiving is associated with subjective sleep complaints and sleep continuity disturbances. In this study, we took a deeper look at these data to try and understand possible mechanisms for the stress-sleep relationship. Our focus was on measures of increased arousal during NREM sleep, as reflected by delta and beta EEG spectral power, as well as spectral measures of heart period variability. We hypothesized that stress would be associated with alterations in EEG spectral power across 3 nights of laboratory sleep studies. We also hypothesized that the chronic stress of caregiving would be associated with increases in autonomic tone during sleep which would, in turn, adversely impact NREM sleep.
Methods: Participants were 13 adults caring for a family member who had received a liver transplant (caregivers) and 12 non-caregiver controls (mean age = 49.8 years). Caregiver stress was quantified with the Intrusion subscale on the Impact of Event Scale (administered on the first night of sleep studies). Measures of NREM sleep included sleep latency, sleep maintenance, percent delta sleep, as well as relative delta (delta band of 0.5-4.0 Hz/total power) and beta (beta band of 16-32.0 Hz/total power) spectral power. Autonomic tone was measured by autoregressive spectra of interbeat intervals. The ratio of low-to-high frequency power was used to quantify sympathetic nervous system activity, and high frequency spectral power (.15 - .4 Hz) was used to measure vagal tone.
Results: Repeated measures ANOVA revealed a significant group effect for EEG beta power ($F = 4.57$, $p<.05$). Beta power was significantly higher in caregivers on Nights 2 ($F = 4.3$, $p<.05$) and 3 ($F = 6.55$, $p<.02$). Among caregivers, autonomic tone was significantly correlated with stress-related intrusive thoughts, sleep continuity and slow-wave sleep. Greater frequency of stress-related intrusive thoughts were associated with higher levels of sympathetic nervous system activity ($r = .61$, $p<.05$) which were, in turn, associated with increased sleep latency ($r = .78$, $p<.01$), poorer sleep maintenance ($r = -.88$, $p<.001$) and reductions in slow-wave sleep ($r = -.58$, $p<.05$). Conversely, heightened vagal tone was associated with shorter sleep latencies ($r = -.60$, $p<.04$) and better sleep maintenance ($r = .71$, $p<.01$). Regression analyses revealed that sympathetic nervous system activity (Beta = .81, $p<.01$) was a significant mediator of the relationship between stress-related intrusive thoughts and sleep maintenance (Beta = .11, $p<.64$) .
Conclusions: Stress was associated with increased arousal during sleep. Among caregivers, beta power remained elevated across study nights, and stress-related intrusive thoughts in caregivers were associated with heightened sympathetic nervous system activity throughout NREM sleep. Significant relationships emerged for autonomic tone and visually-scored sleep as well. Higher levels of arousal were associated with poorer sleep continuity and decreases in slow-wave sleep. Although preliminary, these data suggest that chronic stress does impact physiological arousal during NREM sleep which may, in turn, interfere with sleep continuity and slow-wave sleep.

0790.L

Treatment Outcome of Group Cognitive-Behavioral Therapy for Insomnia
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Introduction: Patients with psychophysiological insomnia frequently report high levels of distress and anxiety over inability to sleep, and they often attribute inadequate sleep to impairment in mood and functioning. Hyperarousal, which manifests in cognitive, affective and somatic domains, has been found to characterize individuals with this disorder. Extended time in bed and fragmented sleep with prolonged wake after sleep onset are thought to contribute to poor sleep quality reported by the patient. This study is a part of a trial validating a portable device (RMEView®) that estimates sleep parameters based on head movements and eye movements. It is hypothesized that treatment would improve sleep quality and sleep efficiency but not necessarily total sleep time.
Methods: The study enrolled a total of 19 participants, of which 7 women and 1 male (ages 31-60; M=44, SD=11) completed all aspects of the protocol. Study patients were recruited from Stanford Sleep Disorders Clinic. Patients met criteria for psychophysiological insomnia and were free of sleep medications throughout the study. Treatment consists of a 7-session multi-component cognitive-behavioral group therapy spanning 9 weeks. Baseline laboratory polysomnogram (2 consecutive nights) was performed before the second group session and post-treatment polysomnogram (2 consecutive nights) was performed during week 8-10. Participants completed a set of questionnaire at baseline and at the end of treatment. Sleep diary was completed daily throughout treatment. This report includes data from sleep log and self-report questionnaires, comparing sleep variables during the 1st and the 9th week of treatment.
Results: Paired t-tests were performed on all variables, based on the 8 participants who completed study protocol. Comparing the first week and last week of treatment, participants showed significantly reduced time in bed (484 ± 46 vs. 423 ± 57 minutes; $p=0.006$) and sleep quality (5.0 ± 1.4 vs. 6.2 ± 1.6; $p=0.009$), which was rated on a 1 (very poor) to 10 (excellent) Likert scale. A statistical trend was observed on sleep latency (36 ± 30 vs. 24 ± 17 minutes; $p=0.062$). Although wake after sleep onset was reduced (75 ± 63 vs. 45 ± 36 minutes), it did not reach statistical significance ($p=.114$). Total sleep time did not change (346 ± 92 vs. 347 ± 51 minutes; $p=.922$). A slight increase in daytime sleepiness, assessed by the Epworth Sleepiness Scale, was reported (8.1 ± 5.1 vs. 10.6 ± 6.8; $p=0.202$).
Conclusions: The results support the hypothesis that cognitive-behavioral therapy is effective in improving sleep for persons with psychophysiological insomnia. Treatment benefits appear to be mediated through improved sleep quality. Cognitive-behavioral therapy focuses on reducing the patient's hyperarousal state. Data from this study support the notion that the patient would experience increased sleepiness subsequent to decreasing cognitive and somatic arousal. The subjective improvement in sleep quality is not accounted by increases in the quantity of total sleep time.

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0791.L

Assessment Of Neurocognitive Functioning, Sleep Quality, And Sleepiness In Older Insomnia Subjects

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Introduction: Literature is inconsistent on the impact of poor sleep on cognitive functioning in nondemented, healthy elderly. In our study of behavioral treatments for insomnia, applicants 55 years and older met primary insomnia diagnosis by questionnaire, objective and subjective sleep measures, and overnight ambulatory sleep apnea monitoring. They were required to abstain from using hypnotic medications and to be cognitively intact enough to carry out study demands, which involved adhering to precise treatment protocols, extensive record-keeping, and self-observation. We explored relations among subjective and objective sleep measures, daytime sleepiness and cognitive measures, expecting that poorer sleep would correlate with greater sleepiness and poorer scores on cognitive testing.

Methods: For screening, applicants (N= 60, mean age= 63.6yrs, 42 female) completed 7 days of daily sleep logs and actigraphy; Epworth Sleepiness Scale (8 items, higher scores indicating greater sleepiness); and were examined on two measures of cognitive function: the Executive Interview (EXIT) and the Mini-Mental State Exam (MMSE). Royall et al's EXIT measures cognitive processes that integrate ideas and actions into complex, goal-directed behavior essential for independent functioning. Eligibility cutoffs were < 26 on the MMSE (30 items, with higher scores indicating better performance) and < 15 on the EXIT (25 items, lower scores are better). Multiple correlations were performed among MMSE, EXIT, Epworth and sleep measures.

Results: Only one participant (scoring 25 on MMSE), scored below cutoffs on cognitive measures. On the MMSE mean=28.8, SD 1.3 and on the EXIT mean=3.0, SD 2.3. Lower MMSE scores correlated with greater sleep log Wake After Sleep Onset (WASO, mean=74.3 min, SD 60.2) $p < .05$. There was a trend toward significance for both the MMSE and EXIT scores and sleep log Sleep Efficiency (SE, mean=68.3%, SD 10.7), but no other significant associations existed between cognitive and sleep measures. Epworth scores (mean=7.7, SD 4.4) were positively related to sleep log SE (greater sleepiness, higher SE) and negatively related to sleep log WASO and Sleep Latency (SL, mean=34.5 min SD 38.0) greater sleepiness associated with less SL and WASO. Epworth negatively correlated with actigraphic Total Sleep Time (TST, mean=378.8 min, SD 59.0) $p < .05$.

Conclusions: The findings, that poorer neurocognitive performance (MMSE) correlated with greater fragmentation of subjective sleep and that sleepiness (Epworth) inversely correlated with objectively measured TST, were in the expected direction. Paradoxically, higher sleepiness scores correlated with less fragmented, more efficient sleep on subjective measures. Possible explanations for this unexpected finding are the hypervigilance or sleep-state misperception often encountered in insomnia patients. These findings were for a highly selected group of relatively healthy older insomniacs screened to be free of sleep apnea and soporific medication. Results could differ in other samples of older insomniacs.

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0792.M

Isolated Sleep Paralysis as a Manifestation of Depression

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Introduction: Sleep paralysis (SP) episodes are thought to originate in sleep-onset REM periods (SOREMPs). Although a symptom of narcolepsy, SP is also found in non-narcoleptic patients and is often accompanied by hypnagogic or hypnopompic hallucinations, typically a sense of a threatening presence nearby. Because the sleep architecture of depressive patients is also characterized by frequent SOREMPs, we compared depression scores for three groups of non-narcoleptic subjects: Control (CTL), Isolated sleep paralysis (ISP), and ISP with sensed presence (ISP+PRES).

Methods: University students (N=47) answered a questionnaire on sleep paralysis and sensed presence hallucinations. Frequency of sleep paralysis was assessed on 1-5 Likert-type responses to the following description: "Just prior to falling asleep or upon awakening, I have been unable to move. At this moment, I was conscious of my surroundings (e.g. room). This experience was brief, i.e. it lasted no more than a few seconds or minutes". The sensed presence was assessed with the following item: "Just prior to falling asleep or upon awakening, I have sensed a presence in the room where I was lying without necessarily seeing or hearing anything". All subjects completed the BDI-II and the SCL-90-R. Finally, subjects completed a Sleep Disorders and Dreams Questionnaire with questions permitting exclusion of narcolepsy (i.e., cataplexy). One subject was excluded because he "sometimes" experienced cataplexy, and another because she did not complete the BDI-II. The final sample consisted of 45 students (21.8±2.5yrs), 17 men and 28 women. The CTL group (N=19) never had ISP or PRES; the ISP group (N=10) had had ISP at least once, but never PRES; and the ISP+PRES group (N=16) had experienced both symptoms concurrently at least once. Age and gender did not differ among groups. BDI-II and SCL-90-R depression scores were normally distributed.

Results: There was a significant correlation between the two depression measures (Pearson $r=.72$, $p<.001$, 2-tailed). A one-way ANOVA for each measure followed by Tukey post-hoc analyses revealed that the ISP+PRES group scored significantly higher on the BDI-II (M=9.44±5.92) than the control group (M=3.16±3.92, $p<.001$) and tended to score higher than the ISP group (M=5.0±3.68, $p=.060$). The same pattern was found for the SCL-90-R depression subscale, the ISP+PRES group scored higher (M=1.11±0.64) than both the CTL (0.45±0.51, $p<.01$) and ISP (0.53±0.45, $p<.05$) groups.

Conclusions: ISP, especially when accompanied by sensed presence, appears to be linked to depressive symptomatology—or depressed mood, since depression scores for all groups were well below suggested cutoffs for clinical diagnosis of depression. The link may be an increased occurrence of SOREMP, which is both elevated in depression and a necessary condition for ISP. Protocols targeting depression scores at the moment of ISP events could be used to test this possibility.

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0793.M

Sleep Paralysis Experienced by Korean Male Teenagers

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Introduction: Although it is well known that sleep paralysis (SP) is very common in the general population and its prevalence shows wide variations according to ethnic background, it has never been studied in Korea. A phenomenon known to Koreans as ¡°Kawinulim¡± is descriptively and symptomatically identical to sleep paralysis. Etymologically, the word is

derived from Kawi (which is the ghost that comes in our soul during sleep and frightens us) and nulim (which means being pressed). We examined the characteristics of the Kawinulim phenomenon experienced by Korean male teenagers.
Methods: Four-hundred forty-two Korean male draftees were selected as study subjects using a simple random selection method. A sleep questionnaire package was administered, comprising a Kawinulim Scale devised after referring to similar questionnaires, the Epworth Sleepiness Scale (ESS), the Insomnia Severity Scale (ISS), and questions about sleep-wake schedule during the previous month. Subjects were divided into SP and non-SP groups according to the presence or absence of the SP experience.
Results: Of all subjects, nearly 78% had known of the term Kawinulim. 150 (33.9%) had experienced at least one attack in their lifetime. Among SP subjects, however, only 5.8% reported having attacks more than once a month. About one fourth of all subjects showed the belief that Kawinulim is related to the ghost Kawi (SP 27.4%, non-SP 26.9%; ¥ö2=0.01, p>0.1). The peak age of onset was in the range of 16-18 years old (51%). SP subjects were significantly sleepier measured by the ESS and also complained significantly more of disturbed sleep (longer sleep latency, more frequently awakening during sleep, and higher scores on the Insomnia Severity Scale) than non-SP subjects. Various hallucinatory experiences accompanied SP. Among feelings, fear (75.2%) was the most common one experienced during attacks. More than half of SP subjects (55.0%) had experienced the attacks in the middle of a sleep period. The main sleeping position during attacks was supine position (63.3%). SP subjects were significantly more likely to have positive family history than non-SP subjects (SP 31.7% vs. non-SP 19.7%, ¥ö2=25.4, p<0.001). Physical and psychological stress, disturbed sleep, irregular life style, and sleep deprivation were reported as preceding events for SP.
Conclusions: Our results show that the word Kawinulim is familiar to Korean people and the incidence of SP among Korean male teenagers is high. Over one fourth of all subjects hold the superstitious belief that Kawinulim is associated with the ghost Kawi. SP subjects have more sleep associated problems, and there is strong familial association in SP subjects. We also found that various horrifying hallucinatory experiences and fearful feelings accompany SP. Our study shows very similar results to those of studies from Japan1) and Hong Kong,2) which are geographically and culturally very close to Korea.

0794.M

REM Behavior Disorder (RBD): Delayed Emergence Of Parkinsonism And/Or Dementia In 65% Of Older Men Initially Diagnosed With Idiopathic RBD, And An Analysis Of The Minimum & Maximum Tonic And/Or Phasic Electromyographic Abnormalities Found During REM Sleep

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Introduction: RBD is a parasomnia with tonic & phasic electromyographic (EMG) dyscontrol during REM sleep. In 1996 we reported (in NEUROLOGY) that 38% (n=11) of 29 men >50 yrs old diagnosed with idiopathic RBD eventually developed parkin- sonism. We present additional findings 7 yrs later.
Methods: Clinical follow-up & medical reports were obtained on 15 of 18 RBD pts previously reported not to have developed parkinsonism. Polysomnograms from 10 RBD pts with eventual parkinsonism & from 13 pts with current idiopathic RBD (selected from a larger pool of RBD pts) underwent analyses of EMG activity: all 7.5 sec REM sleep bins were scored for i) increased tonic submental EMG activity present >50% of each bin; ii) limb twitch bursts (>2 sec) of upper or lower limbs.
Results: 6 of the 15 (40%) pts with persistent idiopathic RBD (n=14) or Alzheimer's disease (AD) (n=1) in 1996 later developed parkinsonism (n=5) (PD [n=2], parkinson's-plus disorder, Lewy body variant of AD, dementia with Lewy bodies), or dementia (n=1). For the series of 26 older male pts diagnosed with idiopathic RBD (from the original group of 29, with current follow-up), 65.4% (n=17) have since then developed parkinsonism &/or dementia. Mean latency between onset of RBD and onset of parkinsonism/ dementia (n=17), 13.3 yrs (range, 3-29). Mean interval between onset of RBD and latest follow-up in current idiopathic RBD (n=9), 20.3 yrs (range, 9-29). Mean age of RBD onset, 57.0 yrs (n=17) vs. 56.7 yrs (n=9). Quantitative REM sleep data of current idiopathic (n=13) vs. eventual parkinsonism (n=10) RBD groups, mean ±SD of individual pt %s: TONIC—% REM time bins with preserved submental EMG atonia, 25.0 ± 33.9 vs. 22.7 ±25.3 (ranges, 0%-95.3%; 0%-66.1%); PHASIC—% REM bins with limb twitch bursts, 44.2 ± 18.9 vs. 39.8 ± 12.9 (ranges, 10.8%-74.7%; 17.5%-56.9%); % REM bins with limb twitch bursts & preserved submental EMG atonia (i.e. phasic-tonic EMG dissociation), 8.1 ±13.6 vs. 9.1 ±9.8 (ranges, 0%-48.5%; 0%-22.6%); TONIC/PHASIC—% REM bins with increased submental EMG tone &/or limb twitch bursts, 83.1 ± 22.6 vs. 86.5 ± 15.7 (ranges, 38.8%-100%; 71.8%-100%). (t-tests & chi-square, NS.)
Conclusions: The predominance, specificity & long latency of eventual parkinsonism/dementia in "idio- pathic" RBD should be noted, along with the very broad range of tonic & phasic EMG dyscontrol in REM sleep, with clinical & basic science implications.

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0795.M

Hypersynchronous Delta Activity and Somnambulism: Effects of 38 Hours of Sleep Deprivation

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Introduction: Our group recently showed that 38 hours of sleep deprivation results in a dramatic increase in the frequency of sleepwalking (SW) episodes recorded in the laboratory. Some polysomnographic studies have documented the presence of hypersynchronous delta activity (HSDA) during the SWS of somnambulistic patients. However, whether or not actual behavioural episodes are preceded by HSDA remains a contentious issue. The goal of this study was to assess the presence of HSDA prior to SW episodes under normal conditions and following sleep deprivation.
Methods: Ten sleepwalkers (3 males, 7 females, mean age: 25.1 ± 4.1) were investigated. After a screening night, participants were monitored during a baseline night (BN) and one recovery night (RN) after 38 hours of sleep deprivation. HSDA was defined according to two methods described in the literature. In the first method, two events were scored: a) delta wave build-up, defined as the presence of the highest amplitude delta wave occurring within 10 seconds preceding a SW episode as compared to 11 to 30 seconds, and b) delta wave clusters, defined as the presence of 2 or more consecutive highest amplitude delta waves within the 10 seconds preceding an episode. The second method required the presence of at least 5 seconds of continuous high voltage (> 150 uV) activity and was scored on 5-minute windows prior to each SW episode. All methods were scored on C3/A2.
Results: Seven behavioral episodes were recorded at baseline and 37 during the RN. There was no significant difference in the proportion of SW episodes preceded by delta wave build-up at BN (57.1%) as compared to RN (62.2%). There was no significant difference in the occurrence of delta wave clusters prior to SW episodes at BN (14.3%) versus RN (10.9%). The mean time spent in HSDA prior to an episode was significantly higher during the RN than BN (32.2 seconds versus 22.5,

p<0.05), but there was no significant difference in the actual number of HSDA events (4.3 versus 3.0).
Conclusions: This is the first study to have investigated the effects of sleep deprivation on sleepwalkers' HSDA. The data indicate that under normal conditions, approximately 60% of SW episodes are preceded by delta wave build-up but less than 15% show evidence of delta wave clusters. Sleep deprivation results in a small, but not statistically significant, increase in the proportion of episodes preceded by delta wave build-up. The observed increase in the mean time spent in HSDA prior to SW episodes during recovery sleep may reflect an enhancement of the homeostatic process resulting from both sleep deprivation and increased sleep fragmentation. A study is currently underway to evaluate this hypothesis.

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0796.M

Rem Sleep Behavior Disorders (RBD): Clinical and Polysomnographic Evaluation of 100 Consecutive Patients

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Introduction: RBD is the main Rem sleep-related parasomnia. However, few studies reported on clinical and laboratory information of large series of patients, as well as longitudinal studies in order to identify whether idiopathic forms at observation may become symptomatic of some neurological syndromes. Aims of our study were firstly to characterize clinically and polygraphically a large series of consecutive chronic RBD patients (both idiopathic and symptomatic) and secondly to start a follow-up evaluation by means of a structured clinical interview and (when possible) of a video-PSG recording.
Methods: We included all the patients studied in our Center for suspected RBD from 1990 to date. The diagnosis of RBD was done according to the criteria of Mahowald and Schenck. Moreover, the patients, at the time of observation, were classified in two groups: idiopathic (iRBD, without clinical and/or neuroimaging signs of neurological illness) and symptomatic (sRBD, with clinical history or neurological examination suggestive of RBD secondary to a neurological syndrome). This in order to verify, at the follow-up, the possible developing of neurological signs and/or symptoms in the previously classified iRBD group. The differences between iRBD ans sRBD have been evaluated by a non parametric test (Mann-Whitney) for demographic, clinical and PSG variables, and by chi-square test for the dycotomic ones.
Results: Seventy nine (79%) of the patients were classified as iRBD and 21 (21%) as sRBD. In the whole group, the male prevalence was 77%, the age at observation was (mean $\pm$ SD) 67 $\pm$ 8 yrs, the age at onset 61.4 $\pm$ 10 yrs: these variables were not significantly different between iRBD and sRBD. Moreover the frequency of the episodes (21.9 $\pm$ 17 per month), the percentage of patients reporting dream contents of aggression or being attacked by someone (61%) and sleep-related injuries to self or to bed-partner (51%) were not significantly different between the two groups. Results in the classical sleep parameters (SL 24.7$\pm$21.7 min; SE 74.7$\pm$15.1%; % St 1NREM 10.1$\pm$6.7; % St 2NREM 49.9$\pm$12.3; % St 3-4NREM 18.5$\pm$9.1; % St REM 22.7$\pm$8.9; REM latency 103.4$\pm$62.6 min) resulted similar in the two groups. A periodic leg movement index >10 was more frequently observed in sRBD than in iRBD (86% vs 58%, p<.05), whilst AHI>10 (33% vs 23%, ns) was not. MRI or CT scan were performed in 48% of the whole group (67% of sRBD and 43% of iRBD). We found lesions in 12 of the sRBD and 50% of these lesions were observed in the brainstem. In iRBD we found aspecific lesions in 53% of the examined case. Among the sRBD, 47.7% had extrapyramidal signs and 23.8% had dementia or cognitive decline plus extrapiramydal signs, 23.8% had MSA. In one case (4.8%) a pontine lesion was found. In 23.8% of sRBD patients RBD preceded the neurological symptoms. Up to now, a follow-up evaluation has been performed in 20 iRBD patients (mean 1 year, range 6 months-10 years): in 36% we found the appearance of neurological symptoms or signs (most extrapyramidal).
Conclusions: The more striking results of our data, out of the absence of significant demographic and PSG differences between iRBD and sRBD, were the high prevalence of iRBD in our series (79%) in comparison with the data in the literature (range 25-43%) (Shenck CH et al, Sleep 2002), and the progression to sRBD of more than one third of our initially classified iRBD. It has to be considered that we used strict criteria to define sRBD: neurological symptoms and signs associated or not with neuro-imaging lesions; lesions alone (i.e. vascular), without symptoms or objective signs, were not considered specific for RBD. Moreover, our patients were mostly self-referred and rarely sent from other neurological department, therefore more frequently in the early stage of RBD. However, the high rate of evolution of iRBD in sRBD confirm the hypothesis that a consistent percentage of patients with RBD become symptomatic after some years.

0797.M

Treatment of Nocturnal and Sleep-Related Eating with Topiramate

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Introduction: Sleep-related Eating Disorder (SRED) and Nocturnal Eating Syndrome (NES) combine features of sleep disorders and eating disorders. Treatment of these nocturnal eating behaviors has been directed towards underlying identifiable sleep or eating disorders using dopaminergic or opioid agonists, or anorectic agents, at times with the addition of sedatives.We now describe effective treatment of four cases of nocturnal eating with the GABA agonist, glutamatergic antagonist, topiramate. This agent has produced weight loss in studies of patients with epilepsy (for which it has FDA indication), binge eating disorder (with marked reductions in daytime binge episodes), bipolar disorder and migraine.
Methods: Two patients with SRED and two with NES (3 females and 1 male, mean age 40 years), who had failed multiple previous trials of pharmacotherapy and psychotherapy, were treated with topiramate in a naturalistic, open-label fashion at a dose range of 100-400 mg at night. None of the patients had a current daytime eating disorder or a polysomnographically defined primary sleep disorder. Topiramate was added to existing medication regimens for sleep or psychiatric disorders in two of the patients. Topiramate was begun at a dose of 25 mg and subsequently increased by 25-50 mg every week according to the patient's response and tolerability of the medication. Reduction in nocturnal eating was graded based on self-report.
Results: One patient with NES had complete elimination of nocturnal eating with topiramate, two patients (one with NES, one with SRED) had a marked response (75 to < 100% reduction in nocturnal eating episodes), and one patient (with SRED) had a moderate response (50 to <75% reduction in nocturnal eating episodes). Average dose of topiramate was 219 mg, with two patients (both with NES) using 75-100 mg and two (with SRED) using 350-400 mg. Benefit of topiramate treatment has been maintained for a period of 8.5 months (range 6-12 months). One patient has used the treatment intermittently, with return of symptoms upon discontinuation, and immediate benefit when he reinitiated topiramate.Mean weight loss was 11.1 kg (range 6.8–15.0 kg). The mean BMI decreased from 30.0 to 26.1. There was no association between topiramate dose and subsequent weight loss, or between initial BMI and treatment-related reductions in nocturnal eating or weight. Topiramate was generally well tolerated, though two patients had dose-limiting side-effects which precluded the planned dose increases to 400 mg (reduction in sexual function, blepharospasm).
Conclusions: The mechanism of action by which topiramate is benefi-

cial for nocturnal eating (NES or SRED) is unclear. Given the poor response of these disorders to benzodiazepine hypnotics alone, the simple sedative effects of topiramate probably do not account for its benefit in NES and SRED. Medications reported to have been effective in other reports for nocturnal eating may do so via suppression of underlying disorders of arousal (eg dopaminergic and opioid suppression of RLS) or due to appetite suppressant effects via serotonergic agonism. Topiramate may also have an anorexigenic effect via kainate/AMPA glutamatergic antagonism.Due to the open, uncontrolled nature of the study, it is possible that the results are due to placebo response, clinican or patient reporting bias, or spontaneous remission. Despite these limitations, our data suggests that topiramate may be of value for patients with NES or SRED. Given that SRED may be present in up to 4% of college students, and NES in 1.5% of the general population, and that both can be associated with substantial weight gain, development of effective treatments is important.

0798.M

Prevalence Of Motor Manifestations And Loss Of REM Atonia In REM Sleep Behavior Disorder Associated With Parkinson's Disease

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Introduction: REM sleep behavior disorder (RBD) is characterized by frequent REM abnormalities and harmful or potentially harmful sleep behaviors. RBD has high comorbidity in Parkinson's disease and often precedes disease onset. Loss of atonia in REM sleep and fragmented REM sleep are the most common polysomnographic markers of RBD. The aim of this study was to investigate the chin muscle tone in REM sleep in different sleep cycles of Parkinson's patients and to assess how this corresponds to the frequency of sleep motor behaviors.

Methods: Forty-eight consecutive patients (32 males, aged 65.6±8.7 and 16 females, aged 66.2±8.9) who were diagnosed with Parkinson's disease participated in this study. All patients were on dopamine agonist therapy. A single scorer blindly reviewed polysomnographic findings according to standardized criteria. The duration of REM sleep episodes and duration of REM sleep with augmented chin muscle tone in each sleep cycle was calculated. Additional interviews were done with the spouses, caregivers and relatives to obtain information about simple or complex motor activities and vocalization episodes during sleep.

Results: Augmented muscle tone was observed in 44 out of 48 patients with Parkinson's disease. The repeated measure procedure showed a high proportion of REM sleep with partial or complete loss of atonia in Parkinson's patients (ranging from 61 to 71% in different sleep cycles). The greatest amount of augmented muscle tone was found in the 3rd REM episode and the least was in the 4th REM episode (71.5±0.33 vs. 61.9± 0.38; p<.05). Review of clinical histories' revealed that 13 out of 48 patients had abnormal motor activities during sleep (acting out dreams, fighting, punching or kicking) and 23 patients had vocalization episodes (screaming, shouting and loud talking).

Conclusions: This study showed that abnormal motor behaviors were present only in approximately 25% of Parkinson's patients. Only half of the patients had episodes of vocalization and frequent nightmares occurring predominantly in the early morning hours of sleep. Polysomnography is a more sensitive method to confirm the diagnosis of RBD since the history is not adequate to detect all RBD manifestations. We hypothesize that loss of REM atonia is a sentinel sign preceding development of florid RBD symptoms.

0799.M

Hypersynchronous Delta Activity and Somnambulism: Differences Between Frontal and Central Leads

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Introduction: We recently found that sleep deprivation results in an increase of the mean time spent in hypersynchronous delta activity (HSDA) on the 5-minute windows prior to sleepwalking (SW) episode on the scoring channel. We have suggested that this augmentation could be linked to the homeostatic process. Studies have shown that the effects of 40 hours of sleep deprivation on slow wave activity are particularly evident over the brain's frontal regions. To our knowledge, no study has investigated differences in the occurrence of HSDA on central versus frontal leads. The goal of the present study was to assess such differences and to evaluate potential topographical effects of sleep deprivation on HSDA prior to SW episodes.

Methods: Ten sleepwalkers (3 males, 7 females, mean age: 25.1 ± 4.1) were investigated. After a screening night, participants were monitored during a baseline night (BN) and one recovery night (RN) after 38 hours of sleep deprivation. HSDA was defined as at least 5 seconds of continuous high voltage (> 150 uV) activity and was scored on 5-minute windows prior to each SW episode. Scoring was performed on C3/A2 and F3/A1+A2 derivations. Since this method of scoring HSDA can only be applied to SW episodes from slow wave sleep (SWS), episodes from stage 2 sleep were excluded.

Results: Five SW episodes from SWS were recorded during the BN and 30 during the RN. For all episodes combined, the mean time spent in HSDA prior to an episode was significantly higher on the F3 derivation as compared to C3 (63.7 seconds versus 30.8, p<0.001). When compared to C3, the F3 derivation also contained a significantly greater number of actual HSDA events (7.8 versus 4.1, p<0.01). The mean time spent in HSDA prior to an episode during the BN was significantly higher on the F3 derivation as compared to C3 (32.3 seconds versus 22.5, p<0.05), but there was no significant difference in the actual number of HSDA events (3.4 versus 3.0). The mean time spent in HSDA prior to an episode during the RN was significantly higher for the F3 derivation as compared to C3 (68.9 seconds versus 32.2, p<0.001). The F3 derivation also showed a significantly greater number of HSDA events during the RN as compared to C3 (8.5 versus 4.3, p<0.01).

Conclusions: Our results indicate that under normal conditions the mean time spent in HSDA prior to SW episodes occur more frequently over frontal leads than central ones. Furthermore, the data indicate that sleep deprivation accentuates these differences by significantly increasing the time spent in HSDA as well as the number of HSDA events over frontal leads as compared to central derivations.

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0800.M

Evaluation of Striatal Presynaptic Dopamine Transporter Binding in Parkinson's Disease with versus without REM Sleep Behavior Disorder - A Pilot Study

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Introduction: Idiopathic REM sleep behavior disorder (RBD) may precede other symptoms of Parkinson's disease (PD) for several years. About half of the patients with idiopathic PD suffer from RBD. The

pathophysiological mechanism of the occurrence of RBD in PD is not yet known.

Methods: We performed IPT-SPECT investigations in 5 patients with PD and polysomnographically (PSG) confirmed RBD and in 6 group-age matched patients with PD, whose PSG excluded RBD.

Results: All patients received dopaminergic treatment at the time of the PSG and stopped dopaminergic treatment at the day of the IPT-SPECT investigation. Presynaptic dopamine transporter binding contralateral to the affected body side in PD with RBD (IPT-SPECT binding ratio: 1.44 ± 0.19, 4 men, age: 68.8 ± 7.8 years, H&Y: 2.5 ± 0.9) was significantly lower than in PD without RBD (IPT-SPECT binding ratio: 1.79 ± 0.26, 3 men, age: 63.8 ± 12.5 years, H&Y: 1.9 ± 0.4), (p=0.030). Mean presynaptic dopamine transporter binding between right and left striatum showed a tendency to be lower in PD with RBD than in PD without RBD (p=0.052).

Conclusions: Progressive loss of striatal presynaptic dopamine transporters in the course of PD without RBD results in decreased stimulation of REM atonia mediating brainstem centers and may cause RBD. Long term follow up with repeated SPECT, MRI and PSG investigations in the course of idiopathic PD is needed to evaluate this hypothesis.

0801.M

Efficacy And Safety Of Oral Splint Devices In The Management Of Sleep Bruxism

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Introduction: One of the most frequently used treatments for sleep bruxism (SB) is the occlusal splint that covers the teeth, thus preventing tooth damage. However, its efficacy has been debated for years and its safety (e.g., potential respiratory disturbance) remains to be assessed. The present study aimed to assess both issues using quantitative measures in a cross-over randomised controlled design.

Methods: The subjects were nine young adults (20-29 years old) who reported frequent tooth grinding (more than 3 nights/week). SB diagnosis was confirmed using the second night of sleep laboratory recording (baseline night) according to published recording methodology and research criteria (Lavigne et al., J. Dent. Res., 1996). Subjects then received either the occlusal or the palatal splint (a control splint offering no tooth protection) and were recorded after two weeks of habituation to the splint. Subjects then received the other splint (cross-over design) and were recorded two weeks later. All subjects were told that the study goal was to establish whether one of the 2 oral devices was better than the other. Scoring for sleep, respiratory events, swallowing and SB outcomes (e.g., SB episodes, bursts) was done blind to splint status. Repeated measures ANOVA were used to evaluate treatment effect. The baseline night was then compared to either occlusal or palatal nights using paired comparisons. Friedman two-way ANOVA followed by Wilcoxon signed ranks tests for paired comparisons were used when the data distribution was not normal.

Results: The duration of sleep stages 3 and 4 was decreased by 30% (p=0.04), while no other change was observed for sleep variables (e.g., sleep stages duration, number of micro-arousals, awakenings, sleep efficiency). A reduction was noted in the median number of SB episodes per hour (6.3 [3.7-10.5] in baseline versus 3.7 [0.2-8.2] and 3.7 [2.8-7.9] for occlusal and palatal splints; p=0.05 for both comparisons). This reduction was more than 25% in 5 out of 9 patients. The number of masseter muscle bursts per hour of sleep was significantly reduced for both splints (45% and 42% reduction from baseline; p<0.05 for both comparisons). Tooth grinding incidents were reduced by more than 50% with both splints (p=0.06 and 0.05 for occlusal and palatal splints). No difference was observed between devices. Moreover, no change in respiratory (apnea and hypopnea; p>0.2) or swallowing variables (p>0.1) was noted between baseline or oral splint nights.

Conclusions: This study suggests that oral splints are safe to use in young SB subjects, after a two-week habituation period, with regard to maintenance of sleep quality and sleep respiratory efficacy. The use of oral devices reduces SB related masseter events. Since the use of such devices is not harmful, the occlusal splint remains useful for mechanically protecting teeth when tooth damage is a major patient complaint.

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0802.M

A Psychological Study on the Patients with Temporomandibular Disorder Who Develop Bruxism

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Introduction: Bruxism is one of abnormal phenomena, which occur during sleep. A tendency toward shallower sleep stages appears after bruxism in EEG recording. It is reported that Stage 1 sleep increases in the patients with bruxism compared with normal subjects, and the decrease is found in Stages 3 and 4 sleep. Temporomandibular disorder (TMD) is a type of disease, in which the patients have main complaints such as pain, noise, or dyskinesia in temporomandibular region. Bruxism is believed to be one of major causes to develop TMD. There have been some reports describing the tendency in personality of the patients with TMD, while there is no unified opinion yet. In the present study, we performed P-F study to find out whether the patients with TMD develop bruxism or not and to evaluate the tendency in personality of the patients.

Methods: The study was performed on the patients who had been diagnosed by oral surgeons as having masticatory muscle disorder (MMD) who had been reported as developing bruxism more frequently among the patients with TMD. The purpose of the study were explained to the patients, and P-F study was carried out to the patients who gave informed consent to the execution of the examination. Since it was aimed to compare the tendency in personality of the patients who have bruxism or not, the patients with MMD were further divided to two groups: bruxism group and non-bruxism group. There were 19 patients in the bruxism group, and 12 patients in the non-bruxism group with 31 patients in total.All patients were female. For statistical analysis, Mann-WhitneyÕs U test was employed.

Results: In the results of P-F study, the patients who developed bruxism had scores as low as 2 points (median value) in extrapunitive reaction (reaction to punish others) (standard value in general adult women; 4.7 points; SD: 2.6 points). On the other hand, the patients developing no bruxism had 4 points, i.e. on the same level as the standard value. In intropunitive reaction, the patients developing no bruxism showed 2.7 points (median value) (standard value: 4.5 points; SD: 1.3 points). In the patients of the bruxism group, it was 4 points, being on the same level as the standard value. In impunitive reaction, it was on the same level as the standard value, while the bruxism group showed 5 points and non-bruxism group had 3.7 points (standard value: 4.1 points; SD: 1.7 points), showing some difference. In the comparison of the two groups in the above 3 items, significant difference was found. In the other 6 items, there was no significant difference.

Conclusions: In the reports describing the tendency in personality of the patients with TMD, MMPI was used to find out whether the patient had a tendency to develop depression or a tendency toward hypochondriasis, while it was reported that there was no characteristics specific to the patients with TMD. In our present P-F study, apparent difference in the

tendency in personality was found depending on whether the patient had bruxism or not among the patients with MMD. In particular, the patient with MMD due to bruxism showed a tendency of being unable to maintain self-assertion when necessary. These results suggest that, for the patient with MMD who developing bruxism, it would be important not only to perform symptomatic treatment to masticatory muscle and to temporomandibular region but also to carry out psychotherapy and pharmacotherapy for the treatment of the behavior to control mental stress.

0803.M

Comparison Of Clinical Characteristics And Polysomnographic Features Between Subjects With Subclinical And Clinical Rapid Eye Movement Sleep Behavior Disorders

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Introduction: Rapid eye movement (REM) sleep behavior disorder (RBD) is commonly diagnosed by both polysomnography findings of REM sleep without muscle atonia (RWA) and history of abnormal behavior during REM sleep. Abnormal REM sleep behavior can often be violent and even injurious. Nevertheless, many patients with RBD do not regard their abnormal sleep behaviors as pathological. In addition, some people who have RWA may not manifest abnormal sleep behaviors. We aimed at studying the possible differences of clinical and polysomnographic findings, depending on the presence or absence of subjective complaint of abnormal sleep behaviors in patients with RWA on polysomnography.
Methods: We reviewed patient record and polysomnographic data of patients referred to the Sleep Laboratory at Seoul National University Hospital from June 1996 through October 2002. Fifty-two subjects had RWA, as detected by polysomnography (42 males and 10 females, mean age of 55.1±19.1 yrs). We defined clinical RBD group (CR group) patients having both complaints of abnormal sleep behavior and RWA on polysomnography. Subclinical RBD group (SCR group) consisted of patients who exhibited RWA in polysomnography but didn't complain of abnormal sleep behavior. Thirty-two subjects belonged to CR group and 20 subjects to SCR group. Clinical characteristics and polysomnographic findings between CR and SCR groups were compared and analyzed.
Results: Subjects in the CR group were significantly older than those in the SCR group (61.59±13.5 yrs vs 44.70±2.76 yrs, unpaired t-test, $p<0.01$). There were significantly more female subjects than male ones in the CR group (28.1% vs 5.0%, Fisher's exact test, $p<0.05$). No significant differences between CR and SCR groups were found in the prevalence of primary sleep disorders (such as obstructive sleep apnea syndrome or periodic limb movement disorder) and brain disorders (such as Parkinson's disease, multiple system atrophy, or narcolepsy). More CR group subjects exhibited abnormal REM behaviors on polysomnographic recording than the SCR group ones did (81.3% vs 50.0%, Fisher's exact test, $p<0.05$). Between the CR and SCR group, we found no significant differences in sleep latency, REM sleep %, slow wave sleep %, sleep efficiency, total sleep time, and REM latency.
Conclusions: No differences in sleep architecture were found between the clinical and the subclinical RBD groups. Only age and the presence of abnormal sleep behavior on polysomnography differentiated the two groups. We suggest that RWA on polysomnography without complaints of abnormal sleep behavior may be early manifestation of clinical RBD. Clinical attention to RWA on polysomnography is necessary for possibly preventing full-blown RBD from developing.

0804.M

Sleep Bruxism is Associated with a Higher Sympathetic and a Lower Parasympathetic Tone Before the Onset of Masticatory Muscle Activation

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Introduction: Sleep bruxism (SB) is reported in 8% of the adult population. It is associated with tooth grinding and normal sleep but also occurs with a higher level of arousal-masticatory muscle activation. Recent data suggests that SB is preceded by cortical (minus 4 seconds) and cardiovascular (minus 1 cardiac cycle) activity (Kato, JDR 01). To further understand the role of subtle autonomic changes in sleep arousal in relation to SB, we analysed heart rate variability in both normal and SB subjects during 3-minute sections of quiet sleep (e.g., no muscle activation) and during periods preceding SB/masticatory muscle activation.
Methods: 16 SB subjects (tooth grinding ³ 3 nights/week) with a mean age of 25 ± 6 (9m, 7w) were compared to 17 normal sleepers with a mean age of 24 ± 4 (10m, 7w). Polysomnographic recordings were made for all subjects over 2 consecutive nights for SB diagnosis and to rule out other sleep disorders (e.g., apnea, periodic limb movement). Sleep variables, masticatory muscle tone of masseter and suprahyoid muscles, and heart rate (HR) were analysed using Harmonie software (Stellate, Canada) as previously published (Kato, JDR 01). The sympathetic (low [0.05 – 0.15Hz] and high [0.15-0.4Hz] frequency ratio [LF/HF]) and parasympathetic (high frequency) activity were calculated from HR variations using a customized MatLab (USA) application. Autonomic activity was compared between groups for the two periods: 1) the 3-minute sections in the absence of muscle (e.g., motor) activity for all subjects in sleep stages 2, 3&4 and REM; and 2) the 3-minute sections preceding the onset of SB/masticatory muscle activation for a subsample (4 normal and 5 SB subjects) in sleep stage 2 only. Statistical analysis was made using ANOVA and t-tests.
Results: For all sleep stages, masticatory muscle tone was not different between groups during periods without motor activity. Neither sympathetic nor parasympathetic tones differ between groups during these periods. However, in the 3 minutes preceding the onset of SB, a significant rise in sympathetic activity was observed in stage 2 for SB subjects (SB = 4.01 ± 0.69, normal = 1.54 ± 0.20; $p<0.001$). In contrast, during the same period, parasympathetic activity was lower in stage 2 of SB subjects (SB = 0.009 ± 0.001, normal = 0.020 ± 0.002; $p<0.001$).
Conclusions: Young SB subjects show normal sleep characteristics as reflected here by normal values in muscle tone and autonomic variation. However, in the period preceding a SB episode, it seems that a rise in sympathetic and a decrease in parasympathetic activity characterises the transient SB-arousal response. Obviously, these preliminary findings need to be validated with larger sample size.

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0805.M

Correlation Between Slow Wave Activity, Rhythmic Masticatory Muscle Activity/Bruxism And Micro-arousals Across Sleep Cycles

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Introduction: Sleep bruxism (SB) is an abnormal and involuntary phasic motor activity occurring during sleep. The prevalence of SB is 8% in adults. Approximately 60% of normal sleepers exhibit rhythmic masticatory muscle activity (RMMA) during sleep, in the absence of tooth

grinding. However, SB patients have three times more RMMA episodes than normal subjects. SB is associated with micro-arousals and mostly occurs during the arousal phase of the cyclic alternating pattern (CAP; Macaluso et al., J Dent Res, 1998). Recently, it was demonstrated that micro-arousals and phase A3 of CAP mainly occur during the transition from deep to light sleep (Terzano et al., Sleep Med, 2002). To further investigate the occurrence of RMMA in association with slow wave activity (SWA) and micro-arousals, we assessed the correlation between these three variables.

Methods: The sleep of sixteen moderate to severe SB patients (9F;7M, 25.1 ± 4.7) and 11 normal subjects (6F;5M, 24.4 ± 4.2) was monitored over two consecutive nights of polysomnographic recording. Data from the second night was used for SB diagnosis and retrospective analysis. Power spectral analysis of SWA (0.75 – 4.50 Hz) was made for the first four sleep cycles of each patient. NREM and REM periods in each cycle were divided into 20 and 5 sections, respectively, to normalize EEG-SWA dynamics. The SWA, the frequency (number/hour of sleep) of RMMA-SB episodes and micro-arousals for sections were calculated. A cross correlation analysis between these variables was made to assess the temporal association.

Results: Across the four sleep cycles, SWA decreased similarly from the first to the fourth cycles in both SB patients and normal subjects. In SB patients, RMMA occurred more frequently in the second and third sleep cycles, while micro-arousals occurred at the same frequency across all cycles. Within each sleep cycle, the frequency of RMMA was significantly higher towards the end of the NREM period compared to its beginning (ANOVA: $p = 0.002$); similar findings were observed for the frequency of micro-arousals (ANOVA: $p = 0.017$). The frequency of RMMA was negatively correlated (coefficients: -0.24 to –0.34; $p<0.01$) with the amplitude of SWA at the preceding time sections. SB and micro-arousals were positively associated (cross correlation: 0.53; $p<0.001$).

Conclusions: These data suggest that the occurrence of RMMA-SB is inversely correlated to SWA. RMMA-SB occur more frequently during transition from deep NREM to REM sleep, and are correlated with micro-arousals. RMMA-SB seems to be strongly associated with arousal activity across all sleep cycles.

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0806.M

Actigraphic and Sleep Diary Assessment of Sleep in Night Eating Syndrome

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Introduction: Night eating syndrome (NES) is a disorder of sleep, eating and mood, characterized by morning anorexia, evening hyperphagia nocturnal ingestions and depressed mood. No published studies have monitored the rest-activity cycles of patients for more than 1 night at a time or compared the sleep timing of patients with NES to controls. This is the first study to present one week of actigraphy and subjective diary data in NES patients and controls.

Methods: A total of (N=39) NES patients (13m 26f; mean age 44.2 ± 9.5y) and (N=43) control subjects (13m; 30f; mean age 39.4 ± 10.9) wore wrist actigraphs (MiniMitter, OR) for 7 days and completed detailed sleep and food diaries at home. Actigraphic data were compared with daily diary data to determine the correlation between objective and subjective assessments of sleep variables. Actigraphic and sleep diary data from NES patients were statistically compared to control subjects for differences in sleep timing, sleep latency, sleep termination and number of nocturnal arousals.

Results: There were no significant differences between NES patients and controls in the time of sleep onset using the actigraphs or sleep diaries. Sleep offset was later in the NES group (07:46h+76min versus 07:09+64min, $p<.05$). As expected, NES patients reported significantly more nocturnal awakenings than did controls (1.4 ± 1.1 per night vs. 0.5 ± 0.4; $p<0.001$), and these arousals occurred significantly earlier in the sleep period for NES patients compared to control subjects (mean first arousal 01:56h vs. 02:58h; $p<0.05$). NES patients consumed food on 74% of the awakenings versus 0% for the control subjects. NES patients ate 35.3% ± 10.4% of their calories following the evening meal, versus 8.8% ± 6.3% of control subjects. In NES subjects there was a significant correlation between subjective assessments from diary records and objective measures of sleep onset ($r=0.85$, $p<.0001$) and sleep offset ($r=0.99$, $p<.0001$) (from actigraphy). Similarly, diary reports of nocturnal arousals were consistent with actigraphy data in NES subjects for 96% of events, compared to 86% for controls.

Conclusions: Week-long assessment of sleep using actigraphy supports subjective reports of more frequent arousals from sleep in patients suffering from NES. These arousals occurred earlier in the sleep period than did arousals in control subjects, and were associated with a decrease in sleep efficiency. Although the timing of the sleep-onset behavior was comparable between NES patients and controls, there remains a possibility that there is an altered (delayed) phase relationship between the sleep-wake cycle and the endogenous circadian rhythm of caloric intake in NES patients.

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0807.M

Sleepwalking and Malingering

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Introduction: Malingering is an important differential diagnosis to be considered in any case where there is legal involvement. The DSM IV suggests that malingering should be considered when there is a medicolegal issue at stake. The purpose of this presentation is to highlight the inherent difficulties facing consultants offering opinions on parasomnias in a forensic setting. The two cases presented here are reflective of the problems in dealing with malingering in the evaluation of a sleep disorder.

Methods: When evaluating these cases of sleepwalking in a forensic context we analyzed them under 3 headings: I. Offender Characteristics 1.look for clinical features related to sleepwalking 2.personality of the offender and credibility issues 3.motivation for an offense 4.history of aggressive or violent behavior 5.cooperation with the investigation 6.history of malingering II. Victim CharacteristicsRelationship to the victim, vested interest in terms of compensation, custody and access and revenge motives. III. Other Environmental CharacteristicsExamination of police records and victims statements.Understanding how the charges are laid, who is bringing forward the defense and what possible outcomes are expected should be looked at.

Results: I. A client (GC) referred for evaluation for the presence of a parasomnia after he was charged with attempt murder of his former girlfriend. The issues were whether a parasomnia was present, how this interphased with the offense and how the issue was resolved by the courts. The interesting factor that tipped the balance in favor of the final legal resolution was the critical information obtained from the victim, that fact that the client had pled guilty, and how sleep walking was conceptualized by the courts as a mental disorder or not. II. A client (RG) referred for the presence of a parasomnia after he was charged with a sexual assault on his teenaged stepdaughter. He had a history of sleep walking and the conclusions were seemingly obvious. The investigator went beyond a polysomnographic evaluation and shrewd investigating of former girlfriends, erotic preference testing (phallometric testing),

uncovered other motivations for offending. The presence of a paraphilia like pedophilia along with a documented history of sleepwalking and polysomnographic confirmation of a parasomnia still did not eliminate malingering and this determined the final legal outcome.
Conclusions: Malingering is a diagnosis of significant importance in the forensic arena. Sleepwalking is no exception too, and when such a defense is put forward, malingering should be considered to be part of the differential diagnosis.

0808.M

REM Sleep Behaviour Disorder – Characteristics of a Series of Consecutive Referrals to a Specialist Sleep disorders Centre in the UK
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Introduction: REM sleep behaviour disorder (RBD) is characterised by vigorous sleep behaviours usually accompanying vivid dreams which occur during REM sleep. This disorder is often misdiagnosed and is infrequently reported in the UK population. We set out to identify salient characteristics of a consecutive sample of patients with a polysomnographic (PSG) diagnosis of RBD.
Methods: We reviewed the case notes and investigations on a sample of 17 consecutive patients diagnosed with RBD. The following were recorded: Age, sex, referrer's presumptive diagnosis, presenting complaint, the presence of co-morbid medical or psychiatric disorders, Epworth Sleepiness Score (ESS), Beck Depression Score (BDI), Sleep Latency, REM Latency, Apnoea Hypopnoea Index (AHI), Routine Biochemistry and haematology profile and HLA Typing. We also examined the PSG and video recordings for secondary sleep disorder diagnoses.
Results: There were 12 men and 5 women who met the polysomnographic criteria for a diagnosis of RBD. Mean age at presentation was 54.1 $\pm$ 14 years (range 28 – 70). The presumptive diagnosis by referrer was Night Terrors in 8 patients, Insomnia in 4 patients and Excessive movements during sleep in 3 and sleep walking in 2 patients. The primary complaint in 14 patients was of violent behaviour during sleep accompanied by altered dreams. Of the remaining 4, 2 complained chiefly of disrupted sleep and the remaining 2 presented with snoring. None of the patients had a co-morbid medical or psychiatric condition. The mean ESS score was 8.18 (range 4-12)' the mean BDI score was 9.87 (range 5 – 19), Mean Sleep Latency was 23.34 minutes with a range of 0 – 99 minutes and, mean REM latency was 100.93 minutes with a range of 58 to 200 minutes. Routine Biochemistry and Haematology screen was normal in all patients and all were HLA-DR2 negative. Five patients presented with co-morbid sleep disorders, two had a periodic limb movement disorder (PLMD), another two had coexisting Obstructive Sleep Apnoea and one patient had Upper Airways Resistant Syndrome (UARS). All patients were treated with Clonazepam and those with OSA or UARS were also treated with nasal positive airway pressure and a dental device.
Conclusions: Although RBD may be suggested by symptoms alone, PSG preferably with Video monitoring is necessary to establish the diagnosis and to exclude coexist respiratory or neurologic causes for the symptoms. It is not uncommon for RBD to be accompanied by other sleep disorders.

0809.M

Arousal Analysis in Sleepwalking Patients after Window Jumping with or without Injury
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Introduction: Like confusional arousals and sleep terrors, sleepwalking is a NREM arousal parasomnia. It is a serious problem in childhood and adolescence (an estimated rate of 15 to 30% of children and adolescents, with peak prevalence at about 12 years). To compare mentioned NREM arousal parasomnias, walking is described in sleepwalking only. Injury connected with this anomaly is mentioned rarely.
Methods: Polysomnography with videomonitoring were used to evaluate sleep, especially microarousals from delta sleep, in four patients with a history of window jumping - Group I (patient No. 1, male, 20 years: age at sleepwalking episodes onset (SEO) 19 years, without trauma after jumping from the ground floor window; patient No. 2, male, 18 years: age at SEO 9 years, paraplegia of lower limbs, monoparesis of right upper limb; patient No. 3, female, 18 years: age at SEO 12 years, trauma of cervical and lumbar vertebrae after accident, without spinal lesion; patient No. 4, female, 12 years: age at SEO 12 years, paraplegia after accident). Mean age in Group I was 17.0 ± 3.0 years, mean age at SEO was 13.0 ± 3.7 years. Sleep efficiency, percentage of sleep stages, delta sleep latency, duration of delta sleep periods, number of arousals from individual delta sleep, duration of arousals and ratio between the number of arousals and duration of delta sleep periods were analysed. The controls - Group II - consisted of 4 age-matched patients diagnosed as sleepwalkers with no injury.
Results: The two groups showed no difference as to sleep efficiency or the percentage of sleep stages. Delta sleep was only slightly prolonged in both groups. Delta sleep latency was shortened in Group I. Latencies of individual delta sleep periods were shorter in Group I. The duration of delta sleep periods was much the same in both groups, decreasing towards the end of sleep in Group I. The number of microarousals from delta sleep was higher in Group I (4.89 ± 6.02), decreasing to the end of sleep in both groups. The microarousals were longer in Group I (24.10 ± 27.73) and prolonged to the end of sleep. Three arousals in Group I alone were longer than 1 minute. The ratio between the number of awakenings and the duration of delta sleep periods was higher in Group I (0.21 ± 0.29). None of the patients of either group had any behavioural manifestations at any time of the recording.
Conclusions: The results found in patients, who jumped from the window (with or without injury) during sleepwalking episodes indicates a lower quality of their delta sleep. As this type of injury is rare, albeit with serious health consequences, other studies are recommended to help prevent this behaviour.

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0810.M

Analysis of REM Sleep Associated Muscle Activity in Idiopathic REM Sleep Behavior Disorder
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Introduction: REM sleep behavior disorder (RBD) is a diagnosis based on patient history of complex, violent behavior during REM sleep. Polysomnography typically reveals increased muscle activity during REM sleep. However, the minimal diagnostic criteria for RBD exclusively include clinical but not polysomnographic features.
Methods: According to a method, described previously, we analyzed long and short lasting muscle activity during REM sleep for limb and chin muscles separately in 8 patients with PSG confirmed idiopathic RBD and 8 age- and sex-matched controls without any history or PSG signs of RBD. 10-second epochs of REM sleep were scored; the percentage of the 10-second REM epochs associated with increased chin or limb muscle activity (long lasting muscle activity or short lasting muscle activity) was analyzed; muscle activity during REM sleep was considered increased if there was an increase in EMG amplitude of at least 50% compared to the immediately preceding atonic EMG baseline; long lasting muscle activity during REM sleep was scored for each 10-second epoch in which persistently increased muscle activity lasted at least 1

second; each single persistent increase of muscle activity lasted at least 0.5 seconds. We chose the 0.5 second criterion according to the definition of a (periodic) leg movement during sleep, since this, at present, is the only commonly accepted time criterion for movements during sleep. Therefore, long lasting muscle activity according to our criteria is more likely to be associated with potentially locomotor behavior, which is a feature of RBD, than short lasting muscle activity. Muscle activity increase of less than 0.5 seconds was defined as short lasting muscle activity. Short lasting muscle activity was scored for one 10-second epoch if at least 10 short lasting muscle activities occurred during this epoch. Long and short lasting muscle activities were analyzed for chin muscles and extremity muscles separately.

Results: Patients and controls were closely age- and sex-matched (RBD: 69.2±7.6 years, 7 men; controls: 68.6±5.9 years, 7 men). Long lasting chin muscle activity and long lasting limb muscle activity were significantly higher in RBD (long chin: 43.6±35.8%, p=0.015; long limb: 30.2±22.9%, p=0.05) than in controls (long chin:5.4±4.1%, long limb:11.8±10.1%), whereas short lasting limb muscle activity was significantly lower in RBD (short limb: RBD: 5.1±9.2%, controls: 20.1±25%; p=0.028); short lasting chin muscle activity did not differ significantly between patients and controls. Multiple logistic regression analysis controlling for REM sleep associated short lasting chin muscle activity, long lasting chin muscle activity, short lasting limb muscle activity and long lasting limb muscle activity identified long lasting chin muscle activity as independent prognostic factor for the polysomnographical identification of idiopathic RBD (p=0.001).

Conclusions: Long lasting chin muscle activity according to our scoring method helps to differentiate between idiopathic RBD and controls and should be included in the analysis of PSG especially if reliable patient histories are absent. Detailed analysis of muscle activity during REM sleep should be performed to further evaluate polysomnographic criteria for RBD.

0811.M

REM Sleep Behavior Disorder: A 2-Year Clinical Follow-up Study

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Introduction: REM Sleep Behavior Disorder (RBD) is a parasomnia with severe, harmful movements accompanying vivid dreams, occurring predominantly in middle-aged man. Amnesia for the violent behavior is present. Degenerative disorders of the central nervous system are suspected in 40 % of the patients. RBD can precede neurodegenerative disorder by up to five years.In this prospective study we describe the clinical status and outcome of 9 medium to severe cases of RBD.

Methods: Since 1998 the diagnosis of RBD was made in 9 patients consulting for extremely disturbing or violent behavior during sleep. A clinical neurological exam, a PSG and MRI were performed. Follow-up of these patient was obtained either by consultations, either by telephonic interview of their GP. Median follow-up since diagnosis in the sleep lab is 2 years (0-4); first appearance of symptoms has a median of 5 years (0-10 y).

Results: Diagnosis of RBD was made in 2 female and 7 male patients consulting for problematic acting out of their dreams. Median age at diagnosis was 66 years (60-77). Symptoms started at the age of 63 years (52-77). The PSG confirmed the clinical diagnosis of RBD in 5 patients.MRI of the brain was performed in 6 patients and was considered within normal limits for 3 patients. One to two small, hyperintense T2 subcortical lesions in both hemispheres were described in 3 patients. Brainstem lesions were not present. None of the patients had symptoms of a neurodegenerative disease at RBD diagnosis. One patient had been treated for Lyme neuroborelliosis and still complained of fatigue and facialis paresis. Another patient was treated for tardive dyskinesias, after use of a phenothiazine for enhancing appetite. One patient had suffered one epileptic fit. In 3 patients, start of the symptoms was concomitant to familial stress. Three patients were known with a neoplasm, curatively treated at the moment of the RBD diagnosis. In all patients, RBD was treated by clonazepam (mean dose 0.5 mg/evening). When adverse effects (daytime drowsiness or incontinence) occurred, the dose was diminished. When not efficacious, oxcarbazepine or citalopram was added, with good result. However, 4 patients stopped taking clonazepam as they considered the frequency or seriousness of their harmful dreams as acceptable. In the 2 years of follow-up since diagnosis (c.q. 5 years since first symptoms), no symptoms of cognitive decline nor of extrapyramidal disease emerged. One patient developed a new cancer. No recidive of cancer occurred in the patients who were on treatment at the time of the RBD diagnosis.

Conclusions: In this prospective study, patients diagnosed with RBD in a sleep-wake disorders clinic did not develop a neurodegenerative disorder within the 5 first years after symptoms started. MRI, when abnormal, showed vascular lesions in the hemispheres, not in the brainstem. Treatment with clonazepam was highly succesful.

0812.M

Quantitative Analysis Of NREM Sleep EEG In Patients With REM Behavior Disorder

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Introduction: It has been suggested that REM behavior disorder (RBD) may be associated to an increase of slow-wave sleep (SWS). Quantitative analysis of sleep EEG across the night is a powerful and sensitive tool for evaluating changes in sleep regulatory processes. To our knowledge, no study has assessed quantitative NREM sleep EEG between idiopathic RBD patients compared to healthy controls. We tested the hypothesis that patients with idiopathic RBD will present a higher delta power during NREM sleep than age-matched controls.

Methods: We investigated twenty-five patients with idiopathic RBD who met the ASDA criteria for RBD and twenty-five healthy controls matched for age and gender: RBD patients (18M, 7W, 51-77 y; mean age: 66.0 y) and controls (18M, 7W, 52-75 y; mean age: 65.7 y). All subjects had one night of polysomnographic recording. None of the subjects were taking medication known to affect sleep architecture. All participants underwent a standard neurologic examination before PSG recording to rule out the presence of neurologic abnormalities, including signs of neurodegenerative disease and concomitant signs of parkinsonism. To quantify the dynamics of NREM sleep EEG over the night, spectral analyses were performed by fast Fourier transforms (FFT) on artifact-free 4-second epochs in N-REM sleep from C3-A2 derivation. Frequency bands were defined as: 0.25-1.0 Hz, 0.5 to 4.0 Hz, 4.0 to 8.0 Hz, 8 to 12 Hz, 12-14 Hz, 14-16 Hz, 16-24 Hz, 24-32 Hz. Student's t-tests were performed to assess between-group differences on sleep architecture and spectral power parameters. Spectral data were log-transformed before statistical analyses to normalize data distributions.

Results: Compared to controls, patients with RBD showed a higher percentage of slow-wave sleep (p=0.04) and of REM sleep (p=0.02). In addition, patients with RBD presented longer sleep latencies (p=0.04) but fewer awakenings compared to controls (p=0.005). No other between-group difference on sleep architectures was found. Patients with RBD showed higher spectral power in the 0.25 to 1 HZ frequency band. This difference was observed for the entire night (p=0.02) and for the first NREM hour (p=0.04). There was no significant change in the other frequency bands.

Conclusions: Our findings corroborate the hypothesis that patients with RBD show more SWS than healthy controls. Interestingly, spectral results demonstrate that the increase in power is not over the entire delta

frequency band but only in the slow oscillation frequency range. The slow oscillation was previously found to be related to distinct neurophysiological processes that originate from cortical areas. Presumably, RBD would not be restricted to the dysfunction of sub-cortical systems, but also to electrophysiological modifications of the cortex.

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0813.M

Neuropsychological Assessment in Idiopathic REM Sleep Behavior Disorder (RBD): Does the Idiopathic form of RBD Really Exist?

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Introduction: Idiopathic RBD was the initial diagnosis after clinical and PSG evaluations in 25-43% of several patient series (Schenck CH et al, Sleep 2002). Several disorders were reported to be linked to RBD, with neurodegenerative disorders being the most common: RBD may be the initial manifestation of Parkinson's disease or of other neurological disorders (multiple system atrophy, MSA or dementia with Lewy bodies, DLB). Cognitive dysfunction is present in PD and DLB, including the early stages of the disease.Aim of our study was to evaluate the cognitive performances of consecutive idiopathic RBD patients compared to controls.
Methods: Consecutive patients with idiopathic RBD and healthy controls have been evaluated. According to the following exclusion criteria (presence of sleep apnea, smoking, alcohol or psychotropic drug use) seventeen RBD patients have been included (mean age= 68 yrs; mean duration of RBD= 5.5 yrs) and compared to 17 age- and education-matched controls. A battery of neuropsychological tests to evaluate a wide range of cognitive functions was administered to each patient and control. This battery includes: Mini Mental State Examination, tests of verbal and spatial short-term memory (digit span forward and backward, Corsi block tapping span), visual selective attention (attentive matrices), verbal fluency with phonemic and semantic cues, memory for prose (short tale), constructional abilities (copy of Rey-Osterrieth complex figure), spatial learning (Corsi supraspan learning), executive functions (Stroop color word interference test, Trail Making Test [A and B], Raven's progressive matrices). Moreover a self-administered depression rating scale (Beck Depression Inventory) was also evaluated.
Results: RBD patients had significantly impaired scores ($p<.005$ with Bonferroni correction) compared to controls in two of the tests: copy of Rey's figure (28.1, SD= 4.8 vs 33.9, SD= 2.4) and Corsi supraspan learning (10.7, SD= 5.6 vs 5.0, SD= 0.8). No correlation was found between the neuropsychological results and RBD duration or polysomnographic findings as NREM and REM sleep percentages, sleep efficiency and periodic limb movement index.
Conclusions: Our results showed that in idiopathic RBD patients a visuospatial constructional dysfunction and a visuospatial memory impairment may be present. These findings give indications that a neuropsychological assessment should always be performed in RBD patients without an evidence of neurodegenerative disorders. They also suggest that the term "cryptogenetic" rather than "idiopathic" may be more indicated for non symptomatic RBD. This is also in agreement with a previous neurophysiological finding where cardiac autonomic sympathetic and parasympathetic activity during sleep was dampened not only in the symptomatic form of RBD but also in the idiopathic ones (Ferini-Strambi L et al, Sleep 1996).

0814.M

Slowing Of The Waking EEG In Idiopathic RBD And RBD Associated With Parkinson's Disease

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Introduction: REM sleep behavior disorder (RBD) is characterized by a loss of muscle atonia and an increase in phasic muscle activity during REM sleep, leading to complex nocturnal motor behaviors. The brainstem structures affected in RBD are also implicated in cortical activation. To verify the hypothesis that EEG activation is impaired in RBD, quantitative analyses (qEEG) of waking EEG were performed in primary RBD and RBD associated with Parkinson's disease (PD). To our knowledge, no study has assessed qEEG in RBD.
Methods: Forty-five subjects were studied, including 15 with a PSG-confirmed diagnosis of idiopathic RBD, 15 non- demented patients with PD (7 with and 8 without RBD) and 15 healthy controls. The three groups as well as the 2 subgroups of PD patients were matched for age and gender. None of the subjects had any associated medical or psychiatric disorder or were taking any medication known to influence sleep or motor activity, except for patients with PD who were treated with dopaminergic agents. Sleep apnea was ruled out in every subject. Waking EEG spectral analysis was performed in the morning following the night recording. Absolute EEG power was calculated for five frequency bands (delta, theta, alpha, beta 1, and beta 2) from frontal, central, parietal, temporal and occipital regions.
Results: During wakefulness, idiopathic RBD patients showed a statistically significant increase of theta power in frontal, temporal and occipital regions with a decrease of beta power in the occipital region compared to healthy subjects. The dominant occipital frequency (DOF) was also significantly lower in RBD patients. Similarly, PD patients with RBD showed a higher theta power in frontal, temporal, parietal and occipital cortex and a slowing of the DOF in comparison to both PD patients without RBD and control subjects.
Conclusions: This study shows for the first time an impaired cortical activation during wakefulness in idiopathic RBD. This study also demonstrates that the slowing of the EEG previously reported in patients with PD is strongly related to the presence of RBD. These observations support the hypothesis of common pathophysiological mechanisms between RBD and neurodegenerative disorders such as PD and Lewy Body dementia.

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0815.M

Parasomnias In The Medical Intensive Care Unit

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Introduction: Studies to date have suggested a relatively high prevalence of parasomnias in the medical intensive care unit patient population. In this regard, the Rem sleep behavior disorder might be expected to be a common finding as the systemic effects of a wide variety of critical illnesses might lead to CNS dysfunction of descending neural pathways which could precipitate such a phenomena.
Methods: An institutional review committee concerning human studies approved this study, where from 1/12/02 to 3/3/02 all patients admitted to the medical intensive care unit (MICU), and deemed to be critically ill, 18 years of age and older were given the opportunity to enroll in a study where polysomnography (PSG) would be performed in the MICU. Forty-four of 128 eligible patients (35%) participated.
Results: The 44 patients studied included 21 men (48%) and 23 women (52%) with a mean ($\pm$SD) age of 57.2 $\pm$21.1 years, with a range of 19 to 91 years. Eleven of the patients (25%) exhibited classical episodes of parasomnia, evidenced as confusional arousals and/or sleep talking (somniloquy). Although most events appeared to arise from stage 3-4

NREM "slow wave" or "delta" sleep, the underlying electroencephalographic (EEG) pattern frequently revealed a waking baseline theta/delta pattern which made clearly distinguishing sleep stages difficult. In addition, for 9 patients (82%) the events of interest often occurred in a close temporal association with either an obstructive sleep apnea {(OSA)found in 7 of these patients} or a hypoglycemic period (in 2 subjects). None of the 44 patients exhibited an event consistent with the diagnosis of the REM sleep behavior disorder.
Conclusions: The high prevalence of parasomnias in this small pilot study of MICU patients suggests that there may be an association between parasomnias and acute illness requiring MICU treatment. We hope to use this study to justify larger, more detailed population studies to further delineate the clinical concomitants of parasomnias in the MICU population, as the presence of a parasomnia may suggest underlying problems with potentially devastating health related effects, such as OSA and hypoglycemia.

Research supported by The University of Iowa Roy J. and Lucille A. Carver College of Medicine

0816.M

The Value Of The Unexplained Polysomnographic Arousal From Slow-Wave Sleep In Predicting Sleepwalking And Sleep Terrors In A Sleep Laboratory Patient Population

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Introduction: Sleepwalking (SW) and sleep terrors (ST) are disorders of arousal from non-REM (typically slow-wave) sleep. Several studies have suggested an increased incidence of arousals from slow-wave sleep (SWS) in patients with these parasomnias. In clinical practice, a polysomnographic (PSG) observation of an otherwise unexplained arousal from SWS may raise a suspicion for a non-REM parasomnia.
Methods: A parasomnia questionnaire and PSG data from 275 patients were collected over a 10-week period. Arousals as defined by the ASDA, 1992 and awakenings (arousals resulting in at least one epoch of wakefulness) were scored during SWS. 42 patients with arousals from SWS explained by other sleep disturbances (sleep apnea, periodic limb movements), 40 patients undergoing CPAP titration, and 69 patients who did not reach SWS were excluded.
Results: Data from 124 patients were analyzed. Age ranged from 3 to 74 years (mean 41.7). 49% were males. 103 of 124 patients were diagnosed with obstructive sleep apnea syndrome and/or periodic limb movement disorder. Of the remaining 21 patients, 2 were diagnosed with upper airway resistance syndrome, another 3 had episodes of snore-arousals. 16 were not diagnosed with a specific sleep disorder. 30 of 124 patients had a history of SW or ST (parasomniacs), 94 patients did not (non-parasomniacs). Arousals from SWS were seen in 96.7% of parasomniacs, versus 80.9% of non-parasomniacs. Awakenings from SWS were seen in 60% of parasomniacs, versus 41.5% of non-parasomniacs. Mean overall arousal index was similar between groups. SWS percentage was higher in parasomniacs than in non-parasomniacs (20.1% versus 14.5%, $p<0.01$). Positive predictive value (PPV) of a SWS arousal for SW or ST was 25.9%. PPV of SWS awakening for SW or ST was 29.8%. Negative predictive value (NPV) of the absence of SWS arousals was 94.7%. NPV of the absence of SWS awakenings was 82.1%. All 16 patients without a PSG diagnosis of a sleep disorder had arousals from SWS. PPV of a SWS arousal for SW or ST was 37.5%. PPV of SWS awakening was 30%. Of note, 24.2% of the 124 studied patients had a history of SW and/or ST, whereas in the excluded group of 69 patients with no SWS, only 10.1% had such history.
Conclusions: 1. The presence of unexplained SWS arousals or awakenings does not seem to be useful in predicting SW or ST in a patient population referred to a sleep laboratory. 2. The absence of SWS arousals may have a useful negative predictive value. 3. Parasomniacs seem to have a significantly higher percentage of SWS on PSG and patients with no SWS on PSG tend to have a lower prevalence of SW and ST.

0817.N

Mechanical Hyperalgesia without Allodynia in Patients with Restless Legs Syndrome

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Introduction: To investigate the unpleasant, sometimes painful sensory symptoms, which are a characteristic feature of restless legs syndrome (RLS) suggesting an alteration of nociceptive processing in these patients.
Methods: 11 patients (10 female, 1 male, mean age 60 ± 12 years) with primary RLS for 18 ± 15 years and 11 age and gender-matched control subjects (mean age 60 ± 12 years) with normal neurological examination were investigated. Stimulus-response function for pricking pain was obtained at the hand and foot dorsums in the morning and evening with a series of calibrated punctate mechanical stimulators (0.2 mm diameter, 8 ± 512 mN), which activate A delta-high threshold mechano-nociceptors. Pain to light touch (allodynia) was tested by stroking with light touch stimuli (cotton wisp, Q-tip, soft brush).
Results: Pin prick pain ratings in RLS patients were on average 6 times more intense than in controls (ANOVA, $p<0.001$) with marginally higher pain rating in morning compared to evening assessments (+6 %, n.s.). A significant leftward shift of the stimulus-response function for noxious mechanical stimuli indicated generalised hyperalgesia to pin prick, while hyperalgesia to light touch (allodynia) was never reported. Administration of levodopa (100 mg) plus benserazide (25 mg) 1 ½ hours prior to the evening assessments resolved patients RLS symptoms (-75 %, $p<0.001$), but left pin prick hyperalgesia completely unaltered. In contrast, hyperalgesia was significantly, though not fully reversed (-68 %, ANOVA $p<0.001$) after long-term dopaminergic treatment at follow-up after 11.4 ± 4 months.
Conclusions: Patients with RLS exhibited a profound mechanical hyperalgesia, mediated by A-fiber high-threshold mechanoreceptors, which is a hallmark sign of neuropathic pain of the central sensitization type.

0818.N

The role of CNS Dopaminergic, Serotonergic and Hypocretin (Orexin) Systems in Restless Legs Syndrome

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Introduction: The exellent response of RLS symptoms to dopaminergic drugs suggests a key role of the dopaminergic system in the pathophysiology of RLS. However, morning CSF investigations showed no abnormalities in HVA values, and PET or SPECT imaging studies also revealed no clear dopaminergic deficit. Recently, significantly increased hypocretin-1 levels were demonstrated in late evening (11 pm) CSF in early-onset (EO) RLS but not in late-onset (LO) RLS. We further evaluated the role of monoamine neurotransmitters and the neuropeptide hypocretin (orexin) in restless legs syndrome (RLS).
Methods: Twenty-two RLS patients (mean age 58,6 ± 13 years) off psychotropic medication and 11 control subjects (mean age 56,6 ± 12,9 years) were investigated. In all RLS patients diagnosis was ascertained

by polysomnography. Homovanillic acid (HVA), 3-o-methyl-dopa (3-OMD), 5-hydroxytryptophan (5-HTP), 5-hydroxyindolacetic acid (5-HIAA), tetrahydrobiopterin (BH4), dihydrobiopterin (BH2), and 5-methyltetrahydrofolate (5-MTHF), neopterin were measured in the evening (5 - 6 pm) CSF using HPLC. Hypocretin-1 (orexin A) levels were investigated in the same samples using direct RIA and RIA on extracted peptide fractions. CSF for hypocretin analysis was available from 13 RLS patients (EO, n = 7; LO, n = 6) and 9 control subjects. In addition serum serotonin, levodopa and aromatic aminoacid decarboxylase (AADC) levels were determined.

Results: There was no significant difference in HVA (p = 0.547), 3-OMD (p = 0.458), levodopa (p = 0.683), 5-HTP (p = 0.272), 5-HIAA (p = 1.000), serotonin (p = 0.950), 5-HIAA / HVA (p = 0.458), BH4 (p = 0.294), BH2 (p = 0.577), 5-MTHF (p = 0.039), and neopterin (p = 0.121). In contrast, hypocretin levels (mean ± sd) as measured by direct RIA were significantly increased in RLS patients (306.5 ± 51.5 pg/ml) compared to controls (217.6 ± 70.7 pg/ml; p = 0.006). Differences were more pronounced in LO-RLS (p = 0.005) than in EO-RLS (p = 0.072) but may be interpreted with caution due to the small sample size. Using the extracted assay, mean values also tended to be higher in RLS patients (375.0 ± 117.4 pg/ml, n = 13) compared to controls (312.22 ± 55.8 pg/ml; n = 9)(p = 0.110).

Conclusions: Both patients with early- and late-onset RLS have increased hypocretin CSF levels. Our results support the hypothesis that the hypocretin system plays a role in the pathophysiology of RLS. The dopaminergic and serotonergic systems seems not to be directly involved.

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0819.N

Urinary 6-Hydroxy-Melatonin-Sulfate Excretion In Restless Legs Syndrome (RLS)

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Introduction: According to the International RLS Study Group (IRLSSG), worsening of RLS symptoms in evening/night is one of the four obligatory criteria for the diagnosis of this disorder. Sleep disturbances are an additional clinical feature. Prevalence of RLS increases with age. The pathogenesis of the syndrome and especially the cause of its circadian rhythm are unknown. Melatonin (MLT) secretion peaks in the early night, exposure to bright light inhibits the production. In the elderly and in insomniacs, a decrease of nighttime MLT and a delay of the serum peak have been shown. Positive treatment effects of oral MLT have been demonstrated in insomnia. As RLS symptoms show a temporary coincidence with the physiologic acrophase of MLT and an increase with age, a lack of MLT might not only be a cause for insomnia but also for RLS.

Methods: Fifteen patients with idiopathic RLS (4m/11f; mean age 52.1+10.8 years) were included. Patients fulfilled the four obligatory criteria of RLS, sleep disturbances were documented by polysomnography and questionnaires (Pittsburgh sleep quality index, Epworth sleepiness scale). Drug-naïve mean PLMS-(periodic leg movements in sleep)-index was 46.2+36.3/h TST (total sleep time), RLS severity index (IRLSSG rating scale) was 25.5+7.6. Patients with an apnea-hypopnea index >5/h TST were excluded, as well as patients taking any medication known to affect MLT metabolism. At the time of MLT measurement, eight patients were RLS-drug-naïve, seven patients had been treated with different medications against RLS for a mean of 20.3+8.4 months. Specific treatment was discontinued for at least 10 plasma half-live times before MLT measurement. Urinary 6-hydroxy-melatonin-sulfate (aMLTs), a useful tool for measuring serum MLT secretion, was measured in two samples. Daytime urine was collected from 7:00-22:00, nighttime urine from 22:00–7:00 next morning. Urinary aMLTs concentration was measured by means of a commercially available RIA (Stockgrand, Guilford, UK), the total amount excreted was calculated. The control group consisted of 11 healthy, sex- and age-matched subjects without any neurological and psychiatric diseases and without any sleep disorder.

Results: Daytime (7:00-22:00) as well as nighttime (22:00–7:00) urinary aMLTs excretion showed normal cumulative values in RLS patients as compared to healthy controls: daytime 6.1+5.2ng vs. 5.0+5.1ng, p = 0.59, n.s.; nighttime 21.1+17.1ng vs. 22.9+16.5ng, p = 0.78, n.s.

Conclusions: This explorative study showed normal cumulative values of aMLTs in day- and nighttime urine samples of RLS patients. These results do not provide evidence for a lack of MLT excretion in RLS. As the night sample was collected between 22:00 and 7:00, the exact time of maximal urinary aMLTs excretion and of serum MLT acrophase cannot be determined. The RLS symptom climax in the evening and early night might be also due to a delay of pineal MLT excretion. Further studies could focus on the time course of MLT metabolism in RLS.

0820.N

Prevalence Of Clinically Significant But Previously Unsuspected Restless Legs Syndrome In Patients With Clinically Significant Obstructive Sleep Apnea: A Prospective Study

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Introduction: Previous epidemiological studies have shown the common prevalence of RLS in up to 15% of the general population. According to Exar and Collop, patients with presumably pure Periodic Limb Movements in sleep (PLMS) may have underlying sleep disordered breathing. Because most patients with RLS also have PLMS,we sought to determine the relationship between RLS and Sleep apnea. Therefore, we determined the percentage of patients who have clinically significant but previously unrecognized Restless Legs Syndrome (RLS) in patients with clinically significant Obstructive Sleep Apnea (OSA).

Methods: One hundred sequential patients who came to a single sleep laboratory for Polysomnography were given a standard MEMO questionnaire including questions related to RLS. Patients who answered positively for RLS on the questionnaire were called and a personal patient interview was conducted over the phone to verify the symptoms of RLS. Clinically significant RLS was defined as symptoms present at least 2-4 days/week and clinically significant OSA was defined as an RDI of more than or equal to 10 or an apnea index of more than or equal to 5. The patients were then given the severity scale for RLS previously validated by the International RLS study group (IRLS Scale of 0-40 points). Only adult patients were taken into consideration for this study.To reduce bias we excluded any patients we saw in our out patient clinic prior to polysomnography.

Results: A total of 100 patients who had come in for PSG were evaluated. Within the group of 100 tested polysomnographically, 76 patients had filled out the RLS questionnaire.Of these 76 patients, 40 had clinically significant OSA. Of these 40 patients, 3 (7.5%) also had clinically significant RLS. None of these 3 patients had a previous diagnosis of RLS. If patients who did not fill out the questionnaire were included, 3 out of 54 (5.6%)of the patients with clinically significant OSA also had clinically significant RLS. Out of those 3 patients who had both clinically significant RLS and OSA,the average RLS rating scale score was 26.6 with a range of 20-32.

Conclusions: The new information from this study is that nearly 5-7.5% of the patients who were found to have clinically significant apnea on PSG also were found to have clinically significant RLS. In all these cases, RLS was unsuspected prior to filling out the questionnaire about

the RLS. We therefore recommend that patients coming into the sleep laboratory for PSG to rule out sleep apnea should also be screened for symptoms of RLS. This study does not suggest an increased prevalence of RLS in sleep apnea, but the reverse association, that is the prevalence of apnea in RLS should be studied in the future.

0821.N

Restless Legs Syndrome in Parkinson's Disease: A Case-Controlled Study

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Introduction: Restless Legs Syndrome(RLS) is a disorder of motor activity that has a circadian pattern and affects onset and continuity of slee, characterized by unpleasant leg sensations mostly at bedtime. The prevalence in general population ranges from 0.1% to 29%,being much lower in Asian populaitons.The prevalence of RLS in Parkinson's disease has been reportd to range from 7-19.5%.It is important to daignose RLS in patients with PD so as to provide effective therapy. The present study aimd to estimate the prevalence of RLS in Indian PD patients .
Methods: One hendred and twenty-six consecutive PD patients attending the Movement Disorders clinic at All India Insitute of Medical Sciences, New Delhi,India formed the study gruop. One hundred twenty-eight age and sex matched healthy individuals were recruited as controls. All were interviewed for the presence of RLS uing the IRLSSG criteria. Details were collected on disease profile, UPDRS, H and Y staging. Depression was evaluated using DSM IV criteria. Presence of accompanying medical illness was noted, Epworth Sleepiness Scale was applied and the John Hopkins Restless severity scale in patients with RLS.Data was analysed using chi square and student's t -test with $p< 0.05$ considered as statistically significant.
Results: Rls was present in 10 out of 126 cases of PD (7.9%) and in 1 of 128 control (0.08%) p=0.01.Pd patients with RLS were older than those without RLS (63.70 ± 7.80 years vs. 57.37 ± 10.04 years, p=0.05) and had a higher prevalence of depression (40% vs 10.3%;p=0.023). No demographic factors or factors related to PD corelated with the presence or severity of RLS.
Conclusions: RLS occurs more frequently in patients with Parkinson's Disease than in control subjects. However there is a much lower prevalence than that reported from the west.

0822.N

Peripheral Nerve Disease in Restless Legs Syndrome

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Introduction: Restless legs syndrome (RLS) is a poorly understood disabling disease, affecting 5-15% of the population. It is characterized by unpleasant sensations in the limbs, worse at night and at rest, and relieved by movement. RLS is associated with peripheral nerve disease (PND), reportedly in 9-37% of RLS patients. The significance of this association is unknown.The objective of this study is to determine the prevalence and type of PND in RLS.
Methods: Patients meeting the International RLS Study Group criteria for RLS were recruited from the Sleep Disorders Clinic over 3 months. All underwent screening blood tests, polysomnography (PSG), and a combination of tests of large and small fiber nerve (LFN and SFN) function: electromyography (EMG) and autonomic screening consisting of quantitative sensory testing (QST), quantitative sudomotor axon reflex testing (QSART), heart rate responses to deep breathing (HRDB) and Valsalva responses (VR).
Results: This is an ongoing study. Eleven patients were recruited (7 female, 4 male), with a mean age of 55 years (range: 31-69). One patient was found to have severe iron deficiency. Two patients without suggestive symptoms were incidentally diagnosed with obstructive sleep apnea syndrome (OSAS). There was no evidence in blood testing for diabetes, renal, liver or thyroid disease, vitamin B12 deficiency or monoclonal gammopathy. All but 3 patients underwent the complete test battery: 2 did not have PSG, 2 were not tested for HRDB and VR. Five (45.5%) had abnormal EMG studies suggestive of large fiber peripheral neuropathy (PN). Seven (64%) had abnormal QST indicating distal SFN. Five (45.5%) had abnormal QSART suggestive of postganglionic sympathetic dysfunction. Three (30%) had abnormal cardiovagal responses (HRDB and/or VR). Overall, 10 of the 11 patients (90.9%) had abnormalities in either LFN or SFN, 7 (64%) had significant abnormalities in both.
Conclusions: The prominence of sensory symptoms in RLS suggests a disturbance of afferent input in its pathogenesis. There are no studies of PND in RLS using a combination of routinely available, non-invasive tests of both LFN and SFN. EMG is a study of LFN, it cannot assess SFN. SFN can be evaluated with QST, QSART, HRDB and VR. The reported sensitivity of QST for detection of abnormal temperature and vibration sense ranges from 40-100%, QSART measures the integrity of the postganglionic sympathetic sudomotor axon, HRDB and VR are sensitive tests of cardiovagal function. Using these three tests combined increases the detection of SFN to approximately 93%. Our findings suggest a much higher prevalence of PND (LFN or SFN) than previously estimated, using a sensitive test battery. This may have been affected by the small sample size, referral bias and the presence of comorbid conditions like OSAS. Comprehensive electrodiagnostic investigation in RLS including studies of autonomic and SFN will increase the detection of potentially treatable PND. A better understanding of the pathophysiology will lead to improved diagnostic and treatment options.

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0823.N

The Burden Of Restless Legs Syndrome (RLS) On Patient Quality Of Life (QOL): Comparison With A Normative Population And Other Medical Conditions

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Introduction: RLS is a serious neurologic disorder with primary morbidities involving sleep loss and extreme discomfort, which may disrupt normal activities. To date, few studies have systematically assessed the burden of RLS on QoL. This study assesses that burden compared with a normative population (norms).
Methods: 200 patients who had attended a specialist clinic within the previous year for primary RLS were mailed the Short Form-36 (SF-36) and other measures; 85 (42.5%) patients returned the surveys. Scores from this group were compared with published SF-36 data from norms and people experiencing other medical conditions (n=2474). The International Restless Legs Syndrome rating scale – Patient Version (IRLS-PV) was used to determine symptom severity.
Results: 64.5% of patients with RLS and 57% of norms were women; patients with RLS were older than healthy norms, but age ranges between patients with RLS and norms with chronic conditions were approximately equivalent. 67.1% of patients reported experiencing RLS symptoms almost daily and first noticed symptoms at an average age (± SD) of 36.6 (± 19.6) years. Compared with norms, the RLS sample had significantly lower QoL scores for all SF-36 scales, even when examined by age and gender, indicating poorer physical, social and role functioning, bodily pain, general health, vitality and mental health. Differences in scores ranged from 8.6 (mental health, $p<0.0001$) to 48 (role-physical, $p<0.0001$). All severity groups experienced significant deficits ($p<0.05$) compared with norms for all SF-36 scales, with the exception of gener-

al health, role-emotional, and mental health, where patients with mild symptoms had approximately equivalent scores to norms. In general, scores for patients with RLS were equivalent to or worse than scores for norms with type II diabetes, depression, arthritis, hypertension, angina or a history of myocardial infarction.
Conclusions: These results suggest a significant burden of RLS on patients' daily lives that matches or exceeds that for other major medical disorders. This should be considered when evaluating treatment needs for RLS. Research using larger sample sizes over longer periods of time will examine further the impact of RLS on QoL in relation to changes in clinical status.

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0824.N

RLS Symptoms in Primary Care: A One Year Follow-up Study

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Introduction: The objectives of the Primary Care Sleep Education and Training Project are to increase awareness of sleep disorders and to determine their prevalence within the primary care community. Data gathered by our group revealed that 24.0% (504/2,099) of the patients within a Moscow, Idaho clinic population reported having symptoms of Restless Legs Syndrome (RLS) at least occasionally. The diagnoses were based on a validated questionnaire, the Restless Legs Syndrome Questionnaire (RLSQ).
Methods: For a one-year duration, each patient seen at the Moscow Clinic was asked to complete the RLSQ. The questionnaire was completed by 79.2% (2,099/2,649) of the population. Next, the RLSQ was scored as either positive or negative for RLS symptoms. Patients were asked to further participate, which included a structured diagnostic interview (SDI) performed by their primary care physician (PCP) and the completion of additional questionnaires. The PCP was blinded to the results of the RLSQ. If the PCP diagnosed the patient with RLS based on the SDI, treatment was considered. If the PCP felt the symptoms were subclinical, if treatment was not addressed, or if the patient refused treatment, the patient was placed in the "no initial therapy" group. Patients who were prescribed a pharmacologic agent or treated with iron were placed in the "initial therapy" group. A total of 176 patients completed the SDI and the additional questionnaires. One year after the initial appointment, follow-up questionnaires were mailed to the patients who completed the additional components; 103 of these individuals completed the follow-up questionnaires.
Results: For the 103 patients who returned follow-up questionnaires, four groups were formed based on the PCPs' diagnoses and therapy decisions: 1) RLS positive patients who continued therapy [13], 2) RLS positive patients who discontinued therapy [12], 3) RLS positive patients with no initial therapy [27], and 4) RLS negative patients with no initial therapy [51]. The RLS positive group that continued therapy for at least one year (RLSC) compared to the RLS positive group that discontinued therapy prior to one year (RLSD) showed significant differences at the one year follow-up, although the baseline measures were similar. RLSD patients reported a poorer quality of sleep ($t = -4.9$, $p<.001$), an increased difficulty staying awake during the daytime ($t= -3.4$, $p<.002$), and increased daytime fatigue ($t = -5.24$, $p<.001$) compared to RLSC patients.
Conclusions: Our results indicate that RLSC patients scored differently than RLSD patients on questionnaire-based measures one year after the initial appointment, even though baseline measurements were similar. RLSD patients appear to have a poorer quality of sleep and increased feelings of sleepiness and fatigue during the daytime. We are continuing to collect follow-up data on this population.

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0825.N

Abnormal Cutaneous Thermal Thresholds in Restless Legs Syndrome

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Introduction: The restless legs syndrome (RLS) is often associated with periodic leg movements and affects up to 10 % of the population. Its etiology still remains unknown, however, there is evidence of small fiber neuropathy which is usually not investigated under routine conditions.
Methods: We assessed small fiber sensory function by psychophysical estimation of cutaneous thermal thresholds (cold, warmth, and pain from heat) with the Marstock thermostimulator method in 22 patients with idiopathic RLS and in 40 healthy controls. The preliminary questionnaire of the International Restless Legs Syndrome Study Group (IRLSSG) was used to assess severity of RLS. Exclusion criteria were pathological nerve conduction, any severe additional neurological, psychiatric or medical disease, and intake of RLS specific medication.
Results: 32% of the 22 RLS patients (mean age 56.4 $\pm$ 13.7 years; 16 female; mean IRLSSG score 16.8 $\pm$ 3.2) and only 10% of the 40 controls (mean age 51.6 $\pm$ 11.7 years; 20 female) showed pathological values in at least one of the three thermal thresholds ($p=0.04$). Thresholds for coldness were significantly reduced ($p=0.035$), for warmth and pain slightly increased in patients with RLS as compared with the controls. 36% of the patients had a positive family history with at least one affected first-degree relative, 59% reported an early onset (< 45 years of age). Cold thresholds were significantly lower ($p=0.038$) and warm thresholds were significantly higher ($p=0.038$) in patients with a negative family history. Severity and duration of RLS as well as age of onset did not correlate with thermal thresholds.
Conclusions: We conclude that a subgroup of patients with suggested ?idiopathic? RLS and typically without family history may have an axonal neuropathic disorder which affects only those unmyelinated small fibers involved in the perception of pain and temperature. The detection of abnormal thermal thresholds may differentiate between sporadic and familial RLS and might influence management of these patients. However, further investigations with increased patient numbers are needed to elucidate the role of sensory neuropathy in RLS.

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0826.N

Restless Legs Syndrome (RLS): Improvements In Disease-Related Quality Of Life (QoL) With Ropinirole

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Introduction: RLS is a neurological disorder characterized by an urge to move the legs and commonly accompanied by uncomfortable or painful sensations. Movement temporarily relieves symptoms but, in many patients, there is considerable impact on sleep and QoL. Disease-related QoL was evaluated as part of a 12-week randomized double-blind placebo-controlled study of the efficacy and tolerability of the dopamine agonist ropinirole in RLS (Protocol number 101468/190).
Methods: Patients (>= 18 years) with primary RLS were randomized to ropinirole or placebo (1:1) for 12 weeks. Patients receiving medication for RLS or sleep disorders before the study undertook a washout period. During weeks 1-7, medication was titrated upwards, through predetermined dose levels (range: 0.25-4.0 mg/day), to reach patients' individual efficacious doses. Dosages remained stable after week 7 or after reaching the efficacious dose. The primary endpoint was the mean change from baseline to week 12 in the International RLS Rating Scale (IRLSRS) total score. The Clinical Global Impression (CGI) scale (part of the primary inferential set), administered at week 12, determined improvements in RLS symptoms. Disease-specific QoL was assessed at baseline, and weeks 8 and 12 using the RLSQoL questionnaire.
Results: A total of 284 patients (43 centres in 10 countries) received treatment. Of these, 76.7% (112/146) of the ropinirole and 79.0% (109/138) of the placebo group completed the study. The mean (SD) daily dose of ropinirole at 12 weeks was 1.90 (1.13) mg. A greater mean improvement in the IRLSRS total score was seen in the ropinirole group (-11.04 points) compared with the placebo group at week 12 (last observation carried forward; -8.03 points; treatment difference=-3.01, p=0.0036, 95% CI -5.03, -0.99). Additionally, significantly more patients receiving ropinirole showed a 'much improved' or 'very much improved' CGI score at the end of the treatment period compared with those receiving placebo (53.4% versus 40.9%, respectively; p=0.0416, 95% CI 1.02, 2.69). The improvement from baseline to week 12 in the RLSQoL questionnaire summary score was superior for the ropinirole group (-13.62 points) compared with the placebo group (-10.11 points; treatment difference=-3.51, p=0.00329, 95% CI -6.73, -0.29). The most commonly reported events were nausea and headache, which were more common with ropinirole than placebo.
Conclusions: Ropinirole was significantly more effective than placebo at alleviating RLS symptoms in adults. Patients receiving ropinirole also experienced superior disease-related QoL (measured with the RLSQoL questionnaire) compared with patients receiving placebo. Ropinirole treatment was well tolerated.

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0827.N

The Impact Of Restless Legs Syndrome Symptoms On Quality Of Life: A Population-Based Survey In The USA

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Introduction: Restless legs syndrome (RLS) is a common movement and sleep disorder in which symptoms present at rest, particularly in the evening and at night, and are temporarily relieved by movement. RLS symptoms therefore can adversely impact on the activities and sleep of sufferers, and affect their quality of life (QoL). The aim of the present study was to determine the impact of RLS on the QoL of adult sufferers using the health-specific QoL instrument, the Short Form-36 (SF-36).
Methods: A random population survey using a diagnostic questionnaire based on International RLS Study Group criteria identified 519 people with RLS symptoms. Of those 519, 424 completed the SF-36 Health Survey (the RLS symptoms group) and rated the severity of their RLS symptoms using a five-response continuum (ranging from very mild to very severe). The mean scores of the RLS symptoms group for the SF-36 dimensions were compared with age- and sex-adjusted normative values for the general population of the USA and also with values for patients with other medical conditions. In addition, the relationship between mean SF-36 scores and RLS symptom severity, diagnosis and treatment status were examined.
Results: Mean scores were significantly lower ($p<0.05$) for the RLS symptoms group compared with the general population for six of the eight SF-36 dimensions: physical functioning 68.1 vs 80.0; role limitations due to physical problems 62.3 vs 76.0; bodily pain 60.4 vs 72.0; general health 58.6 vs 69.0; energy/vitality 48.0 vs 60.0; social functioning 77.5 vs 82.0, respectively. Values for the RLS symptoms group for the remaining two dimensions (role limitations due to emotional problems, and mental health) were also lower than those for the general population. The mean SF-36 scores for the RLS symptoms group were similar to those of patients with other serious chronic medical conditions, such as type-2 diabetes, hypertension, and acute myocardial infarction. Within the RLS symptoms group, mean SF-36 scores decreased with increasing symptom severity and irrespective of whether patients reported using prescription medications to treat symptoms or whether they had been diagnosed with RLS before the study. Patients receiving evidence-supported prescription medications for RLS were too few for separate analyses of the benefits of these treatments.
Conclusions: This population-based survey suggests that, in the USA, adults with RLS symptoms have a worse QoL than the general population and a similar QoL to that of patients with other serious chronic medical conditions. The QoL of the RLS symptoms group was not improved by treatments they were receiving.

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0828.N

Restless Legs Syndrome: Excessive Daytime Sleepiness Caused By Dopamine-Agonists

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Introduction: Restless Legs Syndrome is characterized by a desire to move the extremities, often associated with paresthesias or dysesthesias, motor restlessness, worsening of symptoms at rest with at least temporary relief by activity; and worsening of symptoms in the evening or night (IRLSSG diagnostic criteria). Dopamine-agonists have been proven effective for RLS. However, in patients with Parkinson's disease treated with these drugs, Excessive Daytime Sleepiness (EDS) and incidental cases of 'sleep attacks' have been reported. Aim of this retrospective study is to evaluate whether episodes of EDS or sleep attacks in

association with dopamine-agonist therapy have been reported by RLS patients seen in our clinic, to get an impression of the extent of the problem.
Methods: From a database of 867 RLS-patients seen in our clinic during the past five years, 85 patients currently or previously treated with dopamine-agonists (Ropinirole, Pergolide, and/or Pramipexole) were randomly selected. The data of these patients (48 men, 37 women; mean age 52.6; range 24-82) were screened for subjective reports of EDS and/or sleep attacks.
Results: Overall, 76 patients were treated with Ropinirole, 27 patients were treated with Pergolide, and in 16 patients Pramipexole was administered. The sum is more than 85 because some of the patients have been treated with more than one agent. In most patients (71 out of 85), treatment with one of these agents turned out to be sufficient in suppressing the RLS symptoms (mean effective daily dose of 0,46 mg (Ropinirole), 0,41 mg (Pergolide) and 0,31 mg (Pramipexole), administered between noon and nighttime). All patients were informed beforehand about the possibility of induction of daytime sleepiness. Eight patients had complaints of fatigue and/or feelings of inertia or indolence. Only seven patients (five treated with Ropinirole, one treated with Pramipexole, and one with Pramipexole) explicitly complained of excessive sleepiness, to such an extent that they were restricted in daily life. However, in none of the patients, sudden sleep attacks occurred. Moreover, EDS disappeared after substitution by another dopamine-agonist. No relationship could be found between the occurrence of daytime sleepiness and clinical or demographic features of the patients.
Conclusions: Our results show that induction of sleepiness in RLS is a relatively infrequent complication of treatment with dopamine-agonists. The side effect disappears after changing one drug to another, suggesting that different underlying mechanisms play a role in the induction of sleepiness. EDS can be very stressing and dangerous for the subject involved, e.g. it might increase the risk of traffic accidents. Even though in none of the patients in our study sleepiness occurred without warning, it would yet be better if we could foresee which patients are at risk for this complication. However, in our study, risk of induction of EDS could not be predicted based on demographic and clinical features.

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0829.N

Restless Legs Syndrome: Prevalence in a Family Practice Office Population

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Introduction: Restless Legs Syndrome (RLS) is a movement disorder causing uncomfortable leg symptoms that make it difficult to fall asleep at night. RLS responds to a variety of medications including dopamine agonists. However, if left untreated, severe symptoms can lead to significant impairment. The prevalence of RLS in a Family Practice outpatient population is not known and there may be substantial under-diagnosing of this syndrome.
Methods: To determine the prevalence and to describe the symptom distribution of RLS in a Family Practice outpatient population, we conducted a cross-sectional study using a survey instrument designed to be both sensitive and specific for RLS. A unique feature of this survey was that it included questions about nocturnal leg cramps, neuropathy, arthritis, and muscle aches to differentiate RLS from other conditions common in Family Practice. We recruited a systematic sample (n=1126) of adult patients with scheduled, non-acute office visits from a practice based research network consisting of nine Family Practice offices in Michigan. The survey was validated in a pre-survey pilot and revalidated on a sub-sample (n=50) of survey respondents after survey data was collected. In the post survey validation study, the gold standard was a structured telephone interview based on the International RLS Study Group definition of RLS by a neurologist with expertise in sleep disorders.
Results: The estimated prevalence of RLS symptoms in participating Family Practice offices was 12.5% (95% CI 10-15%). However, 66% of who screened positive for RLS symptoms had only mild or infrequent symptoms. Only 4% of the population had symptoms that were at least moderate in severity and that occurred at least once a week. In our initial pre-survey validation study in a tertiary care neurology clinic population, the survey instrument was 85% sensitive and 86% specific for RLS. In our post-survey validation study, the instrument was 80% sensitive and 42% specific. Thirty participants or about 2 percent of the population had been diagnosed with RLS according to their medical chart. However, almost half of the patients who had RLS as a diagnosis in their medical charts did not meet diagnostic criteria for RLS, and only about 11% of patients who screened positive according to our survey had the diagnosis on their medical chart. Among the 17 patients who were correctly identified as having RLS in their medical charts, only 5 were on medication effective for treating RLS symptoms.
Conclusions: Restless Legs Syndrome symptoms are common in primary care practice and may be confused with other common disorders, such as nocturnal leg cramps or neuropathy. However, relatively few patients have symptoms that are frequent or severe enough to warrant medication. There is significant room for improvement in both diagnosis and treatment of patients with RLS in a Family Practice office setting.

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0830.N

Epidemiology of Restless Legs Syndrome in a Population of 606 Pregnant Women

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Introduction: Pregnancy is considered as a risk factor for Restless Legs Syndrome (RLS). The relationship between pregnancy and RLS is known from the Mussio-Founer and Rawak case report described in 1940. Since then, very few epidemiological studies, performed without unanimous standard diagnostic criteria, have found a RLS prevalence rate that ranged from 11 to 27%. The grounds for the association between RLS and pregnancy are actually unknown.
Methods: 606 women (mean age 31.8±4.6) were interviewed by a medical doctor within two days after parturition. The interview took into consideration the woman's medical history, mother and newborn anthropometrical values, sleep habits/disorders and detailed description of eventual RLS. The day before parturition, iron, haemoglobin and mean globular volume values were checked. Women with specific diseases known to be associated to RLS or receiving drug therapy, except for iron and folati supplementation, were excluded. The International RLS Study Group criteria was used to define if a woman was affected by RLS. A follow up by telephone was performed during the first, third and sixth month after parturition.
Results: 26% of women experienced RLS symptoms during their pregnancy. 42% of them had already experienced RLS before in their life. There were no significant differences between RLS and the healthy group in: age, pregnancy duration, modality of the delivery, smoke, women Body Mass Index, number and weight of babies, and iron and folati supplementation. Haemoglobin and the mean globular volume were significant lower in RLS group; plasmatic iron was lower in symptomatic women but without statistical significance. The highest number of affected women were observed during the third trimester. The symp-

tomatology tended to disappear just around the delivery. RLS was usually not severe but had a significant impact on the women's sleep, increasing the sleep latency and decreasing the total sleep time. Snoring, nocturnal cramps, bruxism, nocturnal eating and others sleep disorders were equally distributed in the RLS and the non RLS women.
Conclusions: This study is the largest performed and the first to use the standard diagnostic RLS criteria. Pregnancy could be considered a strong risk factor in the initial or the worsening of RLS symptomatology. Pregnancy related RLS is usually not severe, transitory and more often accentuated during the third trimester. The decrease in haemoglobin and mean globular volume that was found in symptomatic women suggests that iron metabolism could be implicated in RLS pathogenesis during pregnancy. Fetal request and hemodilution decrease in iron storage during pregnancy with a nadir in the last trimester. The fact that oral iron supplementation did not facilitate patients with RLS, could indicate that iron oral adsorption or iron transportation toward CSF and bone marrow could be defective in RLS pregnant women.

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0831.N

Actigraphic Assessment of the Effect of Melatonin Treatment on Nighttime Sleep in Patients with Parkinson's Disease

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Introduction: Melatonin treatment for patients with age-related insomnia has been reported to improve a variety of objectively and subjectively measured sleep parameters. As part of a larger multicenter trial to examine the effects of two different doses of melatonin (5mg and 50mg) versus placebo to treat sleep complaints in patients with Parkinson's disease (PD), participants provided their subjective appraisals of sleep parameters and were monitored with wrist actigraphy.
Methods: The clinical design was a placebo-controlled, double-blind, double cross-over trial. Patients with PD who complained of poor sleep were screened to rule out primary sleep disorders and depression. Subjects received each treatment (placebo, 5mg, 50mg) for 2-weeks with a 1-week washout between treatments. Throughout each treatment period, participants wore the Mini-Mitter, Actiwatch 64 on the wrist less effected by movements characteristic of PD. Activity was recorded in 30-second epochs and analyzed at high sensitivity using Actiware 3.2. Actual sleep time was defined as the number of minutes asleep between initial sleep onset and final sleep offset; actual sleep percent was defined as the percent of time spent sleeping from sleep onset to sleep offset.
Results: Subjects (n=39) had a mean age of 62 $\pm$ 8 years, Hoehn & Yahr scale score of 2.4 $\pm$ 0.6, and a mean time since diagnosis of 7.5 $\pm$ 4.2 years. Subjects, on average, slept 312 $\pm$ 68 minutes per night on placebo, 318 $\pm$ 68 minutes on 5 mg, and 325 $\pm$ 73 minutes on 50 mg melatonin. Average actual sleep percent was 84 $\pm$ 10% on placebo, 83 $\pm$ 10% on 5mg, and 84 $\pm$ 10% on 50 mg melatonin. Wilcoxon signed ranks analyses revealed no significant differences in actual sleep percent on either the 5 mg or 50 mg dose of melatonin compared to placebo. There was no correlation between actual sleep time or actual sleep percent in any treatment period and Hoehn and Yahr, disease duration, UPDRS ADL or UPDRS motor scores.
Conclusions: Melatonin treatment did not significantly change actigraphically measured sleep time or percentage of sleep during the nighttime sleep episode in this sample of patients with PD. Future analyses will examine the potential effects of melatonin administration on circadian parameters including strength of the rest-activity pattern.

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0832.N

Sleep And Cognitive Functioning In People With Restless Legs Syndrome (RLS): Comparisons With A Normative Population

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Introduction: RLS sufferers experience sleep loss and extreme discomfort, which may impact cognitive abilities. Assessing the burden of RLS on sleep and cognition and the relation between these is critical for evaluating not only clinical significance and treatment benefits, but also whether RLS produces daytime symptoms not accounted for by the degree of sleep loss. Prior studies have not evaluated RLS sleep and cognition compared with a normative population (norms).
Methods: The Medical Outcomes Study (MOS) Sleep and Cognition scales were administered to 85 patients with primary RLS referred to a specialist clinic. Scores were compared with published norms (n=3053). The International Restless Legs Syndrome rating scale – Patient Version (IRLS-PV) was used to determine symptom severity.
Results: 64.5% of the patients with RLS and 61.0 % of norms were women; the mean age was 62.4 (range 26–87) years and 54 (range 18–98) years, respectively. 67.1% of patients reported experiencing RLS symptoms almost daily. At the item level, patients with RLS reported less restful sleep, more trouble falling asleep, greater fatigue, and less quantity of sleep compared with norms, but no differences were observed for sleep-related respiratory problems (shortness of breath/headache, snoring). For cognitive functioning, patients with RLS reported more problems with reasoning, forgetfulness, concentration, confusion, and slow reactions compared with norms. Sleep scores for patients with RLS were 19 points or approximately 1 SD worse than those for norms ($p<0.0001$). Cognition scores for patients with RLS were 14 points or 0.5 SD worse than those for norms ($p<0.0001$). Sleep and cognition scores for patients with RLS were even worse if RLS symptoms first began to appear before the age of 45 years (deficit of 4 additional points). As the severity of RLS increased, sleep problems increased and cognitive functioning decreased ($p<0.0001$). Sleep problems and cognitive functioning scores were moderately and negatively correlated ($r=–0.61$, $p<0.0001$). In multiple regression analyses, RLS severity predicted sleep ($r2=0.25$, $p<0.0001$) and showed that sleep, RLS severity, and age significantly predicted cognitive functioning ($r2=0.46$, $p<0.05$).
Conclusions: RLS poses a clinically significant burden to patients in terms of sleep loss and cognitive functioning, which should be considered when evaluating RLS treatment. The early-onset phenotype was more impaired, consistent with research noting the biological differences between early- and late-onset RLS phenotypes. Our results suggest significant daytime cognitive impairment in RLS not fully accounted for by the sleep loss alone. These data are consistent with the view that RLS affects the daytime functioning directly and not simply as a consequence of the sleep disturbance. This concept needs further evaluation with regard to the effects of RLS pathophysiology.

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0833.N

Sleep Disturbances in the Rotenone-Animal Model of Parkinson Disease

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Introduction: The degeneration and death of dopaminergic neurons in the central nervous system is a fundamental characteristic of Parkinson disease (PD). The herbicide rotenone produces Parkinson's-like anatomical, neurochemical and behavioral symptoms in rats when administered chronically. Clinical studies have repeatedly demonstrated that PD patients have disrupted sleep patterns. The objective in this study was to determine if rotenone administration produces changes in sleep patterns of rats similar to those characteristics of PD.
Methods: Sprague-Dawley male rats (300-350 g body weight) were implanted with Alzet mini pumps under ketamine-xylazine anesthesia (87/13 mg/Kg). An Alzet pump was implanted under the skin on the back of each animal, and a catheter was placed into the right jugular vein (Tygon microbore 0.51 mm i.d.). The Alzet pump was pre-filled with rotenone (RT) (ICN Biomedicals Inc.) dissolved in a mixture of 50% dimethyl sulfoxide and 50% polyethylene glycol. RT was administered in a dose of 2.5 mg/Kg per day for 4 weeks. Control rats received vehicle. The animals were also provided electroencephalograph (EEG) electrodes, a brain thermistor, (model 44008: Omega Engineering) and electromyograph electrodes. Each week rats were sacrificed; brains were removed and processed using a Fluro-Jade histofluorescent kit (Histo-Chem Inc) for detection of neuronal degeneration. Tyrosine hydroxylase immunostained sections were processed for silver staining to demonstrate selective neurodegeneration.
Results: The effect of RT administration on sleep patterns was progressive. The total time spent in non-rapid eye movement sleep (NREMS) (control 574.28 ± 25.34 min vs. 477.58 ± 12.25 min RT) decreased after two weeks of RT exposure. Consequently, EEG slow-wave activity decreased. The mean duration of rapid eye movement sleep (REMS) also decreased significantly (control 7.35±0.49 min vs. 2.71±0.36 min RT) after 2 weeks of RT treatment. The number of awakenings also increased during the light period in RT-treated rats (control 154.67±28.76 vs. 179.50±12.50 RT). Furthermore, selective nigrostriatal degeneration was observed in the rats after two weeks of rotenone administration.
Conclusions: Results suggest that rotenone-treatment in the rat may induce sleep disturbances similar to those characteristics of PD. Further, results suggest that dopaminergic nigrostriatal degeneration may have direct effects on the neuronal substrates regulating sleep.

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0834.N

Periodic Limb Movements in Macrophagic Myofasciitis

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Introduction: Macrophagic myofasciitis (MMF) is an emerging inflammatory myopathy. It includes muscle weakness, joint and muscle pain, and severe fatigue associated with macrophagic infiltration in the deltoid muscle fascia. The macrophage cytoplasm contains abundant aluminic inclusions, possibly brought in through intra-muscular injection of aluminium-containing hepatitis B vaccine. We asked whether sleep abnormalities could contribute to the otherwise unexplained fatigue.
Methods: Eighteen non obese patients (13 women, 5 men), aged 30-59 years and meeting MMF criteria (including a positive deltoid biopsy and no polyneuropathy), underwent an overnight polysomnography with left and right tibialis anterior muscle recordings and 4 multiple sleep latency tests. The Epworth sleepiness scale (ESS), fatigue impact scale (FIS, normal <80) and International Restless Leg Syndrome Study Group (IRLSSG) rating scale were also administered.
Results: Total sleep time was 392 ± 104 min, sleep onset latency was 16 ± 21 min and sleep efficiency was 80 ± 11%. The mean REM sleep was 64 ± 34 min, and slow wave sleep 102 ± 64 min. The mean periodic leg movements (PLMs) index was 24 ± 22 (range 6-80) per hour, and the PLMs arousal index was 23 ± 15 (range 4-63). The PLMs index was greater than 5 in all patients, greater than 15 in half of them and greater than 30 in 22% of them. Thirteen (75 %) patients had a restless leg syndrome. Serum ferritin was lower than 50 microgr/L in 3 patients with a PLMs index lower than 15. There was no polyneuropathy on electromyogram. Two third of the patients were treated with an antidepressant drug. Two patients had a severe obstructive sleep apnea syndrome. The mean daytime sleep latency was 15 ± 8 min, and two patients (one with sleep apnea) had an abnormally short (2.4 min) mean daytime sleep latency.
Conclusions: All patients with MMF have a PLM disease, 75 % of them associated with a RLS. This may explain –at least partially- daytime fatigue in the patients. Since no polyneuropathy or iron deficit was found, the potential causes of PLM/RLS include the frequent use of antidepressant and dopamine central deficiency.

0835.N

Impact Of Restless Legs Syndrome (RLS) On Sleep: The REST (RLS Epidemiology, Symptoms And Treatment) Study In Primary Care

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Introduction: RLS symptoms of leg discomfort and the need to move occur at rest and are most common in the evening and at night. Although these RLS symptoms lead to significant sleep disruption in severely affected patients, the actual degree and type of sleep disturbance has not been documented in a systematic manner. The adverse impact of RLS on sleep was therefore explored as part of REST, the first large international study of the prevalence, impact and treatment of RLS.
Methods: In the REST primary care study, all patients visiting (for any reason) 182 primary care physicians (PCPs) in five countries over a 2-week period were asked to complete a screener questionnaire. Patients who reported at least weekly symptoms consistent with key diagnostic features of RLS were considered positive responders for prevalence calculations and were given a more detailed questionnaire to complete. Their physicians also completed a questionnaire on their medical history. Patients with complete data (matched patient and physician questionnaires) and confirmed symptoms occurring at least weekly formed the study population.
Results: Based on data from the positive responders, the overall prevalence of symptoms consistent with RLS, occurring at least once weekly, was 7.1%. Of 23052 patients screened, 1145 formed the study population. The mean age of this population was 56.1 (SD, 15.8) years and 66.5% were women. Most patients (82.1%; 940/1145) experienced at least one sleep-related symptom and 36.6% (419/1145) considered a sleep-related symptom the most troublesome. Sleep symptoms included disturbed sleep, inability to get comfortable, twitching and/or jerks of the legs or other parts of the body, and inability to fall asleep. When suffering from RLS symptoms, 46.3% of patients (530/1145) stated that they woke up three or more times per night and 58.9% (674/1145) stated that they took more than 30 minutes to get to sleep. Identified consequences of the RLS symptoms occurring the following day included

finding it difficult to sit still or relax, lack of energy and difficulty in concentrating. Of the 390 patients for whom physicians reported a consultation about RLS symptoms, only 93 (23.8%) had received a diagnosis of RLS.
Conclusions: Sleep-related symptoms are common and troublesome in patients with RLS. Patients consider RLS symptoms to have consequences on daily functioning the following day. The high rate of sleep complaints among the patients with RLS and the relatively low rate of diagnosis in patients with frequent symptoms suggest that these patients have significant sleep problems that could be better treated if PCPs' awareness of the condition were increased.

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0836.N

Impact Of Restless Legs Syndrome (RLS) Symptoms On The Health And Quality Of Life Of Sufferers

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Introduction: RLS has been reported to be a common and often troublesome neurological disorder, but large scale studies have not been done to confirm this impression. We have now undertaken a project, REST (RLS Epidemiology, Symptoms and Treatment), to determine the profile of RLS in large multi-national population groups. Two groups were examined, a primary care population and a population survey. The latter was undertaken in France, Germany, Italy, Spain, UK and USA to investigate the prevalence, diagnosis rates, symptoms and burden of RLS and results are reported here. The other study is the subject of a separate abstract.
Methods: Randomly selected individuals were surveyed by telephone or face-to-face interviews. To be classified as RLS sufferers, interviewees needed to respond positively to four of the survey questions based on the International RLS Study Group diagnostic criteria for RLS. They also needed to indicate that symptoms occurred at least once a week. Further questions were included to determine the nature and consequences of these symptoms.
Results: A total of 15 391 questionnaires were returned fully completed. The survey population had an age range of 18–98 years (mean 45.7 years) and a male:female ratio of 48:52. 6.0% of those completing questionnaires (926) fulfilled all criteria for RLS sufferers. Prevalence was higher in women than in men. Additional symptoms identified in the RLS sufferers included inability to get comfortable (50.5% of RLS sufferers; 468/926) disturbed sleep (49.0%; 454/926), pain (43.0%; 398/926), inability to fall asleep (39.8%; 369/926), exhaustion/fatigue (32.1%; 297/926), inability to stay asleep (31.0%%; 287/926), insufficient sleep (29.6%; 274/926), and daytime sleepiness (25.9%; 240/926). A total of 64.3% of sufferers (595/926) reported some form of sleep disturbance. When sufferers were asked about the impact of RLS symptoms, 57.5% (532/926) rated the symptoms as moderately or extremely distressing and 39.3% (364/926) reported a negative effect on mood. The majority (65.8%; 609/926) of the sufferers reported consulting their primary care physician (PCP) about the symptoms of RLS, and 46.4% (430/926) stated they had done so in the last 12 months. However, only 5.4% (33/609) of those consulting their PCP indicated they were given a diagnosis of RLS.
Conclusions: This study, like its companion primary care study, indicates that RLS is a prevalent condition that is associated with sleep disturbance and significant distress. The majority of sufferers with frequent symptoms do seek help from their PCP. However, diagnosis rates for RLS in this group remain quite low, suggesting a need for improved education of medical professionals about this disturbing, but treatable condition.

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0837.N

Sudden Onset Of Sleep (SOS) In Parkinson´s Disease (PD)

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Introduction: It is common knowledge that daytime sleepiness and sleep disorders are widespread problems in PD. In 1999 the discussion arised if SOS is a side-effect of nonergoline dopamine agonists (nonergoline DA). However, recent studies showed that SOS appeared within all kinds of antiparkinsonian medication. Some authors suggested a class effect of all DA, independent of being ergoline or nonergoline.The study´s aim was to estimate the prevalence of sudden onset of sleep in PD (SOS; with and without feeling sleepy before), to determine the role of medication in SOS (type, dosage, duration of intake), to prove their relative impact compared to other associated factors, such as the duration or severity of disease and the quality of night sleep.
Methods: A questionnaire was sent to approximately 12,000 PD patients of which 63% were returned. We analyzed 6,620 complete data sets. The questionnaire of 25 pages contained items about SOS, medication, duration and severity of disease, daytime sleepiness and quality of night sleep.
Results: 42% of the patients reported experiences of SOS; 25% of those suffered currently and daily, further 26% at least twice a week. As SOS risk factors we identified: Epworth Sleepiness Scale (ESS) score above 10, old age, male sex, longer disease duration, intake of DA and sleep troubles. SOS occurred significantly earlier after introducing nonergoline DA and was more strongly associated with nonergoline DA in younger patients (< 70 yrs.) shortly diseased (< 8 yrs.). In patients with a history of disease of four years or less the intake of levodopa was also associated with a heightened risk for SOS. Furthermore, SOS seems to be dosage dependent. High dosage patients were at higher risk of experiencing SOS than low dosage patients. This effect was stronger in younger than in older patients and stronger for ergoline than for nonergoline agonists. In summary, medication was less efficient in predicting SOS than most of other factors considered.
Conclusions: The results of this questionnaire based survey show that the influence of medication on SOS has to be analyzed with respect to moderating factors like age and disease duration since both SOS and medication strongly depend on these factors. At first, our data confirmed a class effect of DA. In addition, nonergoline DA were more strongly associated with SOS than ergoline DA when they were applied to younger patients with a short history of disease. However, numerous mediating and moderating factors mentioned above have a much greater contribution in predicting SOS than type, dosage or duration of drug therapy. Thus, medication by itself cannot explain the SOS phenomenon, it rather seems to be caused multifactorially.

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0838.N

"Sleep Attacks" At The Wheel In Parkinson´s Disease (PD)

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Introduction: So far, only little research was done on the subject of driving ability in PD. The focus of the discussion is not only on the motor disabilities associated with PD but mainly on SOS and daytime sleepiness at the wheel.The study´s aim was to evaluate the prevalence of sudden onset of sleep (SOS) at the wheel in PD. SOS-induced accidents were compared to fatigue-unrelated accidents, driving situations critical for SOS examined and aspects differentiating between SOS with and without feeling sleepy before identified. In particular the study addressed the question whether sleepiness is a required precondition to SOS.
Methods: A questionnaire assessing driving habits, traffic accidents and SOS at the wheel was sent to 12,000 PD patients. Of 6,620 patients who returned complete data sets (response rate 63%) about 400 patients were interviewed by phone. Three groups of patients were compared: patients with SOS at the wheel without feeling sleepy before (target group 1, TG1), patients with SOS at the wheel with feeling sleepy before (target group 2, TG2), and patients without SOS at the wheel but with a recent accident (comparison group, CG). The semi-structured interview included questions about the event's antecedents, circumstances, consequences and other relevant conditions of SOS at the wheel resp. fatigue-unrelated accidents.
Results: 82% of the patients questioned held a driving license, of which 60% were active drivers. 8% of the patients with a driving license had already experienced SOS at the wheel, which was associated with a markedly increased accident risk. Patients involved in accidents were rather those with SOS experiences, with a moderate disease and those who still drove quite a lot. Accident involvement revealed to be independent of age, sex and duration of disease. The interview data yielded big differences between TG and CG patients, but there were no differences between TG1 and TG2: SOS mostly occurred in effortless, fatigue-provoking driving situations (93%) and resulted in the same types of fatigue accidents (84%) like side-swipes, no matter if patients felt sleepy before or not. In contrast, fatigue-unrelated accidents of PD patients mostly happened in difficult traffic settings (81%) involving other road users at cross-roads or emerging from parking areas (97%).
Conclusions: The results do not support the existence of "sleep attacks" in PD but argue for a misjudgment of wakefulness on the background of chronic daytime fatigue. Furthermore, the study revealed SOS and daytime sleepiness as important risk factors for traffic accidents in addition to disease severity. The excellent response rate emphasizes the importance of mobility for the patients and the need for further investigation addressing their driving ability.

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0839.N

Severity of Parkinson Disease and Sleep Fragmentation as Risk Factors for Objective Daytime Sleepiness

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Introduction: Daytime sleepiness is commonly reported in patients with Parkinson disease (PD). The cause of sleepiness in this population may be an intrinsic feature of PD, arise secondary to a nocturnal sleep disturbance or antiparkinsonian medications. To quantify objectively the degree of sleepiness in this population, we recruited patients from a movement disorder clinic for overnight polysomnography (PSG) followed by daytime assessment of sleepiness.
Methods: Consecutive patients with idiopathic PD in a tertiary referral center were recruited. Patients were excluded for dementia (MMSE<23), current use of sedative-hypnotics or antidepressants, or a diagnosed sleep disorder. Patients underwent one night of PSG followed by MSLT and MWT. Patients were divided into two groups based on the MSLT: PD+EDS with mean latency less than 5 minutes; PD-EDS with a mean latency greater than 5 minutes. Comparisons between groups were done using t-tests where appropriate. All values are presented as mean$\pm$standard error of the mean.
Results: Of the 15 PD patients identified as candidates, 10 patients (8 men, 2 women) agreed to participate. Of these, 4 men comprised the PD+EDS groups, and 6 patients were in the PD-EDS. The mean latency on MSLT in the PD+EDS and PD-EDS was 2.4 minutes and 9.7 minutes respectively. The age of the PD+EDS compared PD-EDS (62 ± 9 vs 64 ± 9) and BMI (26 ± 4 vs 28 ± 4) were similar between the groups. The years of disease and Hoehn and Yahr (PD+EDS median 2.5, range 2-3 vs PD-EDS median 2.0, range 1-2.5) were not statistically different, nor were levodopa dose and pergolide equivalents. There were significant differences between the Schwab on (PD+EDS 80 ± 8 vs PD-EDS 92 ± 4,p<.02) and UPDRS Motor score (29 ± 9 and 16 ± 5,p=.02). Subjective measures of sleepiness (ESS) were different between the groups (PD+EDS 14 ± 6 vs 8 ± 3.4, p=.05). The PSG findings in the PD+EDS compared to the PD-EDS group showed: higher percentage of stage 1 sleep (19.7 ± 6% vs 11 ± 6%, p=.05), increased AHI (31 ± 26 vs 1.7 ± 2, p=0.1), and a higher arousal index (40 ± 26 vs 11 ± 5.7, p=0.1). Further comparisons showed sleep efficiency (PD+EDS 80 ± 4% vs PD-EDS 69 ± 14%, p=.17) and total sleep time (PD+EDS 403 ± 52 vs PD-EDS 354 ± 71, p=.27) were not statistically different. Periodic limb movement index was not different (PD+EDS 3 ± 4.7 vs PD-EDS 4.6 ± 7.6), nor was the MWT (PD+EDS 24.9 ± 15.5 vs PD-EDS 30.1 ± 12).
Conclusions: PD patients with a mean latency of <5 minutes on the MSLT had more severe PD than non-sleepy PD. Subjective measures of sleepiness (ESS) were consistent with objective measures of sleepiness (MSLT) and sleep quality (PSG). The group with sleepiness had greater sleep fragmentation, as shown by a statistically significant higher percentage of stage 1 sleep, and a higher arousal index. The cause of the increased sleep fragmentation may be related to sleep-disordered breathing given the increased AHI in the sleepy group. Taken together, these results suggest that the increased CNS dysfunction present in the sleepy patients may contribute directly to daytime sleepiness, or indirectly by causing impaired respiratory control during sleep and associated sleep fragmentation.

0840.N

The Characteristics Of The Restless Legs Syndrome In Persons Initially Diagnosed During A Family Study

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Introduction: The restless legs syndrome (RLS) is a common sensorimotor and sleep disorder, but little is known of the characteristics of the condition in population samples. Epidemiological studies have been performed on general populations to ascertain the prevalence of RLS symptoms, but such studies have generally not validated questionnaire results to be sure individuals actually had RLS. Moreover, most such studies have contained little or no information on the characteristics of RLS responders except their positive responses to screening questions. We sought to determine whether the characteristics of individuals diagnosed with RLS by an expert in a family study would match those of patient populations previously reported.
Methods: 570 adult individuals in the families of 67 RLS probands and 28 control probands were diagnosed by an expert clinician (WAH) blind-

ed to the identity of their families or the proband diagnosis. RLS diagnosis was stratified into definite, probable, and possible RLS. For those diagnosed with RLS, symptom character, measures of severity, provocative factors, any treatment, age of onset, and persistence of the disorder were determined.
Results: 235 individuals (41.2%) were diagnosed with RLS, 154 receiving a definite (27.0%), 60 a probable (10.6%), and 21 a possible (3.7%) diagnosis. 21 of the 235 (8.9%) did not describe uncomfortable leg sensations (categorized probable), while 6 (2.6%) denied an urge to move (categorized possible). 60 (27.9%) of those with leg sensations described them as painful. 47 (21.7%) of those asked reported sitting was more likely to cause discomfort than lying down. 39 (16.7%) of the RLS-diagnosed subjects had daily symptoms, while 93 (39.7%) had symptoms more than once a week but less than daily, and 111 (47.4%) had symptoms less than once a week. Average age of onset was 33.4 (SD 18.1) years, and 92.8% of those who had ever had symptoms still had them at the time of interview. 24 (10.3%) of them reported symptoms typically beginning before 6 pm (most severe group), 105 (45.1%) in the evening, and 104 at bedtime or during the night (44.6%). Only 11.6% of those with current symptoms reported taking any medication to relieve them.
Conclusions: Family members diagnosed with RLS have similar quality of symptoms, age at onset, and persistence of symptoms as patients reported in previous series. They report, however, a lower frequency of symptoms and their symptoms are more often confined to the nighttime hours; only a minority employ any pharmacologic treatment to benefit their symptoms. It therefore appears that RLS of any degree is a chronic disorder with typical onset during youth and middle age, but that individuals with less frequent RLS are less likely to come to medical attention.

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0841.N

Restless Legs Syndrome and Serum Transferrin Receptor and Ferritin Levels in Patients with Rheumatoid Arthritis

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Introduction: Several secondary forms of restless legs syndrome (RLS) have been reported in approximately 25% of patients diagnosed with rheumatoid arthritis (RA). We performed clinical evaluations (FIT test and Actigraph monitoring) on 19 patients diagnosed with rheumatoid arthritis to determine how many may have concurrent RLS symptoms. All patients fulfilled the ACR criteria for the diagnosis of a definite or classic RA.The relationship between iron status and RLS severity was examined. Iron deficiency with or without anemia, is an important contributor to the development of RLS in patients.
Methods: Steps of protocol: 1. Questionnaires, neurological, internal and electrophysiological investigations, (SEP, ENG), familiarity. Routine laboratory tests were also performed, including peripheral blood analysis and determination of erythrocyte sedimentation rate (ESR), rheumatoid factor (RF), serum iron levels, total iron-binding capacity (TIBC), serum ferritin and serum transferrin receptor (s-TfR) levels. 2. Forced Immobilization Test (FIT) designed to quantify leg movements in wakefulness. 3. Actigraphy was used to assess leg movements both during wakefulness and sleep. This method is excellent in the diagnosis of RLS, and in the control of the efficiency of therapy in RLS and PLM. 4. Sleep log
Results: We investigated 19 patients with rheumatoid arthritis. From these 9 patients had been proved the suspicion of RLS. All patients underwent electrophysiological evaluation (EMG) and nerve conduction velocities, 15 had neuropathy of mixed types. On examining the iron status we found lower serum iron levels in all cases. The total iron binding capacity was normal in all patients. The s-TfR levels (mean ± SD, 1,905 ± 623 ìg/l) were significantly higher in all cases. The serum ferritin was lower in 11 patients, and from these 9 cases lower, than 50ìg/l. Patients with higher ferritin levels correlated to active rheumatoid arthritis symptoms. Lower ferritin levels (< 50ìg/l) correlated significantly to greater RLS severity and decreased sleep efficiency.
Conclusions: Serum TfR is a good predictive test of iron responsive anemia in patients with rheumatoid arthritis. Our study suggests that presence of reduced ferritin level does represent secondary forms of RLS.

0842.N

Treatment of Idiopathic Restless Legs Syndrome (RLS) with the D3-Agonist Pramipexole

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Introduction: Most patients with restless legs syndrome (RLS). (approximately 70-80%) studied by PSG have periodic leg movement syndrome (PLMS). The restless legs syndrome (RLS) is a condition characterised by unpleasant limb sensations occurring at rest and associated with an irresistible urge to move and a circadian character. Patients with PLMS may be asymptomatic, but because of sleep fragmentation severely affected patients may have complaints or difficulty maintaining sleep or EDS. PLMS is generally diagnosed by PSG recording. The results of beta CIT SPECT, 123 I IBZM and fMRI investigations demonstrate the hypothesis that the hypofunction of striatal D3 receptors play a major role in the physiopathology of RLS/PLMS.
Methods: 35 idiopathic RLS patients were studied before and after 12 weeks treatments administered 0.5-1 mg pramipexole/day. 26 cases was monotherapy and in nine cases was bitherapy (clonazepam 1-3mg/day). The severity of sensory and motor manifestations was assessed by 1 week of home questionnaires and actigraphy; late afternoon performed FIT test and sleep laboratory recordings (PSG).
Results: Polysomnographic data showed a significant reduction of the number of periodic leg movements (PLM) (187.4±114.3 (baseline) vs. 27.5±28.2 (12 weeks pramipexole monotherapy; p=0.002), PLM arousals (51.7±42.3 vs. 6.4±11.2; p=0.01) and PLM awakenings (13.5±8.3 vs. 1.5±2.4; p=0.001). Total sleep time was prolonged (298.5±48.6 vs. 385.3±67.5 min; p=0.01), sleep latency shortened (51,2±46.7 vs. 17.5±24.4 min; p=0.1) and sleep efficiency increased (59.2±11.3 vs. 82.3±13.7%; p=0.01).
Conclusions: Pramipexole, a D3-receptor agonist is one of the most effective agent for treatment of RLS. In the future we plan larger, controlled trials for pramipexole in patients with RLS, and investigation of polymorphism D3 receptor.

0843.N

Low-density Lipoprotein Apheresis and Restless Legs Syndrome

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Introduction: The restless legs syndrome (RLS) is characterized by a combination of unpleasant sensory symptoms of the legs with an irresistible urge to move them. Symptoms are worse at rest and in the evening or the night, and activity leads to at least temporary relief. RLS may be idiopathic, familial, or symptomatic in association with systemic diseases such as diabetes mellitus, rheumatoid arthritis, uremia, and iron deficiency. To date, there have been no reports of an association of RLS and low-density lipoprotein (LDL) apheresis, a procedure used to treat severe hypercholesterolemia, and/or hyperlipidemia itself. This study

was performed to investigate the prevalence and the etiology of RLS in hyperlipidemic patients undergoing regular LDL-apheresis treatment and to evaluate causative and symptomatic treatment options.
Methods: A clinical interview of all patients currently under treatment with LDL apheresis at the University Hospital Goettingen, Germany was performed. Patients were asked for RLS symptoms according standardized criteria, all patients with the diagnosis of an RLS filled in the RLS rating scale of the International RLS Study Group. Peripheral neuropathy was clinically excluded and by means of nerve conduction measures. Family history was defined being positive if at least one first-degree relative was affected
Results: Altogether, 25 patients undergoing LDL aphereses were included. 12 of these patients (48%) were found to have RLS. The mean score of the affected patients on the RLS severity scale was 17.6 $\pm$ 11.5. 50% of the patients with RLS had serum ferritin levels below 20mg/L as opposed to 15% of the patients without RLS. Other blood tests including urea, creatinine, folic acid, vitamin B12, and TSH did not reveal any differences. Five patients (41%) with RLS had a positive family history of the syndrome, while only one patient (8%) without RLS had a relative with RLS. Substitution of iron lead to a marked reduction of symptoms as assessed with the RLS severity scale. Therapy with levodopa also proved effective in controlling RLS symptoms but lead to a severe augmentation of symptoms in two out of three patients.
Conclusions: Our data suggest that RLS is a common condition in patients treated with LDL-apheresis due to regular elimination of iron-containing LDL-cholesterol. Substitution of iron seems to be an effective causative treatment option in this patient group. Therapy with levodopa is also effective but may lead to an augmentation of symptoms in these patients.

0844.N

Prevalence Of Restless Legs In The General Population Of Sweden
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Introduction: Restless legs syndrome is a sleep disorder characterized by disagreeable leg sensations occurring most often at sleep onset that provoke an urge to move the legs. Several factors, such as age, obesity, alcohol intake, presence of arthritic disease or obstructive sleep apnea were found associated with this disorder.
Methods: A questionnaire assessing sleeping habits, sleep symptoms and health status was developed. The survey was conducted from March to June 2001. Questionnaires were mailed to 1,700 individuals aged 18 years or older, randomly selected according to age, gender and living areas of Sweden. Questionnaires with too many missing answers or that were filled in by someone else than the addressee were rejected. Altogether, 1,209 questionnaires were correctly completed. The participation rate was 71.1%. Participants were asked if they felt discomfort, numbness, restless or pain in legs prior to falling asleep which make them move their legs. Participants answered on a frequency scale.
Results: Restless legs (RLS) occurring at least 4 nights per week were reported by 7.7% of the sample. Another 4.6% of the sample reported having restless legs 1 to 3 nights per week. The prevalence was comparable between men and women and increased with age: it was 6.6% in subjects younger than 45 years and 8.6% after 45 years of age.Difficulty initiating sleep was more frequently reported by subjects with RLS >=4 n/wk (23.7%) or 1-3n/wk (18.2%; p<.001) than subjects without RLS (4.1%). An Epworth score >=12 was more frequently observed in the group with RLS 1-3n/wk (21.4%) compared to the two other groups (RLS >=4 n/wk: 11.8%; no-RLS: 7.0%; p<.01). Daytime fatigue was twice more frequently reported in RLS subjects (60.8%) than in those without RLS (30.4%; p<.001).
Conclusions: The prevalence of RLS symptoms is high in the Swedish population. It is associated with symptoms related to different sleep disorders (narcolepsy, sleep breathing disorders) and chronic physical disease.

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0845.N

Time Course of Arousal Response During Periodic Leg Movements
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Introduction: Periodic leg movements during sleep (PLM) are frequently associated with microarousals (MA) but PLM without changes in the EEG activity or associated with phasic events in slow wave activity, such as K-complex and delta bursts, may be also detected. Despite sleep stage may influence the appearance of MA related to PLM, no data are available on how time of the night may affect the arousal response to PLM. The aim of our study was to investigate the nocturnal evolution of PLM and PLM-arousal response in order to define the factors influencing the PLM occurrence and the associated arousal response. Our rationale was that if recurrence of MA requires variations in arousal threshold and sleep propensity, we should see PLM with MA mostly in the latter part of the night and, on the other hand, a greater number of PLM without MA and with slow wave activity in the first part of the night, when the individual sleep propensity is greater. This was investigated by considering the difference in density of total PLM, PLM with and without MA and PLM with slow wave activity between sleep stages and sleep cycles. Homeostatic sleep influences were studied by spectral analysis of slow-wave activity (SWA).
Methods: The polygraphic recordings of 23 patients (mean age: 55.0 $\pm$ 2.4 yr., mean PLM index of 47$\pm$ 5.2) diagnosed as Restless Legs Syndrome (RLS (n: 11)) or primary PLM syndrome (n:12) patients, were included in the study. PLM were classified into three levels, including PLM associated with microarousal (PLM with MA), PLM not associated with microarousal (PLM without MA) and PLM associated with an arousal response in K- or delta bursts (PLM with slow wave activity). To quantify the dynamics of the SWA during NREM sleep over the course of the night, spectral analysis was performed for the first four NREM sleep cycles
Results: Overall, 60% of movements were associated with MA, 4% with slow wave activity whereas 36% were characterized by no change in EEG activity. Comparison of PLM with and without MA revealed that more PLM were associated with MA during stages 1 and 2 of NREM sleep and fewer during slow wave sleep and REM sleep (ANOVA: ($F(3,13)=7.42$, $p<0.001$).There was a trend for PLM activity to be higher at the beginning of the night, followed by a progressive decline over consecutive sleep cycles. ($F(3.13)=11.2$, $p<0.0001$), similar for all types of PLM. The decrease in the PLM index during the night was not associated with significant changes in duration for the overall PLM, as well as for PLM with and without MA and slow wave activity. The nocturnal evolution of PLM evolution paralleled the dynamic change in SWA throughout the night. The maximal rise in the number of PLM was present during the first sleep cycle when the SWA was greater. Thereafter, a progressive decline was present, for the PLM overall as well as for the PLM associated or not with MA or associated with slow wave activity, reaching the minimum at the fourth sleep cycle when the SWA was lower.
Conclusions: The results of this study firstly indicate that the PLM density clearly decreased during the night with a profile paralleling the nocturnal exponential decay of SWA. Secondly, we demonstrate that the profile of declining PLM rate was similar for PLM associated or not with MA and with slow wave activity, suggesting that the occurrence of the

PLM-related arousal response is independent of night-time changes in arousal threshold and in sleep propensity. This nocturnal trend in PLM-related arousal response may suggest the interference of three factors, sleep instability process, sleep stage effect and circadian influences, all acting on neural and biochemical mechanisms implicated in the PLM occurrence.

0846.N

Comparison Between Submental And Anterior Tibialis Phasic EMG Activity During REM Sleep In Parkinson's Disease With And Without REM Sleep Behavior Disorder

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Introduction: REM sleep behavior disorder (RBD) is frequent in patients afflicted by Parkinson's disease (PD). Patients with PD and RBD (PD-RBD) show a higher submental phasic EMG density during REM sleep compared to both patients with PD without RBD (PD-NRBD) and control subjects. However, some may suggest that EMG activity from anterior tibialis muscles could be a more sensitive measure of phasic EMG density than submental EMG activity. The aim of the present study was to compare the EMG activity from both submental and anterior tibialis in patients with PD-RBD, PD-NRBD and control subjects.
Methods: In addition to a control group of 14 healthy subjects (age: 51.1 ± 7.3 yrs), two groups of patients with PD were studied in a sleep laboratory for one night. One group included 9 patients with PSG-confirmed RBD (age: 66.6 ± 6.6 yrs, PD duration: 5.9 ± 4.9 yrs, Hoehn & Yahr stage: 1.9 ± 0.8), and the other included 15 patients without RBD (age: 53.5 ± 9.0 yrs, PD duration: 5.0 ± 3.5 yrs, Hoehn & Yahr stage: 1.5 ± 0.7). Patients were kept on their usual dopaminergic treatment. PSG recordings included EEG, EOG, submental and right and left anterior tibialis EMG. REM sleep and phasic EMG density from both submental and anterior tibialis with and without periodic leg movements during sleep (PLMS) were scored according to a method described elsewhere. PLMS were scored using a standard method. Differences were assessed by a two-way ANOVA with Group as an independent factor and Localization as repeated measure.
Results: The two groups of patients with PD did not differ either on disease duration, disease severity or medication but patients with PD-RBD were older than the subjects of the two other groups. A significant Group by Localization interaction was found after Huynh-Feldt correction ($F(4,68)=4.8$; $p<0.01$). Simple main effects revealed between-group differences for submental ($p<0.00002$) and anterior tibialis with PLMS ($p<0.03$) phasic EMG density; patients with PD-RBD having a higher submental (27%) and anterior tibialis with PLMS (13%) EMG density during REM sleep compared to patients with PD-NRBD (8% for submental versus 5% for anterior tibialis) or control subjects (9% for submental versus 3% for anterior tibialis). No between-group difference was observed for the anterior tibialis phasic EMG density without PLMS.
Conclusions: The EMG from both submental and anterior tibialis with PLMS are useful to detect excessive phasic EMG activity during REM sleep in patients with PD-RBD. However, the submental EMG seems to be a more sensitive measure than the anterior tibialis EMG.

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0847.N

Recording Periodic Leg Movements in Sleep over Two Nights in 115 Patients with Sleep Disorders: Variability and Relationship to Subjective Sleep Parameters

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Introduction: Periodic leg movements in sleep (PLMS) are a common finding in sleep laboratory investigations of patients with sleep complaints. The number of PLMS may vary from one night to the other and a higher number of PLMS and PLMS associated with arousal (PLMS-A) is supposed to result in a more disturbed sleep. However, there are no reports so far whether fluctuation of PLMS-indices in patients with sleep complaints is associated with alterations of subjective sleep measures and sleep parameters. Polysomnographic recordings of two consecutive nights were therefore evaluated in a retrospective study in order to assess the variability of PLMS and PLMS-A over two nights and to assess their relationship to subjective sleep parameters in patients with sleep disorders.
Methods: The data of 115 consecutive patients were evaluated in the study. Patients were without or on stable medication (psychiatric patients) 4 weeks prior to polysomnography. Five subgroups of patients were separately analysed: patients with restless legs syndrome (n = 42), with insomnia due to a psychiatric disorder (n = 32), with primary insomnia (n = 23), with sleep apnea syndrome (n = 13) and patients with narcolepsy or idiopathic hypersomnia (group HYP, n = 5). PLMS- and PLMS-A-indices were calculated as the number of PLMS and number of PLMS-A per hour of total sleep time.
Results: No systematic differences of PLMS- and PLMS-A-indices were found comparing the first and the second night i. e. no evidence indicating a first-night effect on PLMS and PLMS-A. Individually, however, a large variability of PLMS- and PLMS-A-indices existed over the nights. The highest night-to-night differences of PLMS measures occurred in the group of RLS patients showing a mean difference of PLMS-indices with 16.4/h (min.: 0/h - max.: 61.3/h) and a mean difference of PLMS-A-indices with 6.3/h (min.: 0/h - max.: 30.4/h). Moreover, RLS patients´ percieved sleep quality as assessed by the questionnaire SF-A (subscore "sleep quality") correlated with the PLMS-index and with the PLMS-A-index in the first night (r: -0,486 and r: -0,315; $p>0.01$ and $p> 0.05$, respectively) and albeit not significantly also in the second night. Subjective sleep quality of patients with other sleep disorders did not show such a correlation. PLMS- and PLMS-A-indices were not correlated with sleep efficiency or with the score of the Pittsburgh Sleep Quality Inventory, another measure of subjective sleep quality, in any of the groups.
Conclusions: The high variability of PLMS- and PLMS-A-indices should be taken into account if polysomnography is performed in support of clinical diagnosis especially in patients with a restless legs syndrome. Assessing the patient´s percieved sleep quality by the SF-A may give further information on the frequency of PLMS in RLS patients.

0848.N

Racial Differences in the Prevalence of Periodic Limb Movement Disorder

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Introduction: Previous population-based studies of Periodic Limb Movement Disorder (PLMD) have found a wide range of prevalence estimates for this disorder. The ethnic and racial variability across these studies, suggests that racial differences may be an important factor related to the heterogeneity of prevalence estimates. The present study employed overnight polysomnography to compare the prevalence of

PLMD in African American, Caucasian and other racial groups.
Methods: The participants were randomly selected from the population using random digit dialing techniques. The response rate for the random digit dialing phone interview was 70%. A subset of individuals responding to the phone questionnaire, (N = 419) were evaluated for periodic limb movements (PLM) in the sleep laboratory during an 8.5-hour nocturnal polysomnogram. Periodic limb movements were scored according to standard criteria. The prevalence of individuals with PLM index greater than or equal to 10 was determined in African Americans and non-African Americans.
Results: The group consisted of 141 African Americans, and 278 individuals of other races (90% Caucasian). There was a 4.1% prevalence of PLMD for African Americans, and 11.7% prevalence in non-African Americans, (Chi-Square = 5.51, p = .02). African Americans had a significantly lower PLM index compared to non-African-Americans t(417) = 2.12, p =.03. The above analyses remained significant even after controlling for differences in body mass index, age, gender, socio-economic status, respiratory disturbance index, and additional demographic variables.
Conclusions: This is the first study that has demonstrated racial differences in the prevalence of PLMD. In this population-based sample African Americans had a more than two fold lower prevalence of PLMD in comparison to non-African Americans. The present findings may explain the wide variation in previous population-based estimates of PLMD. Although reasons for this finding are unknown, differences in a variety of demographic variables did not account for the present findings. Future studies of racial differences in PLMD are warranted and would benefit from the assessment of additional sleep related, physiological, and behavioral variables.

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0849.N

Prevalence Of Restless Legs Symptoms In An Elderly American Veteran Cohort

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Introduction: Population surveys have indicated that symptoms consistent with the Restless Legs Syndrome (RLS) are common in the general population. Symptoms are increasingly common in older individuals, at least through the first six decades, and more common in females than in males. Most such studies have examined the prevalence in adults of mixed ages. In the current work, we have examined a group of elderly caucasian World War II veterans (aged 74 to 84) to determine how common symptoms would be in men within this age group.
Methods: Veterans participating in an ongoing longitudinal study were sent questionnaires relative to RLS symptoms. RLS symptoms were probed by asking about urge to move and leg discomfort as well as the state (rest) and time of day (night) when symptoms were most severe and the frequency of symptoms. In addition, they were asked whether they had been diagnosed with diabetes, were current smokers, or had been diagnosed with RLS.
Results: 1161 completed questionnaires were returned. Almost half the subjects reported leg symptoms, but only 297 (25.6%) reported leg discomfort and an urge to move present at rest and worst at night (RLS responders). 34 subjects (2.9%) reported having been diagnosed with RLS. 280 RLS responders reported a frequency of symptoms: 17.1% had daily symptoms, 51.4% had symptoms at least once a week, but not daily, and 31.4% had symptoms less than once a week. Those reporting a diagnosis of diabetes (N=176) and current smokers (N=88) both had an elevated percentage of RLS responders (29.5, n.s. and 37.4%, p<.01, Fisher exact test, respectively).
Conclusions: This study indicates a very high frequency of RLS symptoms in a cohort of elderly American caucasian males. Only a minority have been diagnosed with RLS, although the overall rate of diagnosis is higher than reported from other groups. Consistent with the Hopkins family study (Washburn et al, companion abstract), the majority of the RLS responders show a lower frequency of symptoms than typical patients. Both a diagnosis of diabetes and current smoking was previously reported to be associated with RLS in a population study from Kentucky (Phillips et al, 2000). In future work, a large subset of the subjects will be administered a validated telephone diagnostic interview (Hening et al., 2001) to determine the degree to which endorsing RLS symptoms indicates a diagnosis of RLS.

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0850.N

Restless Legs Syndrome Could Be Overestimated By Questionnaire Based On Standard Diagnostic Criteria

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Introduction: Four core symptoms of restless legs syndrome (RLS) are easy to be understood by full-blown RLS patients, but some insomniac patients due to other causes who stay restlessly in bed at night with anxiety may make a false positive response. On the contrary, people with very mild and/or infrequent symptoms may fail to respond. This should be taken into consideration when we perform epidemiological study by only using questionnaire, but it has not been reported in details in which situation the present criteria brought false positive and negative responses.
Methods: Consecutive 270 people (mean age 53.3 } 13.2, 204 men and 66 women) who came to sleep check-up clinic in our center between Nov 2001-Nov 2002 had a comprehensive health and sleep questionnaire before seeing sleep specialists. The questionnaire included questions asking major RLS symptoms (1-unpleasant sensation, 2-motor restlessness, 3-motor relief, 4-nocturnal worsening) and other supportive clinical features (5-worsening during rest or inactive periods, 6-difficulty initiating sleep). Those who responded positive on all 1-4 were judged as questionnaire-positive (QP). As some patients with mild RLS were expected to be bothered only when they must be immobile, those who were positive on 1, 2, 3, and 5 were also considered QP. On consultation, we checked the questionnaire of all cases, and examined 105 individuals who had been positive at least either on 1 or 2 with special emphasis on ruling in and out the diagnosis of RLS.
Results: There were 35 QP (13.0%) out of 270, but 20 of them revealed to be false positive after the consultation. False positives were attributed to dysesthesia and/or pain in the legs due to neuropathy, spondylosis, or possible orthopedic disorders (6 cases), Binbo-Yusuri (involuntary jiggling of the legs at rest)(5), Komura-gaeri (nocturnal muscle cramps) (3), psychophysiological insomnia (2), mild cognitive impairment (1), temporal dysesthesia due to compression(1), general irritability (1), itching in the legs (1), irritable sensation in the trunk (1). The total number of RLS patients including one false negative case whose symptoms occurred very infrequently was 16 (5.9%) out of 270, but their symptoms were mostly mild, and only two (0.7%) complained of difficulty initiating sleep, requiring further referral for drug treatment.
Conclusions: To the people who have no notion of RLS, individual presentation of four symptoms can cause confusion, especially in the elderly, who are more likely to suffer from other neurological and orthopedic disorders. Explanatory questions asking whether one fs symptoms are the same as Binbo-Yusuri or Komura-gaeri would be helpful to decrease false positives at least among the Japanese.

0851.N

Patients with Restless Legs Syndrome (RLS) Show Reduced Brain Thalamic Creatine On Magnetic Resonance Spectroscopy (MRS)

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Introduction: Thalamic activation related to occurrence of RLS symptoms documented on a prior functional MRI study suggested some involvement of the thalamus in RLS pathology. Proton MR spectroscopy (MRS) can be used to evaluate thalamic metabolism. This study compares controls and primary RLS patients for differences in thalamic metabolic levels on MRS.
Methods: Water suppressed single voxel proton spectra from the thalamus were recorded during the daytime on a 1.5 T GE scanner using the PROBE-P (PRESS) sequence short echo time (35 msec). Peak areas of Choline (Cho), Creatine (Cr) , and N-acetyl aspartate (NAA) were determined. Metabolite concentrations were estimated using water as an internal reference. All measurements were made blinded to the subejct status and diagnosis. Primary RLS patients were off their medications for RLS for at least 14 days prior to the study. Age matched controls had no RLS symptoms, no significant periodic leg movements (< 15 /hr) and no first degree relatives with RLS. Lumbar CSF samples were obtained at night within two days of the MRS and analyzed for homovanillic acid (HVA), tetrahydrobiopterin (BH4) and neopterin (NEOP).
Results: 32 RLS patients (avr ±sd age: 61.0 ± 9.1 years) did not differ significantly from 13 controls (age 61.1 ± 11.6 years) for age or gender distribution. RLS patients compared to controls showed significantly reduced Cr (avr ± sd: 7.1 ± 1.6 vs. 8.3 ± 1.2 mmol/kg, $p<0.03$), but no-significant difference in Chol (2.0 ± 0.62 vs. 2.3 ± 0.35, $p>0.1$) and NAA (12.8 ± 1.7 vs. 12.1 ± 2.3 $p>0.1$). The ratio of NAA/Cr was also significantly ($p<0.02$) increased for RLS compared to controls while the ratio of NAA/Chol did not significantly ($p=0.09$) differ between the groups . For RLS patients Cr correlated significantly with CSF BH4 ($r=0.45$, $p=0.03$) but not with HVA or NEOP.
Conclusions: For RLS patients thalamic creatine was reduced while choline was somewhat but not significantly reduced. NAA, generally believed to be primarily of neuronal and axonal origin, was normal for RLS. Lower creatine levels may indicate a reduction in the high energy phosphate store and. the correlation with lower BH4 indicates a possible relation to dopaminergic metabolism.. The creatine decrease may be secondary to the thalamic activity for symptomatic RLS patients, however the scans were done at a time of day when patients had few symptoms; alternatively, it may indicate some metabolic abnormality reducing these energy stores. Replication and MRS evaluation of other brain regions and comparison with other studies is needed. Overall the results indicate an interesting, previously unknown, possible CNS metabolic abnormality in RLS patients.

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0852.N

Vigilance Troubles in Parkinson's Disease, Compared with a Controlled Population

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Introduction: Increase of interest for daytime sleepiness in Parkinson's disease (PD) was reported since the description of sleep attacks by Frucht (1999). Sleep attacks are described as « periods of sudden, irresistible and overwhelming sleepiness without awareness of falling asleep ». The frequency of vigilance troubles in PD varies between the studies already reported. The aim of the present study is to analyze the prevalence of daytime sleepiness and sleep attacks in PD and to assess the eventual relationships between these vigilance troubles and the quality of sleep as well as the taking of dopaminergic drugs.
Methods: Patients with idiopathic PD according to the criteria of UKPDSBB were included in our movement disorders center. We administrated a questionnaire to every subject to gather the following informations: demographic data, type and doses of antiparkinsonian treatments, subjective sleep pattern, excessive daytime sleepiness and sleep attacks, the Epworth scale sleepiness (ESS) and the Nottingham scale. After that, each patient underwent a telephone interview to elicit information on their daytime sleepiness and on their eventual sleep attacks. All of these results were compared with those of a controlled population.
Results: 160 parkinsonian patients and 120 controls were included. The mean of age was 65.7 $\pm$ 9.3 in PD and 63.6 $\pm$ 8.3 for control patients. Mean ESS score was significantly higher in PD compared with controls (9.1 $\pm$ 5.7 and 7.3 $\pm$ 4.5 respectively) ($p<0.01$). More parkinsonian patients have an ESS score; 10 (45.6% compared with 25% in control population; $p<0.01$). Fourteen PD patients experienced sleep attacks and none in controlled population ($p<0.01$). Furthermore, 30% of PD patients complained about increasing of excessive daytime sleepiness after taking dopaminergic drugs. No significant relationship was observed between excessive daytime sleepiness and quality of sleep or medications. Sleep attacks occurrence was significantly higher when the ESS score was elevated, when the dopaminergic agonist doses increased and when patients took ropinirole. Finally, an increase of excessive daytime sleepiness was observed after taking dopaminergic drugs, especially ropinirole. The occurrence of this secondary effect was significantly related with a short duration of PD.
Conclusions: Vigilance troubles were frequently observed in PD. Sleep attacks were specific to PD since they were not observed in control population. Significant relationships were observed between these vigilance troubles and medications. It is therefore important to talk about the possibility of vigilance troubles after taking dopaminergic drugs in PD.

0853.N

Long-term Safety And Efficacy Of Cabergoline In The Treatment Of Idiopathic Restless Legs Syndrome: Results From A Six Months Clinical Trial

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Introduction: Dopamine agonists (DA) are effective treatment options for Restless Legs Syndrome (RLS). Efficacy of DAs has been shown in previous studies, however, large-scale long-term trials on tolerability and safety are still scant. Data will be presented from a long-term, open-label, multi-center safety trial on cabergoline in the treatment of patients with idiopathic RLS.
Methods: Cabergoline was up-titrated over four weeks to an individually optimized dose. Total treatment duration was 26 weeks. Drug safety was assessed by documenting adverse events (AEs), and efficacy data were acquired using the RLS-6 and the IRLSSG rating scales.
Results: Of 318 screened patients, 302 patients were randomized and treated and 248 patients (82.1%) completed the study after 26 weeks of therapy. All patients fulfilled the diagnostic RLS criteria of the International Restless Legs Study Group; of these, 27% were male and 73% female patients with an age of 61 ± 11 years; they had a history of idiopathic RLS for 14 years, on average. Median treatment duration was 181 days; the median dose of cabergoline was 1.5 mg/day, in 37% of all patients, individual dose was adjusted after the end of the titration period, on average by 0.4 $\pm$ 0.7 mg/day. Severity rating of RLS-symptoms at night (primary endpoint) improved from 6.4 ± 2.9 at baseline to 1.7 ± 2.5 at the study end in the RLS-6 global scale ranging from 0 (no symptoms) to 10 (maximum severity). Secondary endpoints: ratings of RLS-severity at bedtime (baseline: 6.1 ± 3.1; last visit: 1.5 ± 2.3) and during the day (baseline: 3.8 ± 2.8; last visit: 1.2 ± 1.8) as well as the total score

of the IRLSSG Rating Scale (baseline: 26.8 ± 5.9; last visit: 9.7 ± 9.0) improved during therapy. Finally, satisfaction with sleep was increased (baseline: 2.4 ± 1.5, final visit: 5.0 ± 1.8, 7-point scales) during treatment. All these beneficial changes were statistically significant ($p < .0001$, signed rank test), and showed clinically meaningful results both with regard to effect sizes for pre-post changes greater than 1.0 and with regard to no or mild symptoms at study end in the majority of patients.Of all patients, 48.3% suffered from at least one adverse event (AE) which according to the investigator was possibly or probably related to study treatment. Most frequently, gastrointestinal problems like nausea (16.6% of all patients) or gastric complaints (3.6%), symptoms of the central nervous system like dizziness (7.0%) or headache (4.6%) were reported. No patient developed clinically definite augmentation, however, in 9 patients (3.0%), at least one criterion for augmentation was noted. Five percent of all patients were non-responders.
Conclusions: Long-term treatment with cabergoline is efficacious both for night-time and day-time symptoms and safe in RLS patients.

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0854.N

Rotigotine CDS (Constant Delivery System) in the Treatment of Moderate to Advanced Stages of Restless Legs Syndrome - A Double-Blind Placebo-Controlled Pilot Study

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Introduction: Dopaminergic drugs such as levodopa or dopamine agonists are currently considered the first-line treatment for restless-legs-syndrome (RLS). However, treatment with levodopa may cause deterioration of symptoms (i.e. augmentation or time-shifting) in a substantial part of RLS patients. Dopamine agonists (DA) in particular long-acting substances are preferred in moderate to severe RLS but even under DAs augmentation occurs. Different trials suggest an inverse correlation between elimination half-life and incidence of augmentation. We therefore investigated the efficacy and safety of a novel transdermal patch continuously releasing the dopamine agonist rotigotine (RTG) in moderate to advanced stages of RLS.
Methods: We performed a double-blind, 4 arm, parallel group, randomised, placebo-controlled pilot study in 9 German centers. Main inclusion criterion was the diagnosis of idiopathic moderate to advanced RLS defined by a score of higher than or equal to 10 in the IRLSSG severity scale (maximum 40 pts), when untreated, and the presence of day-time symptoms. After a wash-out phase of 7±4 days, patients received 1.125 mg RTG/die, 2.25 mg RTG/die, 4.5 mg RTG/die, or placebo for 7±1 days. Primary endpoint was the change of the IRLSSG severity scale from baseline to the end of treatment.
Results: 63 out of 68 enrolled patients were randomized and used for statistical evaluation. A dose-dependent reduction in RLS severity was observed in all treatment arms resulting in a net benefit of 1.3 (1.125 mg RTG/die; p=0.38), 3.6 (2.25 mg RTG/die; p=0.09), and 6.3 points on the IRLSSG severity scale (4.5 mg RTG/die; p=0.04) as compared to the placebo arm. Obvious differences regarding the topical tolerability of the patch or its systemic side effects were not found between active and placebo patches.
Conclusions: This study suggests a clear clinical efficacy of rotigotine for the treatment of moderate to advanced RLS. Since this investigation was designed as a pilot study, its results are not yet sufficiently powered and will be confirmed by subsequent studies.

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0855.N

Effects of L-DOPA on Dim Light Melatonin Onset in Patients with Restless Legs Syndrome

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Fundacion Jimenez Diaz

Introduction: A dopaminergic dysfunction has been postulated to play a central role in the pathogenesis of RLS, a disorder characterized by a marked circadian pattern of symptoms. Dopaminergic medication may exert chronobiotic effects, as L-DOPA causes a phase advance in the circadian rhythms of body temperature and plasma melatonin in Parkinson´s disease. The objective of this study was to investigate the effects of treatment with L-DOPA on Dim Light Melatonin Onset (DLMO) in RLS patients.
Methods: 8 treatment naive patients diagnosed with Restless Legs Syndrome according to the criteria of the IRLSSG were included in an open study on chronobiotic effects of L-DOPA. Patients underwent the DLMO detection test, and remained awake and quiet in a semi-dark room (<20 lux) between 5PM and 3AM, while salivary samples for determination of melatonin were taken hourly. DLMO was defined as the time at which a salivary concentration of 10 pg/ml was reached. The procedure was repeated following a 3 week treatment period with 400 mg L-DOPA (100 carbiDOPA) administered daily at 8PM. Severity of RLS symptoms was evaluated by means of the International Restless Legs Syndrome Study Group (IRLSSG) rating scale. Patients were also examined clinically for augmentation and classified as AUG-RLS or N-AUG-RLS. In addition, 4 additional patients underwent under randomized, double-blind, cross-over conditions a three week treatment with L-DOPA and placebo. DLMOs were determined at the end of each treatment condition.
Results: The mean (SD) IRLSSG-rating scale total score improved during treatment from 26.3(5.4) points to 11.6(2.1) ($p<0.01$). Four patients were Aug-RLS. Treatment with L-DOPA caused a decrease in sleep latency and periodic limb movements, as well as an increase in total sleep time and sleep efficiency ($p<0.05$). An anticipation of the mean time of onset of RLS symptoms (23.0 vs. 20.5 PM, $p<0.05$) and DLMO (22 vs. 19.7PM) was observed on the entire group. Aug-RLS showed a greater phase advance than N-Aug-RLS (170 min + 32 vs. 100+29). Similarly, preliminary results in the double-blind study showed a mean DLMO time of 22.7 under placebo and 19.0 under L-DOPA, with a mean anticipation of DLMO of 165 min (27).
Conclusions: Our results suggest a phase advance of DLMO following treatment with L-DOPA, which was most pronounced in AUG-RLS. Furthermore, chronobiotic mechanisms seem to be, at least in part, responsible for the symptoms of augmentation. These results are preliminary and require confirmation during long-term treatment.

0856.N

COMT Polymorphism-Associated Modulation of Daytime Sleepiness in Parkinson´s Disease

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Introduction: Daytime sleepiness is an intrinsic part of Parkinson´s disease (PD) and may be aggravated by dopaminergic therapies. COMT polymorphism affects disease severity and clinical manifestations of narcolepsy (Dauvilliers Y 2001) The COMT polymorphism shows two different alleles: a high (H) and a low (L) activity allele. In this study we investigated if a relationship exists between catechol-O-methyltransferase (COMT) polymorphism and daytime sleepiness in PD.
Methods: All nondemented patients with idiopathic PD who had been

part of a previous study of D4 receptor polymorphisms in 1997 (Kronenberg M 1999) were elegible to participate in this study, which included evaluation of daytime sleepiness (Epworth sleepiness Score) and COMT genotyping. From the original sample of 113 patients, 46 were available for COMT genotyping and ESS assessment. Twenty-two met exclusion criteria (dementia n = 20, serious medical comorbidity which might affect daytime sleepiness n = 2). Fourty-three were not available (n = 31 had died, 8 were lost to follow up and 4 refused)

Results: Fourty-six patients were included (27m, 19 f, 68.4 ± 9.9 years, symptomatic disease duration 12.2 ± 5.2 years, Hoehn and Yahr stage 2.6 ± 0.8 in On (mean ± SD). Out of the 46, 13 had LL genotype, 22 HL and 11 HH. ESS scores were 9.5 ± 4.8 in LL, 8.5 ± 4.7 in HL, and 6.8 ± 3.1 in HH (mean ± sd) (n.s.). LL and LH were grouped together assuming an autosomal dominant trait. ESS was 11 or more in 40% of the LL+LH group, compared to 9.1% of the HH group (p=0.039). The levodopa or dopamine agonist doses and the type of agonist did not differ between the combined LL+LH group versus the HH group.

Conclusions: Daytime sleepiness was more severe in PD patients carrying the COMT low activity allele, suggesting that COMT modulates the severity of DS and/or the degree of DS as a side effect of levodopa. Based on these preliminary data from a small group, a dominant effect of the L allele seems possible.

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0857.N

Gender differences in Symptoms of Restless Legs Syndrome

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Introduction: While studies on the prevalence of restless legs syndrome (RLS) in various populations indicate that the percentage of men and women affected is similar, very few have looked at specific differences between the two genders. Men and women presumably have differing life events including known initiators of restless legs, such as pregnancy, and thus may have differing presenting characteristics.

Methods: We report on a questionnaire completed by 158 patients (58 male and 100 female) with restless legs syndrome characterizing demographic information, presentation symptoms and family history. All patients satisfied the four diagnostic criteria set out by the IRLSSG for the diagnosis of restless legs.

Results: The mean age of the respondents at the time of completing the questionnaires was not significantly different at 49.8 (±14) years for males and 48.7 (±16) years for the female subjects. The age of onset of RLS was the same for both genders at 31.4 (±15) for males and 29.9 (±16) years for females. The majority of subjects were early onset RLS sufferers.None of the symptoms examined indicated any significant differences between the genders in that 40% of males and 45% of female subjects had bed partners who complained of regular kicking (presumably periodic limb movements) during the night. This figure excluded subjects who indicated symptoms indicating a high suspicion of sleep disordered breathing (SDB). Involuntary leg movements during the day were experienced by 67% of male and 75% of female subjects. Of the two most prominent sleep disorders associated with RLS, 64% of males and 74% of females had difficulty falling asleep at night and 74% of males and 80% of females woke regularly during the night. The data for the Epworth Sleepiness Scale (excluding those subjects likely to have SDB) was similarly not significantly different with scores of 9.3 for males and 7.96 for females.A non-significant difference was found in the knowledge of a positive family history between the genders (54% males and 69% females) but female subjects were significantly more likely to have affected female relatives. Mothers were affected in 35% of female sufferers against 19% in males and 22% of women had affected daughters versus 9% of daughters in male sufferers.

Conclusions: There are very few significant differences between male and female subjects with restless legs syndrome. Those differences seen in the family history information may be due to better communication about the symptoms among the female gender within families.

0858.N

Restless Legs Syndrome: The Efficacy Of Ropinirole In The Treatment Of RLS Patients Suffering From Periodic Leg Movements Of Sleep

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Introduction: Approximately 90% of restless legs syndrome (RLS) patients experience periodic leg movements of sleep (PLMS), which are repetitive stereotypic movements that affect one or both legs and may be associated with arousal or awakening. These movements disrupt sleep, contributing significantly to the morbidity of RLS. They also represent the primary motor symptoms of the syndrome. This study evaluated the efficacy, safety and tolerability of ropinirole, a dopamine agonist, versus placebo in the treatment of primary RLS patients suffering from PLMS (protocol number 101468/191).

Methods: Patients aged >= 18 years diagnosed with primary RLS who had a PLMS per hour index (PLMSI) of >= 5 at baseline were randomized to ropinirole or placebo (1:1) for a 12-week double-blind study. Patients receiving medication for RLS or sleep disorders prior to the study entered a 7-day washout period. During the first 7 weeks of the study, medication was titrated upwards based on RLS symptoms through predetermined dose levels to each patient's efficacious dose (range: 0.25-4.0mg/day). Dosages remained stable for at least the last 4 weeks of the study. Treatment was administered once daily 1–3 hours before bedtime. Nocturnal polysomnographic recordings of leg movements were made at baseline and at Weeks 6 and 12 and were used to calculate the PLMSI and the PLMS with arousal per hour of sleep (PLMSA/hr). The primary endpoint was the mean change in the PLMSI from baseline to Week 12. A key secondary endpoint was the mean change from baseline to Week 12 in the PLMSA/hr.

Results: A total of 87.5% (28/32) of the ropinirole and 81.8% (27/33) of the placebo group completed the study. The mean daily dose of ropinirole at Week 12 was 1.8mg (SD=1.10). The adjusted mean changes from baseline to Week 12 in the PLMSI and PLMSA/hr of the ropinirole group were significantly better than those in the placebo group (PLMSI: ropinirole -32.94, placebo -5.71, p<0.0001; PLMSA/hr: ropinirole -3.28, placebo 1.05, p=0.0096). Only one patient in the study (ropinirole group) withdrew because of an adverse event.

Conclusions: Ropinirole, in doses up to 4mg per day, is an effective treatment for PLMS in patients with primary RLS. Ropinirole also significantly reduces the number of PLMS causing arousal. Treatment is well tolerated.

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0859.N

Night-to-Night Variability of Periodic Leg Movements in a Community Population

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Introduction: Studies have shown significant night-to-night variability

in periodic leg movement index (PLMI) recorded overnight in community resident seniors. The aim of this study was to describe the night-to-night variability in PLMI in a community sample with a wider age range.
Methods: Unrelated volunteers aged 20 to 70 years were screened to exclude reported sleep problems and overnight oxygen desaturation index ≥ 5 per hour. Included subjects underwent a home study of bilateral leg movements for 3 consecutive nights using actigraphy. Data from the two legs were combined electronically and scored for PLM defined as: (i) movement length of 2-8 seconds, (ii) inter-movement interval of 8-90 seconds, and (iii) at least 4 consecutive movements, and PLMI was calculated for each night. The PLMI's were transformed to normal distributions and within subject, between night variation was assessed using repeated measures analysis of variance. The PLMI's for each subject for each night were also grouped into PLM present (PLMI ≥ 5) or PLM absent (PLMI < 5), and the number of subjects in each group was compared between nights using McNemar tests.
Results: 83 volunteers (41 males) aged 20.4 to 70.5 (median 46.1) years completed the study. PLMIs ranged between 0 and 61.9 movements / hour (median 3.4). The largest difference in PLMI between nights for any one volunteer was 29.4, however, overall within subject PLMI was not different across the 3 nights ($p = 0.192$). Twenty-three subjects fell into a different PLMI group between night 1 and night 2 and/or night 3. PLM was absent during night 1 but present during at least 1 of the second 2 nights in 14 subjects. The highest PLMI on subsequent nights in someone who had a PLMI < 5 on night 1 was 11.7. The lowest recorded PLMI on subsequent nights in someone who had a PLMI ≥ 5 on night 1 was 0.5. There was no statistically significant difference in distribution between groups between the 3 nights ($p > 0.05$).
Conclusions: This assessment has shown that there can be significant variability within individuals in PLMI across three nights. Up to 17% of patients with a PLMI ≥ 5 on nights 2 and/or 3 would have been missed on a single night study, which could have important clinical implications. The sample as a whole did not show a within subject statistically significant difference confirming that there is no order effect with PLM measured by actigraphy in the home.

0860.N

Severity Rating Of Restless Legs Syndrome: Review Of Ten Years Experience With The RLS-6 Scales In Clinical Trials

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Introduction: The RLS-6 scales (formerly RLS severity rating scales) have been used as efficacy endpoints in the majority of German double-blind and open-label trials with dopaminergic drugs for the treatment of RLS. Experiences with the RLS-6 scales in clinical trials with RLS patients are reviewed giving special emphasis to their validity, on sensitivity for change as well as on sensitivity for treatment differences.
Methods: The RLS-6 scales in its final version are six global rating scales using 11 categories from 0 = "no symptoms" to 10 = "maximum" severity. With four scales, severity of RLS "at bedtime", "during the night", "during daytime when at rest", and "during daytime when engaged in activities" is to be assessed by RLS patients. A further item requests the patients to evaluate their "satisfaction with sleep", and the remaining item asks for severity of "daytime tiredness / sleepiness". No total or sub-scale scores are intended but all six scales are evaluated separately.
Results: Psychometric evaluation was performed with the baseline data (301 untreated patients) of a large-scale open-label cabergoline study. Correlations within the RLS-6 severity and sleep quality items were r=0.5 on average and ranged between r=0.4 (severity during the day vs. all other items) and r=0.6 (severity during night vs. at bedtime / sleep quality), it was between r=.25 and r=.40 for the daytime tiredness item. Correlations to the IRLS severity scale were of comparable size (e.g. severity at night: r=.66, quality of sleep: r=.55). Only the items severity at night, at bedtime (both r=0.5) and sleep quality (r=0.6) correlated significantly with polysomnographic (PLM/h, sleep efficiency) and actimetric (PLM/h) data in a levodopa/benserazide study (n=32).Effect sizes for changes between baseline and endpoint after 6 months cabergoline therapy (median dose: 1.5 mg / day) were 1.61 for severity at night, 1.55 for severity at bedtime, 1.38 for sleep quality, and 1.0 for severity during the day indicating high sensitivity of the most relevant RLS-6 items for change. These scales were also sensitive ($p<.05$) for treatment-placebo differences in two levodopa trials, one pergolide study, and one rotigotine CDS trial. Largest effect sizes were observed for severity at night, however, daytime severity was most suitable to differentiate levodopa/benserazide with slight deterioration from the dopamin agonists with clear improvement of RLS daytime symptoms.
Conclusions: The RLS-6 scales are qualified to identify changes over time and are sensitive for differences between active medications and placebo in clinical studies with RLS patients. They allow to describe different profiles of dopaminergic drugs on night- and daytime symptoms and on quality of sleep. In addition to the IRLS severity scale which also reflects quality of life, the RLS-6 scales may point to special qualities of treatments like influence on daytime symptoms.

0861.N

Spinal Cord Injury as a Factor for the Movements of Paws in Rats During the Sleep

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Introduction: The origin of the Periodic Leg Movement (PLM) pattern has not established yet. The occurrence in individuals with spinal cord injury (SCI) indicates that spinal mechanism may be involved.
Methods: Five pairs of bipolar electrodes (2 ECoG, 1 cervical EMG and 2 EMG rear paws) were implanted in 11 Wistar male rats (age 3 months). After baseline recording (24h), the animals were submitted to SCI (level T9). Then, 24 h after SCI, the sleep recording was performed for 7 consecutive days and the rats were filmed everyday at the same time as sleep was recorded. After the last day of the sleep recording, the animals were sacrificed and the spinal cords removed for histological analysis.
Results: Ten of the 11 rats turn to show movements of paws of extension and flexion during the sleep after SCI. The histopathologic analysis, inferred that 4 different rates of extension of the medullary lesion was classified in this way: Group I- parcial lesion of the dorsal column; Group II – total lesion of the dorsal column; Group III- lesion hemi–medullary and Group IV- total lesion of the spinal cord. Two rats showed lesion in Group I, three rats in Group II, three rats in Group III and three in Group IV. The distinct groups of lesion do not influence the appearance of the movements of the paws during the sleep.
Conclusions: Our results suggest that the extension of the SCI in the rats did not influence the appearance of the movements of paws during the sleep, corroborating for one possible function of the spinal cord in the generation of PLM in SCI individuals.

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0862.N

Opioids Protect Against Substantia Nigra Cell Degeneration Under Conditions of Iron Deprivation: A Possible Model for Restless Legs Syndrome

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Introduction: Restless legs syndrome (RLS) presents as leg discomfort that creates an urge to move and movement can relieve the discomfort. The symptoms are worse at night and this disturbs the patient's sleep. Current clinical treatments include dopamine agonists, opioids and other agents which are quite effective, although our understanding as to the mechanism of this disease is very limited. The dopaminergic and endogenous opioid systems have been implicated in the pathogenesis of RLS as has iron deficiency. The major cells in the substantia nigra are dopaminergic and cell cultures of these cells were chosen to create an iron deficiency model of RLS. We then determined the impact of the endogenous opioids on this model.
Methods: Three groups of substantia nigra cells were observed under conditions of cell culture from Sprague-Dawley rats: a). those exposed to the delta opioid peptide [D-Ala2, D-Leu5]Enkephalin (DADLE) at dosages of 1 μM, 10 μM or 100 μM; b). those exposed first to similar doses of DADLE followed 2 days later by exposure to 10 μM of deferoxamine which binds to iron and causes iron deficiency of the cells; c). those exposed to 0.1 μM, 1 μM, 10 μM or 100 μM of deferoxamine alone; and d). a control group exposed to neither DADLE nor deferoxamine. The quantity of cells was recorded for analysis. Each experiement was repeated at least 7 times. Student t-test and ANOVA with a $p < 0.05$ were used to determine statistical significance.
Results: The numbers of cells were significantly reduced at both 10 μM and 100 μM deferoxamine after 7 days and 4 days respectively ($p < 0.01$ for both concentrations compared to control). Over all, deferoxamine causes substantia nigra cell death in a dosage dependent manner. We started the second set of experiments to determine if DADLE is able to rescue some cell death caused by deferoxamine. The following DADLE concentration were tested: 0 μM (control), 1 μM, 10 μM and 100 μM with 10 μM of deferoxamine as the insultant to the cells. DADLE alone (up to 100 μM) did not cause significant cell growth compared to the control ($p > 0.05$). However, DADLE at both 10 μM and 100 μM significantly delayed cell death by 10 μM deferoxamine compared to control ($p < 0.05$). DADLE delayed cell death caused by iron deprivation in a dosage dependent manner.
Conclusions: This study provided evidence that (1) iron deficiency causes damage and cell death of the substantia nigra cells, and (2) that DADLE protects substantia nigra cell damage induced by iron deficiency. Further experiemnts are necessary to determine if this mechanism is specific to dopamine cells or glial cells. Iron deficiency may promote the symptoms of RLS by damaging dopaminergic neurons. An intact endogenous opiate system may be necessary to protect against the symptoms of RLS.

0863.N

Sleep Stages and Oscillatory Cortical Changes During The Periodic Limb Movement

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Introduction: Periodic limb movements (PLM) is a frequent syndrome associated with sleep disorders. The brainstem, the spinal cord and the peripheral nervous system may be implicated in the pathogenesis. The cortical influence has not been confirmed.
Methods: The goal of our study was to probe a cortical change during the PLM, and the relationship with the sleep stage. We focused the study on the analysis of the changes in frequency on the EEG around the PLM.We selected polisomnographic recordings of six patients diagnosed of PLM. We analysed off-line the cortical activity after selecting five-seconds segments having the middle point in the beginning of each limb movement (LM) in non-REM sleep. In each patient were analysed at least 50 LM in slow (stage 3-4) and non-slow sleep (stage 1-2). Phase and non-phase locked-to-PLM changes in the beta and gamma band were determined by means of Gabor time-frequency transforms.
Results: No cortical changes were noted preceding the PLM. After the movement we found an increase in the beta range. This activity was very evident in the stage 1-2, and lighter although present, in stage 3-4. The topography of this activity was different from the location of the alpha rhythm, mainly central and not occipital.

0864.N

Prevalence of Restless Legs Syndrome and it's Association with Quality of Life after Kidney Transplantation

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Introduction: A high prevalence of sleep disorders have been reported in patients on maintenance dialysis. Sleep disorders may impair quality of life (QoL), subjective well-being of the patients and also contribute to their comorbidity. Restless Legs Syndrome (RLS) is very common in this population with an estimated prevalence of 25-35%. It is not known, however, if successful kidney transplantation would reduce the prevalence of RLS in patients with chronic renal failure. The aim of our study was to estimate the prevalence of RLS after kidney transplantation and examine the association between the presence of RLS and health-related quality of life.
Methods: Here we report data obtained in 398 patients living with a functioning kidney graft followed at the transplant center of the Semmelweis University, Budapest. The mean age of the patients was 47±13 years (18-78 years), 57% male, 16% diabetics. The mean serum creatinine level was 156±75 micromol/l, mean hemoglobin level was 135±45 g/l. The patients were administered a battery of questionnaires including a diagnostic questionnaire for the restless legs syndrome (Allen RP and Earley CJ, 2001). Also included in the battery was the "Kidney Disease Quality of Life Questionnaire" (KDQoL) (Hays et al, 1995), a modular, kidney disease-specific, self-administered questionnaire that contains the SF-36, a widely used generic QoL instrument. KDQoL scales measure between 0-100 points, the higher suggesting a better QoL. We also recorded laboratory data (including parameters of the iron status), disease history and medications.
Results: The prevalence of RLS in this population was 4.8 %. The serum albumin of the RLS patients was significantly lower than the rest of the population (39.6±2.7 g/l vs. 41.7±3.6 g/l, $p<0,05$). Serum creatinine level and calculated GFR (Cockroft-Gault formula), and also serum hemoglobin and iron indices were similar between the groups. There was, however, a statistically and clinically significant difference in numerous QoL domains between patients with and without RLS symptoms. The SF-12 Physical Composite score was 36.9±9.2 in patients with versus 43.8±10.2 in patients without RLS symptoms ($P<0.01$). Similarly the SF-12 Mental Composite score (43.6±14.4 vs. 49.8±11.5, $p<0.05$), the "energy/fatigue" score (52.4±22.5 vs. 65.7±23.5, $p<0.01$) and also the "sleep" score (56.7±19.6 vs. 73.8±17.2, $p<0.01$) were sig-

nificantly lower in patients with RLS symptoms, suggesting poorer quality of life.
Conclusions: The prevalence of RLS in our kidney transplant patients was much lower than has been repeatedly published for patients on maintenance dialysis. The presence of the symptoms of RLS was associated with poorer quality of life.

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0865.N

Influence of PLMS on Scoring Phasic Leg Muscle Activity

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Introduction: Phasic muscle activity in the lower limbs has been suggested to be a sensitive marker both of pharmacologic manipulation of, and functional deterioration in, midbrain or spinal dopaminergic circuits. Whether PEM (phasic electromyographic metric) activity is related to the simultaneous occurrence of PLMS, known to occur more frequently in the prototypical condition of midbrain dopamine loss, Parkinson's disease (PD), as well as being suppressed by dopaminomimetics, is unknown. We therefore examined the extent to which PLMS activity impacts upon quantification of PEM in normal subjects and patients with PD.
Methods: Polysomnography from five groups of patients was analyzed and consisted of the following: Young Normals (YN) (X age =21.8 [5.3]); Elderly Normals without PLMS (EN) (X age = 40.4 [8.8]); EN with PLMS (X age = 70.5 [7.6]); PD pts without PLMS (X age 59.9 =[13.6]) and PD patients with PLMS (X age = 66.4 [10.3]). N's for these groups were: YN (n = 29); EN without PLMS (n = 31); EN with PLMS (n = 19); PD without PLMS (n = 28); PD with PLMS (n = 40). Mean PLMS Index (events/hr) for the groups were: YN (0.2); EN without PLMS (0.3); EN with PLMS (50.3); PD without PLMS (0.3); PD with PLMS (30.2). PLMS were scored with conventional AASM rules by one of 2 independent scorers with inter-rater reliability of 0.80. PEM was scored according to the method of Lapierre and Montplaisir by one of 2 independent scorers with inter-rater reliability of 0.77. PEM rates were expressed as the % of 2.5 second intervals with phasic activity for each leg, and individually for NREM- and REM-sleep. PEM scorers were instructed to score EMG activity in the presence of larger amplitude and longer duration leg movements, as long as potentials of at least 100 msec and at least four times background activity were detected.
Results: PEM rates (X, SD) for the right leg for NREM sleep for the 5 groups were as follows: YN (1.7, 1.4); EN (1.2, 1.3), EN with PLMS (6.8, 3.9), PD (12.8, 12.2) and PD with PLMS (16.7, 13.5). Results from the left leg in NREM were similar. PEM rates during REM were slightly higher than NREM for each limb for most groups. The influence of gross motor activity on determination of PEM rates is indicated by the higher percentages within both EN and PD groups when comparing individuals with and without PLMS.
Conclusions: The functional significance of PEM activity remains to be fully determined but the range of values of this metric, its relative independence from PLMS and its sensitivity to nigrostriatal degeneration in the absence of PLMS suggests that quantification of such EMG activity, particularly with digital techniques, may be a metric with potential merit for evaluation of the motor system activity during sleep.

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0866.N

Ropinirole Versus Placebo In The Treatment Of Restless Legs Syndrome (RLS): A 12-Week Multicenter Double-Blind Placebo-Controlled Study Conducted In 6 Countries

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Introduction: RLS is an increasingly recognized neurological disorder. The syndrome is characterized by distressing sensations deep in the lower limbs and an urge to move the affected limbs; the symptoms are worse when inactive, worse in the evening and at night, and improve with movement. Results of several small open-label studies suggest that the dopamine agonist ropinirole effectively alleviates the symptoms of RLS. The aim of the present study was to compare the efficacy, safety and tolerability of ropinirole and placebo for the treatment of RLS (protocol number 101468/194).
Methods: In this 12-week double-blind placebo-controlled study, patients aged at least 18 years with primary RLS were randomized to treatment with ropinirole or placebo (1:1). Patients receiving medication for RLS or sleep disorders before the study entered a washout period. To reach each patient's individual efficacious dose, an unforced dose titration phase was used during weeks 1 to 7 (dose range: 0.25-4.0mg/day). Dosages then remained stable from week 8, or upon reaching an efficacious dose, until week 12. The primary endpoint was the mean change from baseline to week 12 in the International RLS rating scale (IRLS) total score. A key secondary endpoint was the Clinical Global Impression (CGI) scale score at week 12.
Results: A total of 267 patients (47 centers) received treatment; 77.9% (102/131 patients) of the ropinirole group and 78.5% (106/135 patients) of the placebo group completed the study. The mean total daily dose of ropinirole at week 12 was 1.9 mg/day (SD = 1.19). The mean improvement in the IRLS total score at week 12 last observation carried forward (LOCF) was significantly greater for the ropinirole group compared with the placebo group (-11.2 [SE = 0.76] vs -8.7 [SE = 0.75], respectively; adjusted treatment difference = -2.5, p = 0.0197, 95% CI -4.6, -0.4). Furthermore, significantly more patients in the ropinirole group reported themselves as 'much improved' or 'very much improved' on the CGI scale at week 12 compared with the placebo group (59.5% vs 39.6%, respectively). The adjusted odds of being a responder on ropinirole compared with placebo at week 12 LOCF was 2.3 (p = 0.001, 95% CI 1.4, 3.8). A total of 5.3% of the ropinirole group and 6.6% of the placebo group withdrew before completion of the study due to adverse events. Nausea and headache were the adverse events reported most commonly.
Conclusions: Ropinirole, at a single daily dose of up to 4mg, is effective in the treatment of RLS and significantly improves symptoms (as measured by the IRLS and the CGI scale) compared with placebo. Ropinirole treatment is well tolerated.

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0867.N

Prevalence of Restless Legs Syndrome in South Tyrol

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Introduction: A prevalence of 10 % has been described for Restless legs syndrome (RLS) in several recent studies (Rothdach A 1999, Ulfberg J

2000 and 2001, Philips B 2000), but remarkable regional differences are found. Many additional studies are not based on the use of standard diagnostic criteria (Walters A 1995) or were performed in specific populations (e.g. hospital outpatients). The aim of the present study was to evaluate the prevalence of RLS in Southern Tyrol (Northern Italy).
Methods: Cross sectional study of a large stratified representative sample of the population of Bruneck (South Tyrol, Italy) as part of the Bruneck study which started in 2000 (e.g. Kiechl S 2002). A total of 701 individuals (366 m, 335 f) belonging to 4 age groups (50-59, 60-69, 70-79, 80-89 years) participated in the study. The diagnosis of Restless Legs Syndrome was made on the basis of personal interviews based on the minimal criteria for RLS of the Internation RLS study group (Walters A 1995).
Results: A prevalence of RLS of 10.6 % was found in this population. Women were affected twice as frequently as men (14.2 % versus 6.6%). No age related increase of prevalence was seen in this sample. Polyneuropathies, renal insufficiency (creatinine > 1.5 mg/dl), vitamine B 12 or folate deficiency and anemias were not more frequent in individuals who met the criteria for RLS compared to those who did not.
Conclusions: In this large sample of the population between 50 and 89 years an age independent RLS prevalence of 10.6% was found. The prevalence in this central european alpine region is therefore similar to that in other countries with predominantly caucasian populations (Philips B 2000, Rothdach A 2000, Ulfberg J 2000). The study also confirmed a twice as high prevalence in women than in men. It is hypothesized that secondary RLS forms play only a minor role in this population, because possible causes of secondary RLS did not distinguish between affected and non-affected individuals.

0868.N

Operationalization of "Sleep Benefit" (SB) in Parkinson's Disease (PD)

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Introduction: Some patients with Parkinson's Disease (PD) experience "sleep benefit" (SB), the transient improvement of motor symptoms, upon arising in the morning, whereas others, depending upon the time of prior medication, may experience increased dystonia and rigidity upon morning awakening. The purpose of this study was to determine whether PD patients' perception of typical motor function upon morning awakening was validated by results of a brief, bedside motor exam.
Methods: Patients were 11 PD patients with mild-to-moderate (Hoehn-Yahr I-III) disease (1 with Hoehn-Yahr V). Each spent two consecutive (n= 9) or a single night (n = 2) in the sleep laboratory. Upon evening arrival in the lab, all patients completed a brief questionnaire collecting data on perceived sleep benefit following the questions of Merello et al. A board-certified neurologist then performed a 10 to 15 minute motor exam consisting of the following: a) drawing of spiral with R and L hands and copying a simple sentence in script with the dominant hand; 2) 4 10-sec trials of finger tapping alternating between R and L hands; and measurements of 3) tremor and 4) rigidity from the Unified Parkinson's Disease Rating Scale (UPDRS) (score range 0 to 20 with higher score indicating more impairment). Spirals/handwriting were judged independently and blindly by 5 board-certified neurologists who were asked to pick out which, if any, of each PM/AM set indicated "better" function. Data from each night were analyzed separately, yielding a total of 20 PM/AM "pairs."
Results: Of the 11 pts, 8 reported typically better, and 2 typically worse, function in the AM, with one pt experiencing no difference. Blind analysis of spirals/handwriting showed general lack of consensus among better versus worse function with 80% agreement achieved only for 5 pts. Panel consensus judgments were unrelated to the patient's perception of AM benefit. Mean finger tapping showed no PM/AM difference on either dominant or non-dominant hand and was unrelated to perceived sleep benefit. UPDRS rigidity showed similar results. However, UPDRS tremor score indicated a significant reduction in AM relative to PM score ($t = 2.12$, $p < .06$) for pts experiencing SB, relative to those not experiencing SB ($t = 1.00$, NS).
Conclusions: Of the 11 pts, 8 reported typically better, and 2 typically worse, function in the AM, with one pt experiencing no difference. Blind analysis of spirals/handwriting showed general lack of consensus among better versus worse function with 80% agreement achieved only for 5 pts. Panel consensus judgments were unrelated to the patient's perception of AM benefit. Mean finger tapping showed no PM/AM difference on either dominant or non-dominant hand and was unrelated to perceived sleep benefit. UPDRS rigidity showed similar results. However, UPDRS tremor score indicated a significant reduction in AM relative to PM score ($t = 2.12$, $p < .06$) for pts experiencing SB, relative to those not experiencing SB ($t = 1.00$, NS).

Research supported by AT-00611

0869.N

Hypocretin/Dopaminergic Interactions: Pharmacological Studies Of Cataplexy And PLMS In Canine Narcolepsy

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Introduction: D2/3 modulation of midbrain dopaminergic (DA) neurons has been shown to regulate sleep and cataplexy (a REM sleep-like state of muscle tone inhibition) in hypocretin receptor 2 gene mutated narcoleptic dogs. We have also shown that presynaptic enhancement of DA transmission is likely to mediate the wake-promoting effects of commonly used stimulants. In addition, dopamine levels have been shown to be consistently increased in the amygadala and cortex of narcoleptic dogs. DA/hypocretin interactions are thus likely to be involved in the pathophysiology of narcolepsy. Narcolepsy is often associated with periodic leg movements during sleep (PLMS), and we recently reported the occurrence of PLMS-like leg movements during sleep in narcoleptic Dobermans. The involvement of the DA system in PLMS is well-established and dopaminergic agonists (especially selective D2/3 agonists), have been recently used for the treatment for PLMS in humans. In this study, we further examined whether pramipexole and ropinirole (two D2/3 agonists currently used for the treatment of PLMS), reduces PLMS-like movements in narcoleptic dogs. We also studied if established PLMS treatments such as DA agonists (pramipexole, ropinirole, pergolide) or opiate agonists (propoxyphene and tramadol), had a significant effect on cataplexy in narcoleptic Dobermans.
Methods: The effects of pramipexole (0.125, 0.25 mg/dog) and ropinirole (1, 2 mg/dog) on sleep and PLMS-like movements were assessed in 4 narcoleptic Dobermans. These narcoleptic dogs were chronically implanted with electrodes for EEG, EOG, and EMG. The dogs were freely moving in a lighted recording room (3 x 3 m) and were observed from an adjoining room with a video camera. Involuntary movements during sleep were assessed by reviewing the video recordings simultaneously with EEG, EMG and EMG traces. Six narcoleptic Dobermans were used for cataplexy testing. Compounds used for cataplexy testing included pramipexole (up to 0.25 mg/dog p.o.), ropinirole (up to 2.0 mg/dog p.o.), pergolide (up to 0.125 mg/dog p.o.), propoxyphene (65, 195 mg/dog p.o.) and tramadol (50, 100, 200 mg/dog p.o.).
Results: Both pramipexole and ropinirole dose-dependently reduced PLMS-like movements in narcoleptic dogs. All DA compounds (pramipexole, ropinirole and pergolide), significantly aggravated cataplexy in a dose-dependent fashion. However, propoxyphene and tramadol, (two opiate agonists), did not modify cataplexy.
Conclusions: D2/3 agonists used in the treatment of PLMS/RLS significantly reduced PLMS-like movement in narcoleptic dogs. This further

validated the existence of genuine PLMS in our canine model of narcolepsy. The fact that DA agonists (used for the treatment of human PLMS), also aggravated canine cataplexy, suggests that similar DA mechanisms (i.e. D2/3 receptors), may be involved in the regulation of cataplexy (sleep-related muscle inhibition) and PLMS (sleep related-muscle activation). An aggravation of cataplexy with D2/3 agonist has not been reported in humans and further studies would be needed to explore this possibility. Our results also suggest that opiate and D2/3 receptors mediate the regulation of sleep-related motor abnormalities such as cataplexy and PLMS, and may involve different pathways. Taken together with the fact that an elevated hypocretin tonus (high CSF hypocretin levels) is observed in the early-onset cases of human RLS, further studies of hypocretin/ DA interaction in sleep-related motor control is warranted.

0870.N

A Pilot Study Examining the Effects of Neuromuscular Massage Therapy (NMT) on Reported Sleep in Parkinson's Disease (PD)

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Introduction: Patients with Parkinson's Disease (PD) typically have markedly disturbed sleep with conventional treatments showing only minimal success. Recently NMT has been shown to offer beneficial effects on the waking motor function in PD (UPDRS motor subscale) (Svircev and Craig, Amer Pub Hlth Assn, 2002). Massage has been identified previously as offering beneficial effects in spinal cord injury (Diego et al, Int J Neurosci 2002: 112: 133-42) and for improving sleep in hospitalized patients (Richards et al, AACN Clin Issues, 2000, 11, 77-96). The present pilot study examined the effects of NMT on reported sleep relative to a control condition (Music Relaxation Therapy, MRT) in PD patients.
Methods: Pts were 32 mild-to-moderate stage PD patients (mean age 63.1, 23 men, 9 women). Patients were randomized to receive either NMT (n =18) or MRT (n = 14). NMT was administered by certified massage therapists over a 4 week period, 2/week (8 sessions total, 45 minutes each) in an outpatient clinic in a local therapeutic school of massage. During the NMT sessions, specific attention was paid to identification of trigger points and pressured release. A consistent protocol was used for each NMT session, which included music. MRT consisted of an identical protocol but excluded NMT. The Pittsburgh Sleep Quality Index (PSQI) was administered at Baseline and Follow-up, and the PSQI Global Score was used as the primary outcome in this analysis. PSQI subscales served as secondary outcomes.
Results: The NMT group had slightly more advanced PD patients than the MRT group (n = 14) (X Hoehn-Yahr, 1.8 [1.0] vs 1.3 [0.5] t = 1.76, $p < .10$) but did not differ in age or characteristic sleep quality (Baseline PSQI Global = 8.1 [3.6] vs 7.0 [3.6], t = 0.81, NS). Gender composition was equivalent. Repeated measures ANOVA indicated no group by time interactions for either the PSQI Global Score or any of the 7 subscales. With the exception of subscale 5 (subjective sleep quality), absence of even simple time effects suggest the recalcitrant nature of disturbed sleep in this population.
Conclusions: Despite massage-induced improvements in PD motor function reported elsewhere, reported sleep did not show improvement with this alternative treatment modality. Because of the severity of disturbed sleep in PD, possible efficacy of NMT in other conditions (e.g., primary insomnia) might still be entertained using similar or different techniques or different administration schedules.

Research supported by AT-00611

0871.N

Validation Of RLS Diagnostic Questions In A Primary Care Practice

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Introduction: A useful survey questionnaire must be sensitive in identifying sufferers as well as specific enough to minimize false positive results. We have developed and utilized such a questionnaire. The 10-item Restless Legs Syndrome Questionnaire (RLSQ), is a diagnostic questionnaire that can be completed by the patient. In a previous report, the RLSQ had a 93% sensitivity and 84% specificity when compared to the diagnoses by primary care physicians (PCP) knowledgeable about RLS. Currently, the four basic diagnostic criteria can be adequately covered using only four or five questions. For this abstract, we were interested in reanalyzing our data to determine the sensitivity and specificity of the RLSQ vs. the trained PCPs using a smaller set of questions.
Methods: Each patient seen at a Moscow, Idaho primary care clinic during a one-year period was asked to complete the 10-question RLSQ. However, fewer questions were necessary to cover the current diagnostic criteria. These questions are as follows: 1. Do you have or have you sometimes experienced recurrent, uncomfortable feelings or sensations in your legs while sitting or lying down?2. Do you or have you sometimes experienced a recurrent need or urge to move your legs while sitting or lying down? 3. When present, do these feelings or movements improve or go away when you get up and walk around as long as you are walking?4. When present, are these feeling or movements at their worst in the evening or night?5. When present, do these feelings or movement become worse when you are resting (either sitting or lying down) than when you are physically active?
Results: Structured diagnostic interviews performed by PCPs trained to properly diagnose RLS, were completed on a total of 151 patients who responded positively to all five questions and a randomly selected group of 127 patients who responded negatively to all five questions.Question five may overlap question three, therefore, separate analyses were conducted for the first four questions and then for all five questions. The sensitivity and specificity for the first four questions were 82.3% and 89.4%, while the sensitivity and specificity for all five questions were 81.7% and 89.9%.
Conclusions: Our analysis revealed that four questions provide reasonably accurate diagnoses and are suitable for a questionnaire format. This finding provides the basis for developing a simple method for PCPs to screen for this common condition. In the future, items may be added for analyses to enhance diagnostic accuracy. This rural population was almost exclusively Caucasian, therefore, it remains to be determined the extent to which these items will generalize to a wider population or to a population that may have more medical problems confusing the diagnosis.

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0872.O

Prevalence and Clinical Significance of Periodic Leg Movements in the First Night After Cerebral Infarction

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Introduction: The objective of our study was to determine the prevalence and characteristics of periodic leg movements in sleep (PLMS) during the first night after an hemispheric ischemic stroke
Methods: We prospectively studied 47 patients with a first-ever hemi-

spheric ischemic stroke which included at least some motor impairment. Patients with stroke in the brainstem and spinal cord were excluded. On admission all patients underwent a neurological examination, a comprehensive sleep history, and a brain computed tomographic scan (CT) to exclude brainstem and hemorragic strokes. Size (infact area and volume) and location of the stroke was assesed by MRI within the first week after stroke onset. Neurologic severity and functional disability were evaluated by the Scandinavian Stroke Scale (SSS) and the Barthel Index (BI) at admission and at six months after stroke onset. An all-night full polysomnography (PSG), that included right and left anterior tibialis surface electromyographic recording, was performed the first night after stroke onset in all patients. Periodic limb movements during sleep (PLMS) were scored following the Atlas and Scoring Rules by the Atlas Task Force of the American Sleep Disorders Association (Sleep 1993; 16: 748-759).We evaluated the PLMS number, PLMS index (number of PLMS per hour of total sleep time) and the PLM index during wakefulness.

Results: There were 30 men and 17 women with a mean age of 64.8 ± 9.2 (range, 41-80) years. The mean latency between stroke onset and PSG was 11.2 ± 5.5 hours. No one of the patients had restless legs syndrome before stroke onset or developed this disorder during the six months of this study. The mean PLMS index was 44 ± 29, and a PLMS index greater than 5 was found in 27 patients (57.7%). PLMS were observed in the non-paretic (75%) and paretic (25%) legs. Thirty patients had an apnea-hypopnea index greater than 10. The PLMS index and PLMS number were significantly associated with age (p=0.01), higher SSS score at admission (p=0.01) and at six months (p=0.02), lower BI score at admission (p=0.02) and at six months (p=0.02), and greater infarct area (p=0.002) and volume (p=0.004). PLMS were not correlated with gender, vascular risk factors, location of the stroke, apnea-hypopnea index and infarct location. Three patients with a lacunar stroke producing a pure motor impairment did not have a PLMS index greater than 5. PLM during wakefulness was only correlated with age (p=0.01).

Conclusions: PLMS are frequent during the first night after cerebral infarction, predomiantes in the nonparetic limb and are associated with greater age, greater infarct size, severe clinical disability at admission and poor clinical outcome at six months.

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0873.O

The Relationship of Abnormal Sleep Rhythms and Fatigue of Multiple Sclerosis

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Introduction: There is good documentation of variety neurological disorders affecting sleep patterns. Fatigue is a frequent and major symptom in multiple sclerosis (MS) that can be profoundly debilitating. There are no large-scale studies done examining circadian rhythm abnormalities in patients with MS and none looking at the relationship of fatigue to sleep patterns. A few studies in the literature looking at circadian rhtythms and sleep problems in multiple sclerosis have produced conflincting results. The goals of our study were 1) To determine if abnormal sleep patterns are present in patients with MS. 2) If they are present do they correlate with the presence of fatigue. 3) Can a simple sleep questionnaire be used to screen for MS patients with sleep problems and fatigue.

Methods: An actigraph is a simple, non-invasive technique to record activity during waking and sleep over extended periods of time. There is a very close correlation between wake /sleep identified by the actigraph and that determined by a polysomnogram. Three groups of 15 subjects each were identified. The first group was made up of subjects with the diagnosis of definite multiple sclerosis who were fatigued (Fatigue Descriptive Scale(FDS) score of 5 or more. The second group was of subjects with definite multiple sclerosis who were not fatigued (FDS score of 4 or less), and the third group was made up of healthy volunteers who had no sleep complaints, no fatigue, were on no medications that may affect sleep. All 3 groups were roughly age and sex matched. The subjects kept sleep diaries and wore an actigraph for 2 weeks. They also filled out an Epworth Sleepiness Scale and a Modified Fatigue Impact Scale. Exclusion criteria were any subject with diagnosed sleep disorders, any subject who was on any medication that interfered with sleep/wake cycles, and anyone with more than mild depression a Beck's Depression Inventory score of over 16. The subjects will be considered to have sleep abnormalities if the major sleep period was delayed, advanced, frequently disrupted or irregularly timed in relation to the desired sleep time. The actigraphs were interpreted by a blinided physician.

Results: Twelve out of 15 patients with fatigue had disrupted sleep. Three out of 15 MS patients who did not have fatigue had disrupted sleep. The difference was statistically significant p-value of 0.0028 on Fischer exact test. The healthy controls, as of this date, have been all recruited but we have data only on 5. All 5 have normal sleep patterns and are neither fatigued nor sleepy. 10 out of the 12 patients with fatigue and disrupted sleep scored 10 or higher on the ESS. Two patients without fatigue and normal sleep patterns also scored 10 or higher. One patient without fatigue and normal sleep patterns scored 10 or highe. None of the patients with fatigue and normal sleep patterns scored 10 or higher.

Conclusions: 1)Disurpted sleep may be a contributor to the developemnet of fatigue in MS patients.2)ESS may be a good screening tool for disrupted sleep patterns in patients with MS fatigue.

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0874.O

REM Sleep Behavior Disorder in Machado-Joseph Disease

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Introduction: The objective of our study was to evaluate the frequency and characteristics of REM sleep behavior disorder (RBD) in a group of patients with Machado-Joseph disease (MJD) (spinocerebellar ataxia type 1).

Methods: Nine patients with genetically confirmed MJD and nine sex and aged healthy controls were studied. Diagnosis of RBD was performed by clinical history and PSG with audiovisual recording. Patients had to report vigorous sleep behavior and unpleasant dreams and have increased tonic and/or phasic muscle activity during REM sleep associated with excessive movements. Quantification of muscle activity during REM sleep (in chin and limbs) was made following the method described by Lapierre and Montplaisir(Neurology 1992;42; 1371-1374). PSG measures in MJD were compared with those in the control group.

Results: The mean age of the patients was 55.8 ± 17.1 years, and there were five women and four men. RBD occurred in five patients(55%), four men and one women, and in two the RBD symptoms preceded the onset of the MJD cerebellar syndrome by several years. While dreaming, four patients fell out of the bed and other self-injuried his arms. REM sleep without submental atonia, submental phasic EMG activity and anterior tibialis phasic EMG activity were significantly increased in MJD with RBD compared to MJD without RBD and controls.

Conclusions: In Machado-Joseph disease, REM sleep behavior disorder is a common and potentially injurious condition that should be considered part of the clinical spectrum of this genetically determined disease.

0875.O

Analysis of Sleep Parameters and the First Night Effect in Epilepsy Patients

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Introduction: Our objective was to determine the significance of the first night effect in epilepsy patients undergoing overnight EEG-polysomnography (PSG) and report on how sleep parameters in epilepsy patients differ from normative values. Sleep alterations that characterize the first night effect include increased REM latency, decreased REM sleep and decreased slow wave sleep. Recently, studies have refuted this conclusion by showing the lack of a first night effect in healthy volunteers. Performing multiple PSGs to account for the first night effect increases cost of studies and inconvenience to epilepsy patients and caregivers.
Methods: Sleep parameters of 43 epilepsy patients (ages 14-56, mean 34.0 ± 12.0; 19 women, 24 men), most with medically refractory epilepsy, undergoing two consecutive nights of PSG were measured. NREM stage 3 and NREM stage 4 were combined as NREM stage 3/4. Sleep efficiency, sleep latency, REM latency, number of stage shifts, wake minutes, and minutes and percent of total sleep time for NREM stage 1, NREM stage 2 NREM stage 3/4 and REM sleep were calculated for night 1 and night 2 of each patient. These parameters were compared using two-tailed paired t-tests with significance set at $p < 0.05$.
Results: Percent of NREM stage 1 sleep was increased for both nights 1 and 2 (15% and 16% , respectively) as compared to normative values (2-5%). Percent of REM sleep was decreased for both nights 1 and 2 (15% and 14% , respectively) as compared to normative values (20-25%). NREM stage 2 (48% and 47%) and NREM 3/4 (11% and 13%) were within normal ranges given normative values of 45-55% for NREM stage 2 and 10-23% for NREM stages 3/4. There were no statistically significant differences between night 1 and night 2 for any parameters measured except NREM stage 3/4 sleep. NREM stage 3/4 sleep was decreased in absolute time for night 1 (47.3 + 35.7 minutes; mean ± standard deviation) as compared to night 2 (54.5 + 38.4 minutes; $p = 0.03$). Percent of total NREM stage 3/4 was also decreased for night 1 (11.7 ± 9.0) as compared to night 2 (13.6 + 10.1; $p = 0.02$).
Conclusions: These results confirm prior work suggesting that epilepsy patients have increased NREM stage 1 sleep and decreased REM sleep. The majority of sleep parameters are not affected by the first night effect in this sample of patients with medically intractable epilepsy, although NREM stage 3/4 sleep is slightly diminished on night 1. The overall stability of sleep parameters from night 1 to night 2 in our sample may reflect habituation (due to experience with EEG monitoring prior to the PSG). As some ongoing medication trials emphasize changes in NREM stage 3/4 sleep, our results have important implications for the design of clinical trials in sleep and epilepsy.

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0876.O

CSF-Orexin (Hypocretin) Decreases During Intrathecal IFN-Alpha Therapy of the Patients with Subacute Sclerosing Panencephalitis (SSPE)

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Introduction: The recent studies using cerebrospinal fluid (CSF) and postmortem brain of the patients with narcolepsy have shown that dysfunction of orexin (Ox) nervous system is related to its pathophysiology (Nishino.2001). So far, we determined Ox concentration in CSF in cases with various types of neurological disorders other than narcolepsy and have reported that it was normal except for that in GBS (Kanbayashi.2002). In the present study, we determined the CSF Ox level in two patients with SSPE who underwent IFN-alpha therapy.
Methods: The two patients with SSPE both received reservoir placement operation to continuous administration of IFN-alpha into cerebral ventricle. CSF samples were collected through indwelling cannula immediately before IFN-alpha administration and after one cool of IFN-alpha therapy with informed consent. The CSF samples were then stored in a freezer at -80c until Ox level measurement using radioimmunoassay kits(Phoenix Pharmaceuticals, Belmont, CA) as previously reported (Kanbayashi.2002). The detection limit was set to 40 pg/ml (normal range: 160~422pg/ml).
Results: Case 1: A 3-year old boy developed gait disturbance, dysarthria and atonic seizure. Ox level was within normal range (227 pg/ml). After the initiation of IFN-alpha therapy of 3million units twice per week, the symptoms were improved and the frequency of atonic seizures also decreased. Ox level decreased to under detection limit 2 months after treatment. Thereafter, the session of IFN-alpha therapy was reduced to once per week, and Ox level increased to 315 pg/ml. When the patient was 6 years old, his symptoms exacerbated from quadriplegia to decorticate rigidity. Then the session of IFN-alpha therapy was increased to twice per week, and 1week after, Ox level decreased to under detection limit .Case 2: A 4-year old girl developed gait disturbance, aphonia, atonic seizure and myoclonus in limbs. Ox level was in the normal range (311 pg/ml). After the initiation of IFN-alpha therapy 3million units twice per week, the seizures and mylclonus become less frequent, and Ox level also decreased to under the detection limit 3 weeks after. Thereafter, the session of IFN-alpha therapy was reduced to once per week, and 1week after Ox level increased to 387 pg/ml. After 2months, Ox level was still within normal range (191 pg/ml).Both cases had febrile reaction and somnolence after IFN-alpha administration, but cataplexy was never observed.
Conclusions: In the two cases of SSPE reported here, Ox level was in normal range before icv @administration of IFN-alpha and decreased after the initiation of IFN-alpha therapy. IFN-alpha has been used for the treatment with SSPE patients because it is one of cytokines which has anti-viral effect and improves cellular immunity (Garg.2002). Recently, Waleh et al. demonstrated that the production of prepro-Ox, which is a precursor of Ox, was prevented when INF-alpha was given to gene promoter region of prepro-Ox . These results are obtained in vitro but suggest that the production of Ox may be suppressed by similar mechanism as ours. Further studies are needed about the effects of IFN-alpha on Ox production.

0877.O

Multiple Sclerosis And Sleep: Correlation Of A Questionnaire And Polysomnograms

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Introduction: In a previous abstract, a questionnaire study of multiple sclerosis (MS) and sleep was presented. This descriptive study revealed a breadth of subjective sleep problems in these patients, including insomnia, snoring, restless legs syndrome (RLS) symptoms, periodic leg movements (PLMs), as well as MS-related complaints of nocturia and spasms. The current pilot study was undertaken to compare the questionnaire results with polysomnographic data.
Methods: 30 MS patients with the highest overall sleep problem scores were identified from 96 questionnaires. Twenty-two patients either could not be contacted or declined further participation. Seven patients agreed to participate and sleep evaluation (history and physical exam) was performed. All-night polysomnograms were obtained for six of these patients. The polysomnographic measures selected for study included

sleep latency, respiratory disturbance index (RDI), PLM index, oxygen saturation nadir, and sleep efficiency. These measures were correlated with questionnaire scores for MS-related sleep complaints, apnea, insomnia, RLS, PLMD, general sleep problems, total sleep questionnaire values, Epworth Sleepiness Scale (ESS) and expanded disability status scale (EDSS).
Results: Polysomnograms for the six MS patients were interpreted and the following mean values obtained: RDI of 20.4/hour (range 2.3 to 45.5), sleep latency of 42.8 minutes (range 9.3 to 87.7), PLM index 33.3/hour (zero to 98.4), sleep efficiency 54.3% (range 20.6 to 88.6) and oxygen saturation nadir of 85% (range 54 to 95). Pearson correlations were performed to compare questionnaire items with polysomnographic findings. The total sleep complaint score was significantly correlated with sleep onset latency ($r = .78$, $p < 0.3$, one-tailed), and the total MS-related sleep problems score with sleep efficiency ($r = -.74$, $p < .05$, one-tailed). Insomnia was significantly correlated with both sleep latency ($r = .78$, $p < .03$, one-tailed) and poor sleep efficiency ($r = -.75$, $p < .04$, one-tailed). Complaints of periodic leg movements were significantly correlated with PLM index ($r = .81$, $p < 0.03$, one-tailed). Yet, the PLM index was negatively correlated with MS-related sleep complaints and EDSS ($r = -.73$, $p < .05$; $r = -.79$, $p < .03$, one-tailed, respectively).
Conclusions: This pilot study of polysomnography in MS patients provided objective confirmation of the subjective report of sleep problems. Elevated mean RDI, PLM index, sleep latency, and decreased mean sleep efficiency and oxygen saturation nadir were observed. A higher report of overall sleep complaints was related to greater sleep latency; and the higher the number of MS-related and insomnia complaints, the lower the sleep efficiency. A higher subjective PLM score was related to a higher objective PLM index, however, this index decreased in patients with more severe MS. Conclusions are preliminary due to the small patient numbers, and further studies are planned at this time. In-depth sleep questioning and polysomnograms should be considered before medically treating fatigue or sleep complaints in MS patients.

0878.O

Decreased CSF Hypocretin-1 Level In Hypersomnia With Bilateral Hypothalamic Lesion

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Introduction: CSF hypocretin is reported to be markedly decreased in narcolepsy/cataplexy patients. Narcolepy is caused by hypothalamic lesion such as stroke with decreased CSF hypocretin-1. However, hypersomnia without any other narcolepsy-related symptoms due to hypothalamic lesion has not been well documented. The aim of the study was to examine the CSF hypocretin-1 in hypersomnia due to hypothalamic lesion.
Methods: Two patients presented hypersomnia secondary to hypothalamic lesion were employed in the study. Clinical symptoms, brain MRI, and CSF hypocretin-1 level were correlated.
Results: Case1. A 22 year old women suddenly developed hypersomnia. After the onset, her sleep time was 15 hours per day and fell asleep frequently even while eating, talking or riding bicycle. Brain MRI showed FLAIR hyperintensity on both sides of hypothalamus. She had the diagnosis of multiple sclerosis (MS) which had initially started with diplopia one year prior to the hypersomnia. Multiple sleep latency test (MSLT) revealed decreased mean sleep latency (2.8min) and five sleep onset REM periods (SOREMP) out of five sessions. CSF hypocretin-1 level was undetectable (<40pg/ml). Hypersomnia improved within 2 weeks. Two and four months after the onset of hypersomnia, both MRI lesion and CSF hypocretin level recovered to normal. Case2. A 42 year old women gradually developed hypersomnia in one year. She also developed forgetfulness. Brain MRI revealed FLAIR high intensity lesion in the bilateral hypothalamus and basal ganglia. MSLT showed decreased mean sleep latency (7.5 min) with no SOREMP. CSF hypocretin-1 level was decresed (117pg/dl).
Conclusions: Decreased CSF hypocretin-1 in these cases may reflect degree of hypothalamic dysfunction selectively in hypocretin system, and it can explain the mechanism of hepersomnia.

0879.O

Effects of Acetylcholinesterase Inhibitors on Sleep Architecture in Alzheimer's Disease Patients

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Introduction: Patients with Alzheimer's disease (AD) suffer from disturbed sleep and a high prevalence of obstructive sleep apnea (OSA). Acetylcholinesterase inhibitors (AchEI) are commonly used to treat AD and are known to improve symptoms and delay the progression of dementia. Little is know of the effects of AchEI on sleep architecture. In the normal elderly, AchEI is believed to increase REM sleep and reduce REM sleep latency. We hypothesized that AchEI would improve sleep quality in a sample of AD patients with various levels of OSA.
Methods: Twenty-three patients with a diagnosis of mild to moderate AD were recruited to undergo an overnight-unattended home polysomnogram. Subjects were divided based on their use of AchEI with no distinction made between which AchEI they were taking. Sleep records were analyzed according to the Rechtschaffen and Kale's criteria. The total sleep time (TST) and the percent of TST spent in each sleep stage were used to assess sleep quality. T-tests were used to assess differences between groups with Bonferroni correction for multiple comparisons (significant $p = 0.01$).
Results: Eighteen out of 23 were taking AchEI. Forty percent of those not taking AchEI were taking an antidepressant versus 27.8% of those on AchEI. There was no difference in age between the two groups (77 ± 10 years, with AchEI Vs 78.2 ± 6.5 years, without). The mean body mass index (25 ± 2) was in the normal range and there was no difference between groups. The apnea hypopnea index (AHI) ranged from 2.2 to 76/hr and there was no difference in mean AHI between the groups (19.6 ± 18 with AchEI Vs 25 ± 23 without). There was no difference in TST between groups (326 ± 104 minutes, with AchEI Vs 346 ± 96 minutes, without). Stage 1 sleep was significantly lower in patients taking AchEI ($16.7 \pm 13.8\%$ Vs $40 \pm 13.7\%$, $p = 0.003$), while stage 2 sleep was significantly greater in patients taking AchEI ($66.8 \pm 16\%$ Vs $45.5 \pm 12\%$, $p = 0.01$). There was no difference in slow wave sleep or REM sleep between the two groups.
Conclusions: These preliminary data suggest that Acetylcholinesterase inhibitors affect sleep architecture and may affect sleep quality in patients with mild to moderate Alzheimer's disease and obstructive sleep apnea.

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0880.O

Family Aspects of Idiopathic Hypersomnia (Polysymptomatic Form)

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Introduction: A family tendency for idiopathic hypersomnia has long been recognised. In a first study by Nevsimalova and Roth (1972) 9 patients in a group of 23 had one or several affected relatives, and in a second report by Roth (1976), 45 probands in a group of 167 patients (26.9%). An autosomal dominant type of transmission of the disease was suggested.However some limitations applied to these studies: criteria for idiopathic hypersomnia were somewhat loose at that time. The upper airway resistance syndrome was not yet identified. In Roth's study, 79 out of the 167 patients (47.3%) had difficulties in the psychological sphere, thus not fulfilling criterion G of idiopathic hypersomnia in the International Classification of Sleep Disorders (1997). We were interested in evaluating the familial aspect of idiopathic hypersomnia in a group of subjects with the polysymptomatic form (excessive daytime sleepiness consisting of prolonged sleep episodes of non-REM sleep, prolonged major sleep episode and great difficulty waking up)
Methods: 28 subjects, 9 male and 19 female, with the polysymptomatic form of idiopathic hypersomnia, were investigated. All subjects had a complete clinical intervew, one night polysomnography followed by a multiple sleep latency test, and a psychological interview when a mood disorder was suspected. In addition, 23 subjects had a further polysomnography with monitoring of the oesophageal pressure to rule out an upper airway resistance syndrome. All subjects were thoroughly interviewed to establish a detailed pedigree of the family including first and second-degree relatives and to identify those who were affected with the same symptoms as the probands. Neither children below 12 years of age, nor subjects known for loud snoring were included.
Results: 19 patients (67.85%), 6 male and 13 female, with a family history suggestive of the polysymptomatic form were identified. 9 subjects had only first degree relatives affected, 2 had only second degree relatives affected, while 8 had both first and second degree relatives affected. In one family affected subjects were found on both sides and in another, the maternal grand-mother and the mother were affected with idiopathic hypersomnia while the father and the brother were affected with narcolepsy.The segregation ratio was 12/24 = 0.50, suggesting an autosomal dominant mode of inheritance. However two patients had only one sister affected and one patient only one brother. Moreover both parents were affected in one family, in favour of an autosomal recessive mode of inheritance in this particular case.
Conclusions: Our results in a sample of subjects affected with the polysymptomatic form of idiopathic hypersomnia, confirm the high family tendency of the condition and suggest an autosomal dominant mode of inheritance. The presence of subjects with idiopathic hypersomnia and of subjects with narcolepsy in a single family is an incentive for hypocretin CSF assays, in view of further investigating the possible relationship between the two conditions. Furthermore after a deeper identification of the affected relatives, performing a linkage analysis would be of interest to assign a mutation to this phenotype.

0881.O

Sleep, Activity, and Temperature in Genetically Epilepsy Prone Rats

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Introduction: "Genetically epilepsy prone rats" (GEPRs) are a well-studied model of genetic susceptibility to audiogenic seizures. Rats of the GEPR9 substrain develop clonic-tonic seizures in response to a loud tone. Several brain loci that have been implicated in seizure generation in this model are also implicated in the control of rapid-eye-movement sleep (REMS). We therefore characterized the sleep, activity, and temperature patterns of GEPR9 and Sprague-Dawley (SD) rats to assess their suitability as a model for investigating the relationships between REMS and seizure susceptibility and generation.
Methods: Adult male rats (n = 8 per strain) were surgically instrumented for monitoring EEG, EMG, locomotor activity, and core temperature, and were permitted at least 2 weeks for recovery and acclimation. Rats were housed in individual cages placed in sound-attenuating chambers on a 12:12 hour light:dark cycle at 21-22°C. Sleep, temperature, and activity patterns were monitored for 24 hours before and 42 hours after a 6-hour period of enforced wakefulness, beginning at light onset. In subsequent studies, temperatures and activity were evaluated before and after the induction of audiogenic seizures by exposure to a loud noise. All experimental treatments were separated by at least one week. Sleep was scored using standard methods.
Results: Basal circadian patterns of sleep were similar in GEPR9 and SD rats. For both strains, time spent asleep was approximately 60% and 10% of the light phase for slow-wave sleep (SWS) and REMS, respectively, and 20% and 5% of the dark phase. Both strains also showed similar SWS and REMS rebounds after a 6-hour period of enforced wakefulness, although recovery responses were perhaps somewhat greater in magnitude and duration in the GEPR9s. During the recovery period, both strains showed similar increases in SWS and REMS bout lengths, but GEPR9s also demonstrated dark-phase increases in the number of bouts. Recovery sleep was paralleled by modest reductions in locomotor activity and core temperature during the recovery period. In response to seizure induction at light onset, GEPR9s showed a 2-hour period of hyperthermia (1°C) but no change in locomotor activity. In contrast, seizure induction in GEPR9 rats at dark onset produced a reduction in activity for approximately 36 hours, but no change in temperature. Activity and temperature were not altered in SD rats exposed to the tone at either dark or light onset.
Conclusions: Basal patterns of sleep, temperature, and activity, as well as responses to sleep deprivation, were similar in GEPR9 and SD rats. However, GEPR9s demonstrated different physiologic changes in response to seizures experienced at either light or dark onset.

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0882.O

Sleep Disturbances In Multiple Sclerosis

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Introduction: Sleep disturbances, daytime fatigue and depression are common problems in patients with multiple sclerosis. The reasons of fatigue have been repeatedly discussed: physical disability, immobility, spasticity, muscular weakness, depression, MRI-burden of lesions, and sleep disturbances.
Methods: A special questionnaire-set was sent to all members of the Viennese MS society (n³ 1000) comprising the following topics: Demographic data, course of the disease, neurological symptoms, current therapy, present fatigue and depressive symptoms. Completed questionnaires from 504 MS patients (362 females and 142 males, mean age 50.59 ± 14.1) were analyzed. The Pittsburgh Sleep Quality Index (PSQI) (Buysse 1988) was used to evaluate subjective sleep quality. EDSS by phone, an adapted, modified version of the Kurtzke Expanded Disability Scale which allows a rough estimation of patients' disability was used in a questionnaire form. The Fatigue Severity Scale (FSS) was

used for estimation of presence and severity of subjective „fatigue“ (Krupp et al, 1989). Patients rated their tiredness at the very moment of testing on the Visual Analog Scale (VAS). Self Rating Depression Scale of Zung (SDS) was used for quantification of depressive moods (Zung, 1965).
Results: MS-patients showed a reduced sleep quality twice as frequent as controls (61.9% versus 32.1%). The PSQI global score was 7.0 ± 3.9 in MS patients compared to healthy controls (4.6 ± 3.7), and was influenced significantly (p 0.0001) by EDSS-score and age. Sleep latency was longer in MS patients (31 min vs. 19.5 min in controls). Sleep duration did not show any difference concerning EDSS subgroups. Sleep efficiency was lower in MS-patients compared to controls; it was significantly influenced by increasing EDSS and age. Sleep disturbances were reported more frequently by MS patients, increasing with EDSS and age. Compared to healthy controls, sleep quality and sleep efficiency were markedly reduced. Patients who suffered significantly more frequently from sleep disturbances and daytime dysfunction, had a significantly longer sleep latency and used sleeping medication significantly more frequently than controls. The mean FSS score of the patient sample was 5.18 (± 1.41). 98 patients (21.1%) were classified as non-fatigue and 392 patients (79.9%) as fatigue. Regression analysis revealed a significant influence of EDSS-Groups on the VAS-score: it increased from 3.9 (EDSS £ 3,5) to 5.9 (EDSS ≥ 7). The mean SDS Index of all patients was 52.38 (± 13.0). According to the cut off scores of the SDS, 184 patients (36.5%) had no signs of depressive symptoms; 104 (20.6%) showed signs of mild depression; 82 (16.3%) of moderate to severe depression and 9.3% of definite severe depression.
Conclusions: Different factors are involved in the etiology of sleep disturbances and fatigue in multiple sclerosis patients. Sleep disturbances may be three times more common in MS than in the general population (Clark 1992) and are often a reason of MS patients to contact their family physician (Donker 1996).

0883.O

Six-Month Donepezil Treatment Alters REM Sleep Parameters in Alzheimer's Disease Patients: a Double-Blind Placebo Controlled Study

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Introduction: REM sleep is affected by Alzheimer's Disease (AD). Anti-cholinesterase drugs are known to improve cognitive deficits in these patients. We hypothesized that donepezil could improve REM sleep disturbances in AD patients, and that it could correlate with clinical cognitive improvement. Objectives: a) to study the Sleep EEG during REM sleep of AD patients before and after donepezil treatment; b) to assess the effects of donepezil treatment on sleep structure; c) to establish a possible correlation between ADAS-cog scoring improvement and REM sleep variables.
Methods: Thirty-six mild and moderate AD subjects, 24 women (76.5±9.3 years) and 12 men (74.5± 6.5 years) were allocated in two groups: 6-month donepezil and placebo treated groups in a double blind fashion. Polysomnography (PSG) and REM sleep spectral analysis with brain mapping of the AD patients were performed during three nights: basal, after 3 and 6 months of treatment. In all groups basal PSG was preceded by 2 habituation PSGs. FFT during REM sleep was performed in frontal, centro-parietal, temporal, occipital brain areas, and total averaged electrodes. REM sleep EEG slowing index (RESESI) was defined as: RESESI= delta+theta/alpha+beta (absolute power). All the patients undergo to ADAS-cog testing before the 1st PSG, and after 3 and 6 months of treatment. Statistics: Two-way ANOVA followed by Duncan's multiple range test, Kruskal-Wallis and Spearman correlation were used.
Results: REM sleep percentage was significantly increased after 3 and 6 months of donepezil treatment compared to baseline and placebo ($p<0.01$). REM sleep EEG spectral analysis showed a significant decrease in global theta ($p=0.04$), frontal delta ($p=0.03$) and theta ($p<0.01$) bands absolute power, in donepezil group. ADAS-cog scores significantly decreased after donepezil intake (p=0,02). There was a negative correlation between ADAS-cog scores and REM sleep percentage in AD patients before treatment [R= 0,35; t(n-2)= 2,18; p=0,04], and a positive correlation with stage 2 NREM sleep [R= 0,39; t(n-2)=2,51; p=0,02], theta frontal absolute power [R= 0,32; t(n-2)= 1,99; p=0,05], temporal theta [R= 0,33; t(n-2)= 2,06; p=0,04], and temporal delta [R= 0,46; t(n-2)= 2,99; p<0,01]. There was also a positive correlation between ADAS-cog and RESESI in temporal [R= 0,37; t(n-2)= 2,38; p=0,02] and occipital areas [R= 0,37; t(n-2)= 2,34; p=0,02]. However, no correlation was found between ADAS-cog and REM sleep variables after donepezil treatment.
Conclusions: Donepezil was able to improve AD REM sleep related alterations, both in PSG and spectral analysis. This improvement was parallel with cognitive improvement. Cognitive tests did not correlate with REM sleep parameters after donepezil treatment.

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0884.O

Prevalence Of Residual Movement During Sleep, In Patients With Diurnal Quadriplegia Secondary To Severe Spinal Cord Injury

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Introduction: There has been one documented case of quadriplegia {American Spinal Injury Association (ASIA) grade A} where 2 ASIA grade improvements have occurred more than two years after spinal cord injury. Despite clinical paralysis, it is suspected that residual intact spinal cord (which cannot be differentiated from scar by magnetic resonance imaging) may exist. In such cases, functional electrical stimulation (FES) of the extremities may allow spontaneous regeneration of neural signals below the level of injury.
Methods: Our research in the critically ill has allowed us to record electromyographic (EMG) activity in quadriplegia/paresis from spinal cord injury during full polysomnographic (PSG) examinations.
Results: In four patients studied, we observed no waking clinical or EMG motor activity, but marked activity in sleep. In our normal, healthy, volunteer adult population, without spinal cord injury, body movements decrease in sleep, but generally persisted to a lesser extent. In our population of 12 males, 5 subjects had body-movements in sleep with a mean body-movement index {the average number of body-movements per hour of sleep (BMI)} of 10, and in our population of 14 women, 9 subjects had body-movements in sleep with a mean BMI of 20.
Conclusions: These findings suggest that in quadriplegics, connections between cortex/brainstem sleep centers and spinal movement centers exist. Using PSG/EMG, these connections might be quantified and qualified. Patients with such findings might be more successful candidates for FES. Hopefully this data will be used to obtain extramural funding for large, prospective, therapeutic studies, where PSG will be performed in complete quadriplegics.

0885.O

Acute Ischemic Stroke And Sleep Apnea: Evolution Of Clinical Findings, Diffusion-weighted MRI, And Blood Pressure In The First 3 Days After Stroke Onset

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Introduction: Sleep apnea (SA) is present in about 50% of patients (pts) with acute ischemic stroke. Hypoxia and hemodynamic changes accompany SA. Diffusion-weighted magnetic resonance imaging (DWI) detects ischemic injury early after stroke onset. The extent of DWI changes correlates with stroke severity and predicts stroke outcome. The objective of the study was to test the hypothesis that in the acute phase of stroke moderate-severe SA leads to an enlargement of the ischemic volume on DWI that is more pronounced than in pts without SA.

Methods: We include pts with neuroradiologically proven ischemic stroke and hospital admission within 12 hours after stroke onset. Stroke severity is estimated by NIH and Scandinavian stroke scale (NIHSS, SSS) at admission (day 1), day 2 and day 3. Clinical stroke progression is defined as a decrease >= 2 points in conscioussness or motor power or >= 3 points in speech scores in the SSS. Sleep breathing is assessed by an intelligent CPAP device (Autoset® Portable II plus, ResMed) the first night after admission. Moderate-severe SA is defined by an apnea hypopnea index >25. Blood pressure (BP) monitoring is performed at intervals of 30 minutes with an ambulatory device (bp one, Cardiette) from 7 p.m. of day 1 until 7 a.m. of day 3. Mean systolic and diastolic BP values are calculated for daytime and nighttime. Nighttime BP dipping is defined by a ratio of nighttime/daytime mean systolic and/or diastolic BP values of <0.9. MR imaging is performed on a 1.5 T MR system at 7 p.m. of day 1 and again 7 a.m. of day 3. Stroke volumes are measured on DWI.

Results: We included so far 8 pts with a mean age of 64 years (range 44-83). Sleep breathing and blood pressure recordings were performed in all pts, acute and follow-up MRI studies were completed in 4 pts. At admission the mean NIHSS was 12 (range 2-17) and the mean SSS was 35 (range 24-56). Moderate-severe SA was present in 5 pts. Three of these 5 pts had a clinical stroke progression which was accompanied in two pts by a clear-cut increase of stroke volume on DWI (from a mean value of 18 cm3 to 39 cm3). In three pts SA was mild or absent. None of these pts had a clinical stroke progression and only one of them had an increase of stroke volume on DWI. Mean values of blood pressure were not statistically different in pts with and without moderate-severe SA (daytime values: 159/102 vs 148/94; nightime values: 147/91 vs 150/94). A nighttime BP dipping was absent in 2 of 5 pts with, and in all 3 pts without moderate-severe SA.

Conclusions: Preliminary results of this ongoing project suggest that in pts with acute ischemic stroke moderate-severe SA may lead to 1) clinical stroke progression, and 2) increase of stroke volume on DWI within the first 3 days after stroke onset. These detrimental effects may not be related to the presence or absence of a nighttime BP dipping.

0886.O

Orexin-A (Hypocretin-1) Levels in Cerebrospinal Fluid of Patients with Sleep and Neurologic Disorders

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Introduction: An association of low (<200 pg/ml) or undetectable (<10 pg/ml) CSF orexin-A levels with classical narcolepsy (narcolepsy with cataplexy) was observed in several recent studies. A few patients with other neurologic and sleep disorders and with both low and high CSF orexin-A levels have been reported. The objective of this study was to verify the theory that orexin transmission dysfunctions (as assessed by CSF orexin-A determination) may be present in neurologic and sleep disorders other than narcolepsy with cataplexy.

Methods: In 73 patients with a variety of neurologic and sleep disorders CSF orexin-A levels were determined by a highly sensitive radioimmunoassay. Based on our overall results and data from recent studies, orexin-A levels were classified as undetectable (<10 pg/ml), low (< 200 pg/ml), normal (200-600 pg/ml), and high (>600 pg/ml).

Results: In the entire population CSF orexin-A levels ranged from undetectable to 1280 pg/ml, with a mean value of 469 (median 491) pg/ml. In 56 patients with such diagnoses as narcolepsy without cataplexy (n=6), idiopathic hypersomnia (n=10), Creutzfeldt-Jakob disease (n=5), and limbic paraneoplastic encephalitis (n=3) orexin-A levels were considered normal. In all 7 patients with narcolepsy with cataplexy, orexin-A levels were low (mean 70 pg/ml, n=2) or undetectable (n=5). Low orexin-A levels were also found in one patient with posttraumatic hypersomnia (176 pg/ml). High orexin-A levels were observed in 8 patients including such diagnosis as diffuse Lewy body disease (mean 1136 pg/ml, n=3), Guillain-Barré-Syndrome (1117 pg/ml, n=1) and idiopathic hypersomnia (1130 pg/ml, n=1) .

Conclusions: Our data confirm that undetectable and low CSF orexin-A levels are highly sensitive and specific to narcolepsy with cataplexy. Preliminary results of this ongoing project suggest, in addition, the presence of an altered orexin transmission in a variety of other sleep and neurologic disorders including posttraumatic hypersomnia, diffuse Lewy Body disease and Guillain-Barré syndrome. The clinical and pathophysiological implications/significance of these findings remain unclear at present time.

0887.O

Normal CSF Hypocretin-1 Levels in Autopsy-Proven Alzheimer's Disease ± Lewy Body Disease

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Introduction: Recent studies indicate that most patients with narcolepsy have reduced levels of hypocretin-1 in cerebrospinal fluid (CSF), with values <200 pg/ml generally considered abnormally low and characteristic of narcolepsy. Such studies have involved comparison groups of patients with neurologic disorders other than narcolepsy, which have included some patients with clinically diagnosed AD. There are no data on CSF hypocretin-1 levels in autopsy-proven Alzheimer's disease (AD) or Lewy body disease (LBD) patients. We therefore sought to determine if hypocretin-1 levels can be quantified from stored samples of CSF of autopsy-proven AD ± LBD patients, and to determine if any difference in hypocretin-1 level exists between AD versus AD+LBD samples.

Methods: We measured CSF hypocretin-1 levels in a sample of patients with dementia enrolled in either the Mayo Alzheimer's Disease Patient Registry, the Mayo Alzheimer's Disease Research Center, or the Mayo Oldest Old Study who had undergone autopsy. CSF samples had been taken <72 hours after death and were frozen. The CSF (1 ml) was extracted and hypocretin-1 assays were performed with a radioimmunoassay (Phoenix Pharmaceuticals, Belmont CA).

Results: This sample involves 24 patients who had dementia, underwent autopsy between 1992 and 2001, and frozen CSF was available for analysis. The neuropathologic findings of AD were present in 17 and combined AD/LBD in 7. In the AD group, mean age at the time of death was 86 years (range 62-100 years), and the mean hypocretin-1 level was 645 ± 267 pg/ml. The mean age of death for the AD/LBD group was 90 years (range 85-94 years), and the mean hypocretin-1 level was 765 ±

200 pg/ml. There were no significant differences between the AD and AD/LBD groups for age or hypocretin-1 level ($p>0.05$). Only 1 patient among the 24 had a hypocretin-1 level below 200 pg/ml (159 pg/ml); she had AD pathology at her death at age 91, but there were no antemortem features of narcolepsy.
Conclusions: These findings indicate hypocretin-1 can be measured in the CSF of patients with AD ± LBD despite their advanced age, moderate to severe dementia at the time of death, and long duration from the time of CSF collection and freezing to CSF hypocretin-1 quantification. Hypocretin-1 remains above 200 pg/ml in the vast majority of patients with AD ± LBD. The clinical significance of the low hypocretin-1 level in the patient with AD is not known.

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0888.O

Persistent REM Sleep Reduction after Hemispheric Stroke

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Introduction: The role of cerebral hemispheres in REM sleep generation/modulation remains controversial. The aim is to report a persistent REM sleep reduction following focal hemispheric lesions.
Methods: Among a series of 27 consecutive patients with hemispheric stroke prospectively assessed by repetitive polysomnography (Vock et al., 2002) 5 patients with a first hemispheric ischemic stroke and persistent reduction of REM sleep were found. Severity of stroke was assessed by the NIH stroke scale (NIHSS). Stroke outcome was estimated by Barthel Index and modified Rankin score. The stroke volume was calculated from diffusion-weighted MR images. The sleep EEG was recorded over the non-affected hemisphere in the acute (3-8 days; n=5), subacute (10-35 days; n=4), and chronic phase (5-25 months; n=5) of stroke. The sleep EEG was visually scored according to international criteria. Data were compared with published norms (Williams et al., 1974).
Results: There were 3 men and 2 women with mean age of 50±12 years (range:34-68). Stroke was right-sided in 3 patients. Stroke topography was variable (2 deep, 2 superficial, 1 multiple). The mean stroke volume was 30±24 ml (6-56 ml). The median NIHSS was 7 (2-11). The Barthel index was 99 (95-100) and the modified Rankin score was 1 (1-2). Amounts of REM sleep were significantly decreased (>2 standard deviations from published norms) in all phases of stroke: 38 min (range: 14-39) acutely; 82 min (77-109) subacutely; 44 min (32-52) chronically. These REM sleep changes were invariably associated with a significant reduction in sleep efficiency (SE): 64% (49-76) of total sleep time acutely; 86% (77-95) subacutely; 80% (67-92) chronically. Changes in NREM sleep did not parallel the reduction of REM sleep and SE.
Conclusions: Amounts of REM sleep can be reduced after isolated hemispheric stroke over up to 25 months. These changes do not seem to correlate with specific stroke severity, topography, volume, or outcome. These data suggest a role of the cerebral hemispheres in the control of REM sleep generation.

0889.O

Low Hypocretin 1 (Orexin A) and Delayed Phase of Melatonin in a Patient after Subarachnoid Hemorrhage

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Introduction: Low CSF hypocretin is diagnostic for narcolepsy (Mignot 2002) and has also been found in a patient with secondary narcolepsy after diencephalic stroke (Scammell 2001). Moreover, cerebral ischemia has been found to alter orexin 1 receptor mRNA expression (Irving 2002).
Methods: We serially assessed hypocretin (CSF from ventricular drain) and sulfatoxy-melatonin (urine) every two hours during a period of 7 consecutive days in a patient with an external ventricular drain and in whom serial CSF sampling was performed as part of another protocol. Additionally core body temperature, sleep and wake behavior and ambient room temperature were recorded at every sampling time. The patient was a 60 year old male who suffered a spontaneous SAH in October 2001 and developed secondary complications with hydrocephalus and PICA infarction. At the time of the sampling he was awake, obeying commands but still bedridden. He had no sleep disordered breathing.
Results: Hypocretin 1 values in CSF were generally very low (63-110 pg/ml) and showed a circadian variation with its minimum at 12pm and maximum at 4am. Sulfatoxy-melatonin in urine peaked at 8am. Core body temperature reached its nadir at 2pm. Peak illumination was at 12am with 288±182 lux. Behaviorally the patient showed a high probability of sleeping (80-100%) at 0, 2, 4 and 10am, and a low probability (0-40%) at 8am, 2 and 6pm. Sleep probability was intermediate (40-80%) at 6 and 12am and at 4 and 10pm.
Conclusions: In this critically ill patient remarkably low CSF hypocretin was present although diurnal variation and phase were maintained and similar to findings in other animal and human studies (e.g. Yashida 2002). Melatonin phase was delayed compared to published findings in normals and melatonin peak was paralleled by falling core body temperature. The delayed peak of melatonin secretion occurred during the daylight period and is therefore probably not attributable to melatonin supression by residual night time illumination in the ICU. Sleep wake behavior did not follow a clear mono- or biphasic pattern but depended on time schedules for social interactions at the ICU.

0890.O

Sleep Disorders in Autosomal Dominant Spinocerebellar Ataxia (SCA): A Genotype-Phenotype Study

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Introduction: SCA is a group of familial diseases with dominantly inherited cerebellar ataxia causing olivopontocerebellar atrophy. Clinical signs include a progressive and severe cerebellar ataxia, and sometimes ophtalmoplegia, upper motor neuron palsy, parkinsonism, and areflexia (1).
Methods: Since patients complained of fatigue and occasional dyspnea, we explored sleep –using overnight polysomnography- and diaphragm function –using magnetic cervical and transcranial stimulation of the diaphragm and oesophageal pressure- in 13 patients with an identified inherited ataxia.
Results: The molecular analysis identified an abnormal expansion of trinucleotide CAG repeats coding for polyglutamine in SCA 1 gene (6 patients), SCA 2 gene (2 patients) and SCA 3/Machado-Joseph Disease (5 patients). The mean age of the group was 42 ± 16 years and the mean disease course was 11 ± 5 years. Two SCA 1 patients had a severe central diaphragm dysfunction associated with a reduced REM sleep duration (14 min) in one patient. The mean arousal index of the group was 35 ± 19 per hour, the apnea-hypopnea index was16 ± 11 and the periodic leg movement index was 27 ± 26 (table) . Seven patients, mostly SCA 1 (5/6) had a periodic leg movement syndrome. Six patients had a

moderate obstructive sleep apnea syndrome (2/2 SCA 2; 3/5 SCA 3).
Conclusions: Although motor symptoms may be similar, periodic leg movements is a feature of SCA 1 patients while obstructive apnea characterize SCA 2 and SCA 3 patients.

0891.O

High Incidence of Sleep Disorders in Multiple Sclerosis Patients

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Introduction: Fatigue is a frequent and debilitating symptom in multiple sclerosis (MS). We routinely screen all of our patients for sleep disorders with a simple questionnaire. If appropriate, polysomnography (PSG) is scheduled. The frequent findings of previously unrecognized sleep disorders in our MS patient population suggested that sleep disorders might contribute to the high incidence of the symptom of fatigue in this population. The present study was undertaken to determine the frequency of concurrent sleep disorders in our MS patient population.
Methods: The present study involved a retrospective chart review of 102 sequential patients who had a diagnosis of clinically definite MS (CDMS), in order to investigate the incidence of sleep disorders confirmed with PSG (and MSLT when appropriate). Besides obtaining patient demographics, we tabulated the duration of symptoms of MS, the length of time since the diagnosis of CDMS and the type of sleep disorder. Other variables were also tabulated including the specific treatment for the sleep disorder found, Respiratory Disturbance Index (RDI), and Epworth Sleepiness Scale (ESS).
Results: Of the 102 patients, 31 were male and 71 were female with a mean age of 45.6. Adjusting for missing data the mean duration of MS symptoms was 10.8 years (range 1-45) and the mean length of time since confirmed MS diagnosis was 7.6 years (range 1-44). The average male weight was 191 lbs and the average height was 70.9 inches; the average female weight was 178 lbs and the average female height was 65.2 inches. In reviewing the 102 MS patients, 45 patients had a concurrent sleep disorder diagnosis confirmed by PSG. The sleep diagnoses found were as follows: 32 with obstructive sleep apnea (OSA), 3 with upper airway resistance syndrome (UARS), 15 with periodic limb movement disorder (PLMD), 1 with idiopathic hypersomnia, and 5 with abnormal PSG with elevated arousal index due to unknown etiology. Several of the patients had two diagnoses (9 with OSA and PLMD, 2 with UARS and PLMD).
Conclusions: Sleep disorders appear to be more prevalent in the MS population than has been reported in the general population, occurring in 44% of the MS patients in this series. This striking finding suggests the need for screening for sleep disorders in MS patients complaining of fatigue. Further research into the influence of successful treatment of sleep disorders on fatigue in MS is warranted.

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0892.O

Prevalence and Characteristics of Sleep Disturbance in Patients With Partial Seizures

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Introduction: Subjective sleep disturbance has been reported to occur with greater prevalence in patients with epilepsy than in the general population, although the exact prevalence is unknown. Even less is known about the characteristics of sleep disturbance in epilepsy and the impact sleep disturbance may have on quality of life, functioning and epilepsy itself.The study here reported was undertaken to:(1) Evaluate the prevalence and characteristics of subjective sleep disturbance in patients with partial seizures (partial seizures)(2) Identify factors contributing to sleep disturbance(3) Evaluate the relationship between sleep disturbance and quality of life.
Methods: The following questionnaires were sent to 1183 patients with PS, being treated with one or two antiepileptics, registered in four Dutch epilepsy and neurology clinics: Demographic- and Short-Health-Questionnaire; WHO-Epilepsy-Questionnaire; SF-36 Health Survey (Quality of Life, QOL); Sleep-Diagnosis-List (SDL, evaluating last 6 months); Medical Outcomes Study-Sleep Scale (MOS, last four weeks); Groningen-Sleep-Questionnaire (GSQ, previous night); and Epworth-Sleepiness-Scale (daytime sleepiness). Each patient was asked to find two matched controls.
Results: Questionnaires were completed by 486 patients (mean age: 45; range 19-85 years) and 492 controls (43; 18-81). All SDL-subscores (primary insomnia, periodic leg movements, excessive daytime sleepiness, narcolepsia, psychiatric SD, obstructive apnea) were significantly higher in patients than in controls, even after correcting for factors influencing sleep. MOS and GSQ showed similar differences. SD (based on SDL) occurred in 38.7% of patients and 17.9% of controls. Compared with controls, patients had lower QOL-scores on mental health (-28.2 [95%CI -38.8, -17.6]). Independently, SD were associated with diminished mental health QOL-scores of -75.3 [-85.9, -64.8]. Similar differences were found for physical health QOL-scores.
Conclusions: Sleep disturbance is associated with a significant impairment in quality of life. Both sleep disturbance over the previous 6 months and poor previous night's sleep are twice as prevalent among patients with partial seizures compared with matched controls. Patients with partial seizures and sleep disturbance have greater impairment in quality of life than those without and than controls. The possible impact of sleep disturbance on the diagnosis and management of partial seizures may often be overlooked. Further study should be undertaken to better understand the relationship between sleep disturbance and partial seizures and its potential impact on the optimal management of epilepsy.

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0893.O

Polysomnographic Evaluation of Sleep Disturbance in Neuropathic Pain

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Introduction: Sleep disturbance is often associated with chronic pain, but the nature of the relationship is poorly understood. Previous studies of sleep disturbance associated with non-neuropathic chronic pain have not uncovered a consistent relationship between subjective levels of sleep disturbance and objective findings by polysomnography (PSG). This study was designed to evaluate sleep disturbance in neuropathic pain using PSG and sleep and pain questionnaires in subjects who had reported disturbed sleep of at least 3 months duration immediately prior to entry into the study and who had not taken drug treatment for these conditions in the previous week.
Methods: 11 men and 8 women with moderate to severe levels of postherpetic neuralgia (PHN) or painful diabetic peripheral neuropathy (DPN) and comorbid sleep disturbance were enrolled. Sleep disturbance was evaluated subjectively via daily diary and MOS-Sleep Scale and objectively via PSG at home on two consecutive nights. Pain and mood

questionnaires were also completed (daily diaries, Short-form McGill pain and the Profile of Mood states). Mean scores were compared with normal reference values (PSG and questionnaires), with values previously reported for patients with chronic non-neuropathic pain, and with baseline values in large clinical trials of pregabalin in neuropathic pain (questionnaires).
Results: Subjects reported significant disturbance of sleep quantity, and adequacy as well as interference with sleep. The objective PSG measures indicated disturbance of sleep quantity, continuity, and architecture. Patients reporting sleep disturbance also reported elevated pain.
Conclusions: Self-reported sleep disturbance in subjects with neuropathic pain co-exists with PSG- demonstrated sleep disturbance. This is in sharp contrast to subjects with chronic non-neuropathic pain, in whom there is no consistent relationship between PSG findings and subjectively reported sleep disturbance. The relationships between neuropathic pain syndromes and sleep disturbance warrant further exploration, as the extent of their independence and interdependence may have implications for the pharmacologic treatment of neuropathic pain.

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0894.O

Epworth Sleepiness Scale (EPSS) and Sleep Apnea Questionnaire (SAQ)in Patients with Acute Stroke
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Introduction: Several studies have appeared in the literature identifying sleep disordered breathing as a risk factor for cardiovascular events. Patients with acute stroke appear to have a higher prevalence of sleep-related disordered breathing. Yet little is known regarding the premorbid prevalence of sleep apnea in these patients.
Methods: We asked 20 patients or family members, during either a hospital stay for an acute stroke or at their initial outpatient follow-up appointment after recent inpatient admission for acute stroke, to complete the SAQ, the EPSS, body mass index (BMI), neck size, hip width, abdominal girth and smoking history. Patients were instructed to answer the questionnaire based on symptoms experienced prior to their stroke event. Descriptive statistics were calculated and subgroups were compared using paired t-test ($p<0.05$).
Results: 20 patients surveyed had an average EPSS of 10.1, with 9 patients having a score greater than or equal to 10 and 4 patients were over 15. The mean SAQ score was subtotalled 18.5 out of a potential 40. 14 patients snore and 7 noted nightly loud snoring. 8 patients noted difficulty breathing in the supine position and 5 patients experienced witnessed apneic spells on a nightly basis.
Conclusions: We found a high prevalence of excessive daytime sleepiness preceding the acute event of stroke. This suggests that sleepiness and potentially sleep apnea may be a premorbid condition for those at risk for stroke. Further studies are needed to delineate the relationship of sleep-disordered breathing and stroke.

0895.P

Sleep Disorders in Pregnancy
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Introduction: Several physical, emotional and social changes during the life span can lead to sleep disorders. Pregnancy is example of morphologic, functional and psychological changes. In the different trimesters of pregnancy, the mainly clinical complains are sickness, giddiness, somnolence, emotional changes and decreased libido. During this critical period, alterations are determinated by organic modifications, expectations due to the new condition and preoccupations with professional changes. Pregnancy can lead to sleep disorders that are due to physiological parameters, including mechanic and hormonal factors. The main goal of this research is to verify the frequency of sleep complaints during the three trimesters of pregnancy in comparison to the pre- gestational period.
Methods: Three hundred pregnants were interviewed at Obstetrician Center of UNIFESP-EPM, in São Paulo, Brazil. We analized one hundred patients in each trimester. The pregnants range from 11 to 40 years. Two of the authors applied a pregnant sleep disorders oriented anamnestic sheet. Independent variables: insomnia, respiratory disturbance, parassomnia, severe daytime somnolence, mild daytime somnolence, non-specific awakening, specific awakening and general or mood symptoms, according to The International Classification of Sleep Disorders - (ICSD 1991). We applied Chi-Square and Fisher Tests to the data.
Results: Insomnia was significant during the second trimester. Mild Daytime Somnolence showed significance in the second and third trimesters. To Severe Daytime Somnolence, non-specific Awakening, Specific Awakening and General or Mood Symptoms were significant statistically in all trimesters.
Conclusions: Pregnancy has significant impact in the pregnant sleeping quality. There is an important increase of sleep complaints during the pregnancy when compared to the pre-gestational period, except Respiratory Disturbance and Parasomnia.

0896.P

Self-Reported Sleep Problems in Patients with Asthma
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Introduction: People with asthma will often report nocturnal symptoms such as cough and are prescribed medicines such as prednisone, that promote sleep disruption. In addition, snoring and apnea are reported to occur in many asthmatics and treatment of sleep apnea will improve asthma control. Despite this literature, there is no consistent recognition strategy for sleep problems in asthma clinics. Objective: To utilize the Cleveland Sleep Habits Questionnaire as a means of identifying patients with chronic symptoms that would be associated with a high pretest probability for sleep apnea (OSAHS), restless legs syndrome (RLS), narcolepsy, and insomnia in patients with asthma
Methods: Surveys were distributed to patients waiting for an appointment in the asthma clinic at the MetroHealth Medical Center, Cleveland, Ohio. Items addressed included; the frequency of snoring behavior, waketime sleepiness or fatigue, history of obesity/hypertension for composite high risk for sleep apnea (Netzer et al 1999); several other symptoms were scored as positive vs. negative risk for insomnia, narcolepsy, and restless leg syndrome. Data were also collected on the asthma severity using the National Asthma Education and Prevention Program guidelines for diagnosis and management of asthma. Data were analyzed using SPSS 10 Software (Chicago, Illinois).
Results: 179 consecutive patients completed the questionnaire. Mean age was 48 yrs (range 19 to 82); with 46, males and 129 females, mean BMI, 33 (range 15 to 78); and Epworth Sleep Scale; 8 (range 1 to 24). The mean FEV1 was 73% of predicted, mean FEV1/FVC ratio was 89% of predicted. 39% met high-risk criteria for OSAHS; 41% for insomnia; 19 % for restless legs syndrome; and 4.4% for narcolepsy. 9.4% reported use of sleeping pills or bedtime alcohol every day. Based on patients BMI there was a difference in the prevalence of self-reported sleep problems as shown below: OSA Risk(%) Insomnia(%) RLS(%) Narcolepsy(%)BMI>30 53 36.6 20.8 4BMI<30 23 46.7 16.2 5.4 Bivariate analysis showed no correlation between the severity of

asthma and self -reported sleep disorders

Conclusions: Many patients with asthma have a high pre-test probability for sleep problems and disorders, specifically obstructive sleep apnea hypopnea syndrome. An elevated BMI(>30)substantially increases the probability of being at a high risk for OSAHS, but did not alter the risk for other sleep disorders. The severity of asthma was independent of a composite score for these self-reported sleep disorders.

0897.P

The Relationship Between Fatigue and Light Exposure in Breast Cancer

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Introduction: Fatigue is one of the most common and long-lasting complaints among cancer patients undergoing chemotherapy. One theory is that the fatigue is secondary to disturbances in circadian rhythms. Disturbed circadian rhythms can also result from poor light exposure, however, little is known about the association between fatigue and light exposure in this population.

Methods: Data were collected as part of a larger study. 34 women (mean age 51.0 yrs, SD 11.0 yrs, range 34-79 yrs) diagnosed with I-IIIA breast cancer and scheduled to receive 4 cycles of adjuvant or neoadjuvant anthracycline-based chemotherapy were included. To evaluate fatigue, a short form of Multidimensional Fatigue Symptom Inventory (MFSI-SF) was administered before the start of chemotherapy (week 0) and during weeks1-3 of cycle 1 and 4. A higher total suggests more severe fatigue. Light exposure was measured with Actillumes (Ambulatory Monitoring, Inc.), worn for 72 consecutive hours before (week 0) and during chemotherapy (week1). Lux value was calculated by 3 time periods: out-bed (out of bed time according to patients' diaries), in-bed (in bed time according to patients' diaries) and evening (a portion of out-bed time between 6pm and midnight). Correlations between total scores of MFSI-SF and light exposure intensity (lux) of week 0 and week1 were computed.

Results: There were no significant correlations between fatigue and light during week 0. However, during week 1, there was a significant correlation between mean lux and total MFSI-SF scores (r=-0.44, p=0.01) for out-bed period. The total scores also correlated significantly with percent time >1000 lux (r=-0.37, p=0.03), as well as percent time> 2500 lux (r=-0.35, p=0.04). There were no significant relationships for in-bed or evening time.

Conclusions: These data suggest a relationship between fatigue and light exposure in breast cancer patients during their first week of chemotherapy. Although the causality of fatigue and light exposure in breast cancer patients is not confirmed, it may be possible that less light exposure desynchronizes patients' circadian rhythms which then causes or deteriorates fatigue, and fatigue further leads to less light exposure. If this negative feedback loop does exist, increasing breast cancer patients' light exposure adequately during daytime may be an effective way to improve their quality of life by decreasing fatigue.

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0898.P

Changes in Sleep and Fatigue During Radiation for Prostate Cancer

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Introduction: Cancer-related fatigue is a significant clinical problem. When it occurs and its pattern and severity are not evident from prior studies. In addition, few studies have examined changes in sleep patterns that may contribute to fatigue. The purpose of this study was to describe changes in sleep and fatigue during radiation therapy (RT) for prostate cancer, from pre-radiation simulation to the end of RT.

Methods: Data were collected from 52 men (42 White, 7 Black, 3 Other); 24 were Stage 1, 22 were Stage 2, and 6 had Stage 3 prostate cancer. Wrist actigraphy (Ambulatory Monitoring, Inc., Ardsley, NY) was used to estimate sleep for 48 hrs each wk. Other measures included an 18-item Fatigue Scale (completed morning and evening) and a 21-item Sleep Disturbance Scale. Data from the 2 nights were averaged and repeated measures analyses of variance were used to test within-subject changes over time (9 weeks) in: time in bed (TIB), total sleep time (TST), wake after sleep onset (WASO), daytime sleep, evening/morning fatigue, and perceived sleep. Post-hoc Scheffé tests were used to determine peak changes.

Results: A total of 38 men had complete fatigue data and 29 had complete actigraphy data for all 9 time points. Evening fatigue was lowest at baseline (3.5 ± 2.48) and increased significantly (Fs8,296s=2.75, p=.006) by the last wk (4.4 ± 2.62). There were significant peaks at 5th wk (p=.02) and 8th wk (p=.03). Morning fatigue was lower than evening fatigue, but increased (Fs8,272s=3.85, p< .001) over time at a higher slope (from 1.65 ± 1.66 to 2.92 ± 2.52), and also peaked the 5th wk. Self-reported disturbed sleep increased from baseline 34.8 ± 15.9 to 45.2 ± 22.1 the last wk (F=12.2, p<.001). TIB increased slightly over the 9 wks (477 ± 57 to 494 ± 68 mins) with a peak at 4th wk of RT (498 ± 57 mins). TST also peaked 4th wk (397 ± 60.4 mins), and only slightly decreased from baseline 383 ± 7.8 mins to last wk (378 ± 88.4 mins). WASO steadily increased, from $14.8 \pm 11.1\%$ at baseline to a peak ($20 \pm 14.7\%$) 6th wk of RT and $19.7 \pm 16.6\%$ the last wk (F=2.86, p=.01). Bladder irritation, frequent voiding, and hot flashes were the primary reasons cited for awakenings.

Conclusions: TIB (8 hrs), TST (6.5 hrs) and day sleep (36 mins) did not change over time, while WASO increased from baseline15% to peak at the 6th wk of RT and stayed at 20%. Morning and evening fatigue peaked during 5th wk of RT and continued high until the end of RT. The higher slope for morning compared to evening fatigue indicates that sleep may not be as restorative at the end of 8 wks of RT as it is pre-radiation. To reduce fatigue, persons undergoing RT for prostate cancer should be advised to increase their night's sleep to compensate for increased awake time during the night.

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0899.P

Anterior Cervical Spine Fusion And Sleep Disordered Breathing: An Unreported Complication

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Introduction: Anterior cervical spine fusion is a regularly performed surgical procedure. The fusion can be performed between different vertebrae. If C2 to C4 are involved, the surgeon can access the vertebrae from the anterior neck and thus operate at the level of the upper airway. Obstructive sleep apnea syndrome (OSAS) may be caused by abnormal anatomy of the upper airway. The Bernoulli effect is the decrease of air

velocity at a constriction when the volume of flow remains constant. The lower pressure at a narrowing will increase the tendency for a soft tube collapse. Anterior spine fusion may lead to reduction of the size of the upper airway.
Methods: A retrospective evaluation was performed of 12 patients with complaints of fatigue and daytime sleepiness, using patient and bed partner interview, Visual Analog Scales, polysomnography and Multiple Sleep Latency Test. Subjects were treated with nasal CPAP. This investigation was followed by a prospective investigation of 4 patients using similar subjective and objective scales and tests. These patients were investigated before anterior cervical spine fusion, and post-operatively.
Results: Retrospective and prospective patients presented similar clinical history and evaluation findings following anterior cervical spine fusion involving C2 to C4 with progressive development of upper airway obstruction during sleep and related daytime symptoms. Symptoms and objective findings were controlled with nasal CPAP. The placement of the anterior cervical plates led to size reduction of the upper airway behind the base of the tongue. Upper airway obstruction develops during sleep as suggested by the Bernoulli principle.
Conclusions: Specialists should be aware of this potential risk and monitor for this secondary complication.

0900.P

Sleep-Activity Profile and Quality of Life In Patients With Stable Coronary Disease

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Introduction: Previous studies have examined the relationship between initiation sleep difficulties and quality of life. However, when reviewing the literature in this area we found no reports of a relationship between evening physical activity and health related quality of life in patients with coronary disease. This study was designed to investigate assumed sleep, circadian rhythm, evening physical activity and health related quality of life.
Methods: Twenty-six men and 21 women, mean age 64.0 (SD 8.9) years and 63 (SD 9.3) years, respectively, with stable angina pectoris were included. For assessment of health related quality of life the patients completed the SF36 questionnaire. The data were compared with those for men and women in the general Swedish population. Physical activity was continuously recorded at home, using actigraphy with an integral light recorder (Model AW-L, Cambridge Neurotechnology Ltd, UK) in 1-minute epochs during one week. The data were downloaded by Actiwatch Reader and imported to the Actiwatch software for Windows 98.
Results: Average time of going to bed was 22.37, sleep latency 27 minutes, assumed sleep duration 7.59 hr, time in bed 8.56 hr and sleep efficiency 79.2%. No differences were found during the seven nights. Non parametric analysis of the circadian rhythm showed that 39 of 47 patients had the lowest 5-hour count activity onset at 00.00 p.m. and 41 of 47 patients had the maximal 10 hr count onset 08.00 a.m. or later. Sleep analysis indicated reduced activity in the evening (p.m. 06.00-09.00). Some actigraphic parameters of the evening activity associated significantly with circadian rhythm parameters. Compared to the general Swedish population, the patients´ health related quality of life was poor. Linear stepwise regression analysis showed that reduced activity 3 evenings/week significantly explained health related quality of life in 32.3% of role function outcome, due to physical causes ($p=0.0001$) and in 24.7% ($p<0.01$) of social function, whereas reduced activity 2 evenings/week explained 20% ($p<0.01$) of body pain.
Conclusions: These data indicate that sleep-activity profile is associated with health related quality of life in patients with stable angina pectoris.

0901.P

Comparison Of Sleep-Wake Complaints In Whiplash Associated Disorder And Fibromyalgia

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Introduction: Sleep-wake complaints are frequently observed in patients with Late Whiplash Syndrome and have been studied previously (Schlesinger et al., Guilleminault et al.). Pain (neck, shoulder and back region) is the most common complaint in these patients and nocturnal pain can play a major factor in this sleep disturbance. In this study we compared the subjective sleep-wake complaints in a group of WAD patients with an active control group. Fibromyalgia (FM) patients were chosen as they suffer from chronic pain and as sleep disorders have been evidenced repeatedly in these patients. A major difference between these two chronic conditions is that in contrast with FM, WAD started with a trauma.
Methods: Fifty-two patients who received an ICD-9 diagnosis 847 (whiplash) or 723.1 (cervicalgia) at the emergency department of the University Hospital during 2001 were contacted for this study. 24 (11 males, 13 females, mean age 33,2, SD=11.9) agreed. Neuroimaging (CT, RX, MRI) was available from 23 patients.12 patients were on chronic medication (analgesics, hypnotics and sedatives).23 FM patients agreed to participate (3 males, 20 females, mean age 43.7, SD=8.2).Subjective sleep quality was derived from the Pittsburgh Sleep Quality Index (PSQI). A cut-off score of 6 was used. The Epworth Sleepiness Scale (ESS) assesses daytime somnolence in eight common situations. A cut-off of 10 was used. The Profile of Mood States (POMS) assesses five aspects of mood. The chi-square statistic was used to compare observed vs. expected frequencies in each category (under/above cut-off and patient group).
Results: Epworth: 8 on 24 (33.3%) of the WAD patients had a EES >10 compared to 19 on 23 (82.6%) of the FM ($2 =11.67$; $p<0.001$). Pittsburgh: 12 on 24 (50.0%) of the WAD patients had a PSQI >6 compared to 20 on 21 (95.2%) in the FM group ($2 =11.16$; $p<0.001$). As some questionnaires were not filled out completely, some missing data exist. Significant differences between the two patient groups were found in the POMS subscales Tension ($p<0.06$), Depression ($p<0.03$) and Fatigue ($p<0.01$) each time indicating a worse mood state in the FM groups vs.WAD.
Conclusions: Although chronic pain is common in the two medical conditions studied, sleep-wake complaints are far more frequent in FM patients than in WAD. In fact both sleep problems and daytime somnolence occur in nearly all FM patients. Although the prevalence of sleep-wake complaints in WAD patients is much lower, it is a matter of scientific and clinical importance as half of the patients studied report sleep problems and one in three has daytime sleepiness. In addition to being part of a post-traumatic syndrome their sleep problems should also be investigated to exclude sleep-related breathing disturbances as already reported by Guilleminault, but also PLM due to axonal stretching or even minor lesions in sleep regulating brain areas due to the traumatic impact.

0902.P

Neuropsychiatric Longterm Outcome In Patients With Kleine Levin`s Syndrome And Periodic Hypersomnia

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Introduction: To assess personality features and neurocognitive functions in patients with Klein-Levin`s syndrome (KLS) and periodic hypersomnia (PH). These rare disorders are characterized by periodic

hypersomnia, hyperphagia and abnormal behavior in variable combinations. Their potential association with persistent neuropsychiatric/neurocognitive impairment is controversely discussed in the literature.
Methods: All patients (n=10) recieved the diagnosis of KLS (n=7) or PH (n=3) at the University of Berne between 1965 and 2001 according to international criteria and were available for a follow-up assessment. A clinical interview and standardized self-assessment scales including personality features (FPI-R), depression (BDI), sleep (PSQI) and daytime sleepiness (Epworth Sleepiness Scale=ESS) were performed. Cognitive assessment included measures of intelligence, attention, memory and executive functioning.
Results: Concerning personality features, in five or more patients Stanines were below average for frankness (6/10), inhibition (5/10) and emotionality (5/10). BDI sum score was low compared to published norms (3.44 vs. 6.45, p=0.035, two-tailed). PSQI global score was higher than in normal controls (mean 4.3 vs. mean 2.67, p=0.014, two-tailed), whereas no difference was found in daytime sleepiness (ESS scores for both). IQ and neurocognitive functions were within normal range in 7 out of 8 patients.
Conclusions: Our findings show that LKS and PH are not associated with long-term/permanent neuropsychiatric/neurocognitive dysfunctions. Personality features such as frankness, inhibition and emotionality may differ, however, compared to the normal population.

0903.P

REM And Slow Wave Sleep (SWS) In Different Sleep Cycles In Patients With Prader-Willi Syndrome

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Introduction: The sleep/wake cycle disruption has been reported in patients with Prader-Willi syndrome. The aim of the present study was to investigate the distribution of REM sleep (regulated by circadian mechanisms) and SWS (regulated by homeostatic mechanisms) in Prader-Willi patients throughout the night. We hypothesized that patients with Prader-Willi Syndrome would have aberrant circadian rhythms of REM distribution in different sleep cycles and normal distribution of deep sleep across the night.
Methods: Six non-medicated consecutive patients (3 males and 3 females, aged 17.8±9.8) with an established diagnosis of Prader-Willi syndrome were investigated in the study. A single scorer blindly reviewed the polysomnographic findings according to standardized criteria. The duration of REM sleep and slow wave sleep episodes in each sleep cycle was calculated. Statistical analysis was performed using general linear procedure (SPSS for Windows).
Results: Data were derived from the analysis sleep cycles in six patients. There was a statistically significant decrease in SWS duration from the first to the subsequent sleep cycles (F=11.2 p=0.01). The highest amount of SWS was observed during the first sleep cycle in all patients. Amount of REM sleep did not significantly differ from cycle to cycle (F=3.5; p=0.09) and the amount of REM sleep in the latter cycles was not significantly increased over the previous cycles.
Conclusions: REM sleep in non-medicated Prader-Willi patients had an abnormal pattern of distribution in different sleep cycles without a clear increase in REM sleep towards the early morning hours indicating disruption of the circadian oscillator. In contrast, slow wave sleep distribution across the night was normal with the highest amount of deep sleep in the first half of the night and the least amount of SWS towards morning hours.

0904.P

Fatigue And Perceived Sleep Quality In Women With Breast Cancer

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Introduction: Fatigue during cancer and its treatment is a debilitating and common symptom. Cancer fatigue has been defined as a form of tiredness that does not abate following rest, and likely involves mental, emotional, and physical domains. Its etiology is unknown but has been proposed to involve age, stage, time since diagnosis, and/or possible abnormalities in muscle metabolism, vagal nerve afferents, or an HPA axis/serotonin feedback loop. Complaints of disturbed sleep are also common in cancer, but little is known about whether the fatigue bears any relationship to quantity of sleep or to the sleep/wake circadian rhythm.
Methods: 42 women with newly diagnosed breast cancer participated in the study (age range 34-79 years, mean=51;SD=10). Stages of disease included I (n=14), II (n=16), III (n=7), and III-A (n=5). During the week prior to initiating chemotherapy, these women completed the Multidimensional Fatigue Symptom Inventory (MFSI) and the Pittsburgh Sleep Quality Index (PSQI).
Results: MFSI fatigue ratings in these patients were comparable to published values in cancer populations, and suggest substantial fatigue (range=-24–67, mean=7; SD=20 with higher scores indicating greater fatigue and negative scores indicating very low fatigue and high vigor). PSQI scores also suggest a fair amount of sleep disturbance (range=0–15, mean=7; SD=3.3). MFSI fatigue scores were highly correlated with PSQI scores (Spearman's rho=0.524, p<0.0005), but were not significantly correlated with patient age (p=0.16). An ANCOVA of total MFSI fatigue as the dependent variable (using PSQI and age as continuous covariates and stage as a class variable) shows that PSQI scores significantly contribute to fatigue ratings (F=14.73, p<.0005), that patient age contributes marginally to fatigue (F=3.83, p=.058), and that disease stage is unrelated to fatigue (F<1).
Conclusions: These results suggest that fatigue and disrupted sleep are experienced by women with breast cancer even prior to chemotherapy, and further, that perceived sleep disturbance is strongly associated with feelings of fatigue. Interestingly, the high degree of association between disturbed sleep and fatigue is not solely determined by patient age nor stage of disease. It remains to be determined whether objective sleep amounts or daily timing of the sleep period or exposure to bright light are related to fatigue in cancer patients.

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0905.P

Association Between Sleep Complaints and Visual Impairment: A Verification Study

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Introduction: Recently, we showed a relationship between self-reported visual impairment and sleep complaints in urban older Americans. This finding is important as visual impairment might cause circadian rhythms abnormalities. However, it remains unclear whether individuals

reporting sleep complaints have in fact eye diseases that can be verified with ophthalmic tests. It may be that eye diseases compromise light input to the suprachiasmatic nucleus, which controls melatonin, body temperature and sleep wake cycles. Thus, sleep complaints reported by older adults may be a sequela of circadian malsynchronization. This study further explored the relationship between sleep complaints and visual impairment as defined by standard ophthalmic examinations in a community-based sample of older adults.

Methods: A total of 70 volunteers from a biracial cohort participated in the study (mean age = 68.27 ± 5.97 years; mean BMI = 27.68 ± 5.72 kg/m2); 73% were female and 27% were male. Participants completed baseline questionnaires soliciting information on sociodemographic characteristics and physical health. The physical health questionnaire included questions on whether or not the volunteer experienced sleeping difficulties and visual impairment. Volunteers meeting study criteria were scheduled for a comprehensive eye exam at SUNY Downstate Medical Center.

Results: Forty-six percent of the participants reported visual impairment at baseline. Twenty-seven percent were visually impaired according to American criteria (best corrected vision less than 20/40 and better than 20/200 in the better eye). Twenty percent of the volunteers received an eye diagnosis; specifically, 5.8% had glaucoma; 7.2%, cataract; and 7.2%, ocular hypertension. To verify whether volunteers with a sleep complaint (i.e., difficulty initiating sleep, difficulty maintaining sleep, early morning awakening, or daytime napping) also had eye dysfunctions, Fisher¡¦s Exact tests were used. Results indicated that those (35%) who reported napping were more likely to receive an eye diagnosis vs. those that did not (12%) [Fisher¡¦s value = 4.45, df = 69, p = 0.04]. No significant relationships were found between eye diagnosis and the other sleep complaints.

Conclusions: Our findings indicated that individuals with visual impairment may not necessarily experience difficulty initiating sleep, difficulty maintaining sleep, or early morning awakening. The finding of a greater likelihood of daytime naps among volunteers with an eye diagnosis is interesting, and may have two different explanations. One possibility is that older adults with visual impairment may be spending more time indoors, thus providing them with a greater opportunity for napping. Another possibility is that eye diseases might diminish light-induced regulation of the sleep-wake cycle. Accordingly, the sleep-wake period would be redistributed throughout the 24-hour day, such that sleep is attempted both at night and during daytime to compensate for sleep loss due to nocturnal awakenings. Previous research has shown that some older adults take naps both in the afternoon/evening as well as in the morning after final awakening without their awareness. It is of interest to examine further the relations between visual capacity and circadian synchronization in the elderly.

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0906.P

Comparison of Objective and Subjective Sleepiness in Monozygotic Twins Discordant for Chronic Fatigue Syndrome

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Introduction: Chronic fatigue syndrome (CFS) is a disorder of debilitating fatigue of ≥ 6 months duration in the absence of a medical or psychiatric etiology. Fatigue and sleepiness can be difficult to differentiate, with patients often using these terms interchangeably. We sought to identify the role of objective and subjective sleepiness in CFS via the Multiple Sleep Latency Test (MSLT) and Epworth, and Stanford sleepiness scales (ESS and SSS, respectively) in monozygotic twins discordant for CFS. This co-twin control study design allowed us to adjust for the strong genetic influence on sleep.

Methods: Nineteen pairs of monozygotic twins (mean age 42, 89% female) in which 1 member had CFS and the other was healthy underwent overnight polysomnography followed by a 4 nap MSLT. Sleep diaries were filled out and all drugs known to affect sleep were discontinued for 2 weeks prior to the MSLT. The ESS was completed prior to the naps and the SSS was filled out immediately after each nap. In addition, the twins were asked categorical questions regarding their perception of daytime sleepiness and alertness. Data were analyzed using matched pair t-tests, intra-class correlation estimates, and mixed effects linear regression models.

Results: There was no difference in the MSLT mean sleep latency between the CFS twins (9 minutes, 95% CI 7-11) and their healthy siblings (10 minutes, 95% CI 7-12, intra-class correlation estimate = 0.63). No sleep onset REM periods were appreciated. In contrast, the CFS twins more often endorsed sleepiness as measured by the ESS (CFS = 11, 95% CI 9-13; healthy twin = 8, 95% CI 6-11; p £ 0.05, intra-class correlation estimate = 0.23) and SSS (CFS = 3.4, 95% CI 2.8-3.9; healthy twin = 2.1, 95% CI 1.6-2.5; p £ 0.001, intra-class correlation estimate = 0.23) than their healthy co-twins. These differences in subjective sleepiness remained significant in a linear regression model after controlling for total sleep time as measured by the 2-week sleep diary. Twins with CFS more frequently endorsed the statements “Now, I am very sleepy during the day and I struggle to stay awake” (p £ 0.001), and “I have not liked how sleepy I have been” (p £ 0.001). Lastly, no significant sleep disorders were present on the pre-MSLT overnight polysomnogram and total sleep time, sleep architecture, arousal index, sleep efficiency, and sleep latency were similar in both CFS and healthy twins.

Conclusions: Both the CFS and healthy twins had MSLT scores at the lower limits of normal, but CFS twins reported significantly more subjective sleepiness. The reason for this mismatch between objective and subjective sleepiness is unclear but CFS twins appear to experience a heightened awareness of sleepiness, perhaps accentuated by their underlying disabling fatigue.

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0907.P

Autonomic Cardiovascular Control In REM Sleep As A Marker Of Negative Risk In Coronary Artery Disease

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Introduction: Cardiac death during sleep was shown being mostly related to REM sleep which is mainly pronounced at morning hours. One of the reasons of cardiac events during REM sleep is related to increased adrenocorticotropine activity during REM sleep. From the other hand, there was shown clear-cut decrement of parasympathetic activity in REM sleep. The goal of the study was investigation of autonomic HR control in parallel to baroreflex sensitivity (BRS), QT interval and hemodynamics changes during REM sleep in coronary artery disease (CAD) patients.

Methods: Fifty six healthy subjects and 1335 CAD patients underwent polysomnography as well as 6-lead ECG, heart rate (HR) and stroke volume monitoring during sleep. Autonomic control was evaluated using HR power spectrum analysis. BRS was assessed as the slope of the regression line between spontaneous modifications of RR intervals and finger blood pressure fluctuations in 15 healthy subjects and 80 CAD pts. QT interval and QT dispersion, reflecting myocardial instability, were calculated from 6-lead ECG in 5 healthy subjects and 10 CAD

patients.
Results: HR modification during non-REM sleep were dependent on an increase of parasympathetic input and a decrease of sympathetic one; while HR changes during REM sleep were more dependent on a withdrawal of parasympathetic input rather than on an increase of sympathetic one. REM sleep, as compared with slow wave sleep, was characterized by significant decrease of stroke volume, especially in CAD patients displaying cardiac abnormalities. From the other hand, more frequent transitory ST-T segment depression was observed during REM sleep, especially in patients showing permanently reduced parasympathetic control. Wakefulness was characterized by more long JT interval and more high QT dispersion for CAD patients, as compared with healthy. Healthy subjects demonstrated a decrease of QT dispersion during non-REM sleep and a further decrease in REM sleep while post-MI patients and heart failure patients were characterized by significantly higher QT dispersion in parallel to augmented QT interval and HR frequency during REM sleep. CAD patients, as compared with healthy subjects, demonstrated depressed BRS in wakefulness and sleep. Nadir of BRS was seen during REM sleep for CAD patients, while healthy subjects demonstrated only non-significant changes. Thus, REM sleep, as compared to non-REM sleep and wakefulness, demonstrated the highest HR frequency and HR variability dependent on relatively increased humoral-adrenergic control due to decreased parasympathetic one followed by the lowest hemodynamics and BRS and increased QT interval dispersion and blood pressure in CAD patients, especially in patients displaying congestive heart failure. Decreased parasympathetic control, depressed BRS and increased QT interval dispersion in parallel to low hemodynamics' level were seen as negative prognostic markers for CAD patients.
Conclusions: Autonomic cardiovascular control, expressed as HR variability, baroreflex sensitivity, myocardial refractoriness as well as depressed hemodynamics demonstrate mostly negative prognosis having the highest risk for cardiovascular events, including cardiac death, during REM sleep for CAD patients.

0908.P

Wrist Actigraphic Measures In Adults Hospitalized For Severe Burn Injuries

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Introduction: Sleep disturbances, such as poor sleep quality, repeated awakenings and nightmares are often reported in hospitalized burn patients. The purpose of this study was to objectively evaluate activity and sleep disturbances throughout hospitalization, as well as to identify disturbing factors, especially pertaining to pain intensity and medication intake.
Methods: Sixteen oriented and non-ventilated burn patients (13M, 3F), between the ages of 21 and 49 years (mean = 36.3 $\pm$ 9.4) participated in the study. Patients wore a MicroMini Motionlogger actigraph (Ambulatory Monitoring, Inc.) on their wrist during hospitalization (mean = 10 days, range = 3-18) and were interviewed in the morning to assess subjective quality of sleep (10 cm visual analogue scale (VAS)), duration, fragmentation) and nighttime pain intensity (10 cm visual analogue thermometer (VAT)). Pain intensity during the day was evaluated at rest and during therapeutic procedures with the same VAT. A research nurse reviewed patients' medical charts to record analgesic and sedative medications. The actigraph data, collected in HI Proportional-Integrating Mode, were uploaded into the computer and then analyzed in Action-W software by applying the UCSD sleep algorithm. Data were analyzed with descriptive statistics, and time series regression analyses were used to examine temporal relationships between sleep, pain and medication variables.
Results: Patients reported sleeping an average of 391 minutes a night (SD = 142) with frequent awakenings (mean = 3.8 $\pm$ 7.5), and quality of sleep VAS scores averaged 5.2 (SD = 2.9). Between 23:00 and 08:00, actigraph data revealed that the length of sleep episodes varied from 14 to 257 minutes (mean = 60 $\pm$ 36.4). On average, patients slept 332 minutes (SD = 105) with numerous wake episodes (mean = 25.8 $\pm$ 9.5). Subjective and objective sleep variables were significantly positively correlated. All but one patient reported pain during the night with an average intensity rating of 2.6 (SD = 2.7) on the VAT. Pain at rest and during therapeutic procedures averaged 2.3 (SD = 2.2) and 3.6 (SD = 2.8) respectively. Significant negative relationships were observed between actigraph measured sleep variables, pain intensity, and analgesic medication , such that patients presenting worse sleep in terms of duration and fragmentation had more pain and received higher doses of analgesic medication (all Ps <.05). There were no significant relations between sleep variables and sedative medication.
Conclusions: To our knowledge, this is the first study to objectively determine sleep in burn patients with actigraphic measures. These preliminary results support previous findings that subjective sleep quality following burn injuries is poor, and strengthen the evidence of a relationship between sleep and sensitivity to pain. Nonetheless, further analyses are necessary to determine and dissociate the effects of pain intensity and analgesic medication on sleep.

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0909.P

Sleep Complaints Among Breast Cancer Survivors

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Introduction: Complaints of fatigue and sleep disturbance are common among individuals undergoing treatments for cancer. These complaints are to be expected due to the emotional and physical sequelae of a diagnosis of cancer and its subsequent treatment. Recent research, however, suggests that sleep complaints and fatigue persist for months, even years, after the initial treatment phase. A recent review of the literature found insomnia complaints among cancer patients and cancer survivors as high as 60 percent of those surveyed. Furthermore, one recent study found that breast cancer survivors meet the diagnostic criteria for chronic insomnia at twice the rate of the general population. Sleep disturbance, particularly chronic insomnia, among cancer survivors may play a deleterious role in recovery, recurrence, and return to baseline levels of daily functioning. The purpose of this study was to survey the health behaviors, risk perceptions, and quality of life of breast cancer survivors.
Methods: Women who had completed treatment for breast cancer at the Dana Farber Cancer Institute were asked to complete a 120-item survey regarding their current psychosocial functioning, including several sleep-relevant questions. These included the amount of time spent sleeping and/or reclining (hours/day), whether the individual continued to experience fatigue (5-point likert scale), whether the individual had any difficulty falling asleep (5-point likert scale), and whether the individual felt she experienced good sleep quality (5-point likert scale).
Results: The following results are from a sample of 238 women, with a mean age of 55.0 (sd=10.6). The women had completed their initial cancer treatments a mean of 26.2 (sd=18.2) months before completing the survey. Seventy-one percent of the sample was post-menopausal.Women reported sleep/reclining a mean of 8.1 (sd=1.5) hours per night. Sixteen percent of the sample reported frequent (sometimes or often) difficulty falling asleep at night. Forty-one percent of the sample reported that they did not sleep well either quite a bit or very often. Another 31 percent reported that they did not sleep well some of the time. Sixty percent of the sample reported continued fatigue.
Conclusions: The initial results (data collection is ongoing) of this sur-

vey indicate that many breast cancer survivors continue to experience poor sleep quality, difficulty falling asleep, and fatigue months, or even years, following the initial diagnosis and treatment of cancer. Further research is needed to clarify the degree of sleep disturbance, course of complaints, etiologies of the complaints, and impact on daily functioning and physical health and well-being.

0910.P

Association of Gastrointestinal Disorders with Sleep Disorders in a Random Adult Sample

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Introduction: Most studies that have examined the association between sleep disorders and gastrointestinal (GI) disorders are based on clinic samples with specific GI disorders studied in the sleep laboratory. The aim of this study was to define the relationships between GI and sleep disorders using a large random sample of the general population, which was designed to determine the prevalence of sleep disorders in the general population.
Methods: 12,219 women and 4,364 men (ages 20-100) were interviewed by random survey via telephone. From these, 1000 women and 741 men were selected for further study based on the presence of risk factors for sleep disordered (SDB) breathing. Each provided a structured history, had a physical examination and spent one night in the sleep laboratory. GI diagnoses were obtained directly from the physical examination and history, which included GI-related questions, and indirectly from the medication list and symptoms. Sleep disorders were categorized as excessive daytime sleepiness (EDS), insomnia (INS), and SDB. These data were evaluated using logistic regression with the GI disorder as outcome and sleep disorders as independent variables while controlling for age, BMI and gender.
Results: The GI diagnoses in the studied population were grouped into 7 categories, the most prevalent being acid peptic disorders (26.3%) and motility disorders (2.9%). The prevalence of each of the other 5 categories (liver disease, inflammatory bowel disease (IBD), anatomic alterations, neoplasia, and other) was £1.1 %. Acid peptic disorders were further divided into gastro-esophageal reflux disorder (GERD), peptic ulcer disease (PUD) & hiatal hernia (prevalence 24.3%, 3.3%, and 2.4% respectively). Six of the nine GI disorders were significantly associated with sleep disorders. Insomnia was associated with GERD, PUD, hiatal hernia and liver disease. EDS was associated with motility disorders and sleep apnea was associated with IBD. In addition, female gender was significantly associated with GERD, hiatal hernia and motility disorders. BMI was associated with GERD and hiatal hernia while age was associated with PUD, hiatal hernia and liver disease.
Conclusions: In a large random population study focused on sleep disorders it was ascertained that a significant association existed between GI disorders and sleep disorders. Specifically, acid peptic disorders were primarily associated with insomnia. This association supports the link between emotional stress and acid peptic disorders. In contrast, motility disorders were associated with EDS while IBD was associated with SDB. Further investigation is warranted to understand the link between specific sleep and GI disorders.

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0911.P

Impact Of Orthodontic Appliances On Sleep Quality - A Pilot Study

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Introduction: Young patients are often required to wear headgear, frankel or twin block appliances during sleep as part of their orthodontic treatment. The objective of this clinical study was to assess the impact of these orthodontic appliances on sleep quality.
Methods: Twenty-two subjects (14 female / 8 male) between 10-15 years of age and wearing either one of the appliances for 3 to 12 months were enrolled. Informed consent from their parents was obtained. Each subject participated in two overnight sleep studies (with and without their appliance), with a one week interval after an adaptation night. A standardized hospital based sleep laboratory was used and each subject served as his /her own control. There were 12 subjects with an extra-oral (headgear) appliance and 10 subjects with an intra-oral (5 frankel and 5 twin block) appliance. No subject reported any sleep or medical disorder. The primary outcome variable was sleep efficiency (SE). SE was 91.2% (SD 4.31) and 91.2% (SD 4.49) with and without appliances respectively.
Results: Comparing sleep with and without the appliance, analysis of variance using a crossover design revealed no significant difference in SE (p=0.74) or any other sleep variables such sleep onset latency (0=0.86), REM onset latency (p=0.96) or respiratory disturbance index (p=0.63). The RDI with the appliance was 2.1 and without the appliance was 1.3. Gender and body mass index were not confounding variables.
Conclusions: Previously, the influence of orthodontic appliances on sleep was based on descriptive subjective reports. In this study, objective criteria were examined. In young orthodontic patients, there appears to be no difference in sleep quality with or without the overnight use of these specific appliances after the appliances have been worn for a few months.

0912.P

Impact of a Cognitive-Behavioral Pain-Management Group on Sleep Complaints in a Chronic Pain Population

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Introduction: Prevalence rates of sleep complaints in chronic pain populations ranges from 40% to 80%. Depression, pain severity and cognitive arousal predict sleep disturbance, albeit with inconsistent findings. Cognitive-behavioral pain-management treatments (CBT) decrease both pain severity and depression. However, no studies have explored the effect of such treatments on sleep complaints.
Methods: From 1996-2002, self-report data were collected from 188 patients attending a 10-session pain-management group in a clinical behavioral medicine service. Measures included the Multidimensional Pain Inventory (MPI-2), Pain Anxiety and Symptom Scale (PASS), and Center for Epidemiologic Study-Depression scale (CESD). Dependent variables were the weekly nights of restless sleep (CESD item), and degree that pain interfered with sleep (MPI item). Treatment completers (n=68) were compared to non-completers (n=120) on these sleep items using the Mann-Whitney test. The impact of treatment on the two sleep items was assessed using the Signs test (n=65). Independent variables were regressed onto the dependent variable of restless sleep for all patients at pre-treatment using ordinal regression. A similar regression was conducted for treatment completers at post-treatment. A 19-item CESD score was derived by subtracting the restless sleep item from the CESD score.
Results: 78% of our sample complained of restless sleep at least 3 days per week (50% 5-6 days per week); 77% reported pain interfered with sleep at least moderately (49% extremely). There were no significant differences at baseline between treatment completers and non-completers on basic demographic factors, pain parameters, or mood except that non-completers were more likely to have a legal case pending. Com-

pleters did not differ from non-completers on the two respective sleep complaints (z=-.399, p=.690; z=-.106, p=.915). The pain management group, despite significantly decreasing pain, depression, and pain-related anxiety measures, produced no significant change in restless sleep or pain interfering with sleep (Sign Test z=-.530, p=.597; z=-1.249, p=.211). Finally, in regression models, duration of pain, depression, and pain-related anxiety accounted for 11% variance in restless sleep (Cox & Snell's pseudo R square), while pain severity and activity level did not contribute to the variance. At post-treatment, duration of pain, pain severity, pain-related anxiety and depression accounted for 40% variance in restless sleep.
Conclusions: This is the first study to test whether the benefits of CBT for pain would generalize to improving sleep. As expected from clinical experience, sleep was not significantly impacted despite reductions in pain and depression. Our predictive models of sleep contribute to the growing literature of inconsistent ability or minimal ability of pain severity and depression to predict sleep. Our findings do lend support to an arousal-based component of sleep complaints in that pain-related anxiety did predict sleep at both pre- and post-treatment. Using sleep items rather than scales tempers these findings and post-treatment regressions are limited by a small n. Nonetheless, these findings suggest that residual sleep complaints, even after successful CBT for pain, need to be addressed in chronic pain patients.

0913.P

Ratings Of Fatigue And Soluble ICAM-1 Levels In Breast Cancer Patients Pre- And Post-Chemotherapy

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Introduction: Fatigue is a common and distressing complaint in women with breast cancer. While impaired quality of sleep and/or depression may contribute to the increased fatigue, there has also been a concerted effort to identify underlying biochemical factors. Intercellular adhesion molecule 1 (ICAM-1), a glycoprotein from the immunoglobulin supergene family, is important for immune cell-mediated lysis of tumor cells. Levels of the soluble form of ICAM-1 (sICAM-1) are elevated in breast cancer, correlate with disease severity, and are predictive of treatment outcomes. This study examined fatigue and sICAM-1 prior to and following chemotherapy.
Methods: Twenty-one women (age range 34-79 years) diagnosed with stage I-IIIA breast cancer were studied. Fatigue and sICAM-1 levels were determined prior to and following cycle 1 (C1) and cycle 4 (C4) of adjuvant or neoadjuvant anthracycline-based chemotherapy. Ratings of total fatigue were determined by the Multidimensional Fatigue Symptom Inventory. sICAM-1 levels were determined by ELISA.
Results: Ratings of fatigue were increased following the first week of C1 chemotherapy [19.2 (SD=2.3)] as compared to pre-treatment ratings [6.11 (SD=21)], p=0.001). sICAM-1 levels were decreased following the first week of C1 chemotherapy [281 pg/ml (SD=73) vs. 311 pg/ml (SD=85)], p=0.003). By the second week after treatment, fatigue and sICAM-1 values were no longer significantly different from pretreatment values. Compared to C1, fatigue ratings were elevated during C4 of chemotherapy (p's=0.002). sICAM-1 levels were also significantly elevated at the start of C4 (p=0.038) and, as with C1, were decreased following the first week of treatment of C4 (p<0.001).
Conclusions: The findings suggest that sICAM-1 levels may be related to feelings of fatigue in women with breast cancer. Compared to pretreatment values, both sICAM-1 and fatigue were elevated at the start of fourth cycle of chemotherapy. These findings are promising in that they offer a potential new biochemical index of fatigue in breast cancer patients, an index with significant clinical linkage and which may track the ebb and flow of subjective reports of fatigue in response to standard therapy

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0914.P

Prevalence Of Sleep Complaints In Maintenance Dialysis Patients With End-Stage Renal Failure In Korea

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Introduction: Patients with end-stage renal diseases (ESRD) have an increased risk of sleep problems such as daytime sleepiness, insomnia, restless legs syndrome (RLS), and obstructive sleep apnea syndrome (OSAS). However, presently there is limited data available, particularly in Asia.
Methods: To investigate the prevalence of sleep complaints in ESRD patients, 100 patients at the maintenance hemodialysis (HD) and 100 patients at the continuous ambulatory peritoneal dialysis (CAPD) were surveyed using a specific questionnaire which included questions from the Stanford Sleepiness Scale, Epworth Sleepiness Scale, Insomnia Severity Index, Restless Legs Syndrome questionnaire, Pittsburgh Sleep Quality Index, etc. We have translated and validated the specific sleep questionnaire tools to Korean.
Results: Patients had a mean age of 50.58 $\pm$ 14.03 years, with a mean body mass index (BMI) of 21.8 $\pm$ 3.5 kg/m2. The mean duration of dialysis was 44.56 $\pm$ 49.74 months. Fifty-six percent of the dialysis patients were poor sleepers. Daytime sleepiness occurred 24% (by Epworth Sleepiness Scale) to 34% (by Stanford Sleepiness Scale), and insomnia occurred in 35% of the patients, while restless legs syndrome was reported in 44% of the patients. The insomnia group, compared to the non-insomnia group, showed a lower BMI statistically and tends to be more depressed ($p < 0.05$). The RLS group, compared to the non-RLS group, showed a lower blood urea level statistically and tends to be more depressed ($p < 0.05$).There was no difference in the prevalence of sleep disturbances between the HD and CAPD patients groups.
Conclusions: Complaints of sleep disturbance and daytime somnolence are very common in dialysis patients and likely contribute to the impaired quality of life experienced by many of these patients. Identifying and treating the sleep complaints in dialysis patients could contribute significantly to their quality of life and avoid potential side effects of nonspecific sedatives.

0915.P

Influence Of Pain And Opioid Analgesics On Nighttime Sleep And Daytime Functioning In Medical Oncology Patients

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Introduction: Although both cancer pain and its treatment with opioids have the potential to independently affect nighttime sleep and daytime wakefulness, their possible interactive effects remain to be described. The situation is complex in that opioid analgesics may improve sleep through reductions in pain intensity but are also known to interfere with sleep through other mechanisms. Some of our early work in this area suggests that opioids may specifically disrupt sleep regulatory processes by inducing increased daytime sleep and subsequent nocturnal sleep disruption. Therefore, the purpose of this ongoing descriptive-correlational study is to examine relationships among pain, opioids, and day and nighttime sleep in medical oncology patients, using both objective and

subjective measures.
Methods: The sample includes 41 adult oncology outpatients with solid tumor cancer diagnoses, who have at least one current opioid analgesic prescription and a Karnofsky Performance Status score of 50 or greater. Outpatients receiving radiotherapy or immunotherapy are excluded from study participation. Activity and rest patterns are objectively assessed over a seven-day period in the subjects' home environments using wrist actigraphy (the Mini Mitter Actiwatch). Subjects also complete the Brief Pain Inventory (BPI), the Pittsburgh Sleep Quality Index (PSQI), and the Epworth Sleepiness Scale (ESS).
Results: Data analysis reveals that this sample of medical oncology patients taking opioids has poor nighttime sleep characterized by decreased sleep efficiency (mean=78.4%, SD= ±9%) and increased intervening wake time during the night (mean=1 hour, 12 minutes, SD= ±29 minutes). In addition, subjects sleep an average of 3 hours, 11 minutes (SD= ±1hour, 50 minutes) during the day. Using the BPI, worst pain intensity reported in the last week is considerable—7.1 (SD= ±2.2) on a scale of 0 (no pain) to 10 (worst pain imaginable). Subjects with higher worst pain intensity (greater than 4) sleep one hour, 19 minutes longer during the day than those reporting lower worst pain intensity (4 or less). The PSQI global component mean score of 10.8 (SD= ±4.5) suggests that cancer patients taking opioids experience moderate to severe sleep difficulties, and the ESS total score mean of 9.9 (SD= ±4.8) indicates a greater than normal chance of dozing during the day.
Conclusions: These results are consistent with our previous findings that both pain and opioid use have adverse effects on day and nighttime sleep patterns. Future research designed to more closely examine the independent and interactive effects of pain and opioid use on day and night sleep/wake parameters in cancer patients is warranted and will ultimately provide a basis for the development of population-specific interventions to maximize pain relief while minimizing the side effects of sleep disruption.

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0916.P

Sleep and Headache: A Time-Series Analysis

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Introduction: Sleep disturbance is frequently cited as a precipitant of migraine and tension-type headache. Evidence for this relationship derives principally from retrospective surveys or cross-sectional designs that preclude conclusions regarding causality and obscure individual variability. Thus, the strength and direction of the association remain unclear. This prospective longitudinal study examined temporal relationships between daily sleep pattern and headache activity using time-series analysis with lagged correlations.
Methods: Participants were 49 recurrent headache patients presenting for treatment to a specialty university-based head pain center. Each participant had stable headache patterns for at least one year prior to their participation. Migraine (n = 25; 88% female; Mean age 46.0; range 24 - 68 years) and tension-type (n = 24; 79% female; Mean age 44.1; range 22 - 69 years) headache patients recorded sleep and headache activity daily for 28 days. Daily rating of headache severity (peak headache) was the dependent variable. Four lags of sleep (i.e., hours sleep per night) were tested as predictors of headache peak within each subject. To compare the headache groups on the temporal patterning of sleep-headache association, patients were classified into two groups based on the lag that produced the "most characteristic" correlation: (1) Lag = 0, if the correlation was lag 0; (2) Lag > 0, if the correlation was lag 1, 2 or 3, or (3) No Correlation.
Results: Large individual differences were observed in the sleep-headache correlations (r's = -.65 to .49). Sleep accounted for significant variance in headache over time for 46% of tension-type and 60% of migraine headache patients. For 21% of tension-type and 33% of migraine patients with a sleep-headache association, headache peak severity was best predicted by the preceding night's sleep. For the remaining patients (79% and 66% respectively), headache was best predicted by sleep from the preceding one to three days.
Conclusions: These findings suggest that sleep patterns play an important role in precipitating or exacerbating headache in approximately half of migraine and tension-type headache patients. Headache was best predicted by the prior night's sleep for only about one-fourth of the patients with a significant sleep-headache association. For the remaining patients, headache was best predicted by hours of sleep one to three nights earlier. These prospective data support anecdotal observations regarding the temporal patterning of the sleep-headache associations.

0917.P

Prevalence of Fibromyalgia and Sleep Complaints in Women with Systemic Lupus Erythematosus

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Introduction: The aim of this study was to ascertain the prevalence of fibromyalgia (FM) in patients with Systemic Lupus Erythematosus (SLE), and also to describe the associated sleep complaints and the degree of functional disability.
Methods: Consecutive outpatients from the Immuno-Rheumatology Department at the National Institute of Medical Science and Nutrition Salvador Zubirán (INCMNSZ) followed regularly at the clinic between February 2001 to October 2002 were asked to participate in the study. The study was approved by the local ethics committee and all patients gave their informed consent. One hundred eighty-nine SLE patients comprised the final sample of the study with a mean age of 38.5 years (range 16 from to 78) and a mean Body Mass Index (BMI) 25.6± 4.4 Kg/m2. All fulfilled at least 4 of the American College of Rheumatology (ACR) revised criteria for SLE. Disease activity was scored according to the MEX-SLEDAI. Fibromyalgia was diagnosed using the ACR criteria, by two trained examiners. The Sleep Disorders Questionnaire (SDQ), the Spanish Health status- Functional Disability (HAQ-DI), the Fatigue Severity Scale, and the Beck Depression Inventory (BDI) were administered the same day after the tender point and pain threshold determinations were obtained. Patients were receiving corticosteroids plus immunosuppressives (mean dosage of prednisone 8.7 mg/day, azathioprine 112.5 mg/day) and antimalarial (cloroquine 101 mg/day) plus nonsteroidal antiinflamatory drugs, and nine patients received no medication at all. Complete blood count, serum chemistry as well as urinalysis were obtained the day of exam. Patients were classified into 3 subgroups for analysis. All patients meeting the ACR 1990 criteria for the classification of Fibromyalgia were in the FM group (patients experienced pain on palpation of at least 11 of the 18 tender points examined, as well as reporting history of widespread pain). Patients who were noted to have more than four tender points in at least four areas were considered to have probable Fibromyalgia (PFM). All remaining patients not meeting criteria for either FM or PFM were classified as having no FM (non-FM)
Results: Eighteen of the SLE patients (9.5 %) met the ACR criteria for the classification of FM. Patients with PFM were 29.6% and the rest of the patients had no tenderness at any specific 18 tender point sites. An analysis of the principal-components of the SDQ yielded 4 meaningful

factors labelled: sleep fragmentation, narcolepsy-like symptoms, snoring and excessive sleepiness. FM group reported having more sleep fragmentation than the other groups (FM=3.1±0.8; PFM=2.4±0.9; non-FM=2.1±0.8, F=9.6, p<0.0001). Both the FM and the PFM groups differed from the non-FM group in the fatigue level and disability index (Fatigue non-FM=2.8±1.6, PFM=4.0±1.7, FM=4.4±1.8, F=14.7, p<0.001; HAQ-DI non-FM=1.8±2.9; PFM=5.2±5.4; FM=6.5±5.5, F=18.9, p<0.0001). A low correlation was found between depression and tender points (Spearman rho=0.36, p<0.001).
Conclusions: The results of this study demonstrate that fibromyalgia is uncommon in Mexican SLE patients, but considering that over time PFM patients may meet the criteria for FM the prevalence would then be approximately 39%, which is similar to the one reported in other populations. The presence of FM is a major determinant of the sleep fragmentation complaint and the severity of fatigue and functional disability in SLE patients.

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0918.P

Sleep Duration and Obesity

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Introduction: Introduction: Conventionally the major consequences of insufficient sleep are thought to be neurocognitive. Data suggest that insufficient sleep also alters endocrinologic and autonomic status. For example, 6 days of sleep curtailment associated with multiple consequences including decreased glucose tolerance and increased cortisol (Spiegel et al, 1999). Taken to its natural conclusion, insufficient sleep might lead to obesity. Recent data associated sleep <6 hours with an increased risk of obesity (Shigeta et al, 2001). This large pilot study investigated the hypothesis that shorter sleep duration correlated with increased BMI.
Methods: Methods: Approximately 250 patients were recruited from each of four primary care practices. The patients answered an anonymous questionnaire with the aid of nursing staff or a research associate. The questionnaire reviewed basic demographics (age, sex, weight, height), presence, duration and frequency of napping, shift work, bedtime and waketime and total hours in bed on weekdays and weekends including naps. It further inquired about general medical problems: DM, HTN,GERD, CHD, arthritis and asthma and weight loss preparations.. It canvassed for sleep disorders to include OSAS, narcolepsy, RLS, PLMS and insomnia. Finally, inquiries were made about basic sleep hygiene habits as caffeine, alcohol and smoking.
Results: Results: 1001 subjects took the survey. Age was 48 + 16.1 years, mean weight 187 + 47.4 lb, mean height 66.8 + 14.7 inches and mean BMI 30.2 + 7.3 kg/m2. 16.6% of the patients had DM, 39.2% HTN, 24.3% GERD, 9.2% CHD, 33% arthritis and 14% asthma. Mean sleep duration on weekdays was 461.8 + 109 minutes. Men admitted to 23 minutes less sleep on weekdays than women ($p < 0.001$). Significant relationship occurred between BMI and the prevalence of DM ($p < 0.001$), HTN ($p < 0.001$), GERD ($p=0.019$) and arthritis ($p = 0.005$). Total weekday sleep time (TST) within BMI groups of <25, 25-29.9 and 30-39.9 was associated with declining amounts of sleep (8.1, 7.9, 7.7 hours respectively). At BMI > 40, TST rose to 8.0 hours. $F(df = 3, 923) = 2$, $p = 0.043$) with a significant difference between the TST in the 30-39.9 BMI group and the <25 BMI group ($t(df = 551) = 2.003$, $P = 0.046$). With the exception of CHD medical problems were not associated with differences in sleep duration.
Conclusions: Conclusions: Our sample patients manifested obesity and a high prevalence of medical problems. Overall, the data suggests a trend towards decreasing duration of sleep until severe obesity is attained when sleep duration again increases. Previous data reveals that severe obesity in itself may cause excessive daytime sleepiness perhaps through inflammatory cytokines (Vgontzas, 1998). The authors postulate that insufficient sleep leads to hormonal and autonomic changes that predispose to obesity but that at levels of severe obesity is perhaps overcome by the aforementioned factors.

0919.P

Nocturnal Sleep, Daytime Sleepines, and Quality of Life in Patients on Chronic Hemodialysis

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Introduction: Despite the progress that has been made in the treatment of chronic renal failure, compromised quality of life remains a significant problem for many hemodialysis (HD) patients. Numerous factors likely contribute to this problem including stress, anemia, and vocational inactivity. Sleep disturbances are also very prevalent but their impact on the quality of life of these patients has never been examined. We thus studied a sample of HD patients to explore relationships between quality of life and measures of nocturnal sleep and daytime sleepiness.
Methods: The sample included forty-six stable HD patients, 24 men and 22 women, with a mean age of 51.6 (10.8) years. All subjects underwent one night of laboratory-based polysomnography followed the next morning by a Multiple Sleep Latency Test (MSLT) and completed a brief nocturnal sleep questionnaire and the Epworth Sleepiness Scale. Subjects also completed the Ferrans and Powers Quality of Life Index (QLI, Dialysis Version), an instrument that yields an overall quality of life score and four related subscale scores, including Health and Functioning (H&F), Social and Economic (S&E), Psychological & Spiritual (P&S), and Family (F). The range of scores on each scale is 0 to 30, with higher scores indicating better quality of life.
Results: The QLI scores obtained were similar to those previously reported in larger studies and were as follows (mean ± SD): overall QLI - 22.8 (4.0); H&F - 21.0 (4.7); S&E - 22.0 (4.8); P/S - 24.5 (4.4); and, F - 26.8 (3.5). Although ESS scores were unrelated to QLI scores, greater subjective difficulty falling asleep and waking up too early in the morning were significantly and negatively correlated with all four subscales scores and overall QLI ($r = -0.387$ to -0.490, $p = 0.004$ to 0.000). Feeling rested in the morning was positively related to S&E ($r = 0.325$, $p = 0.014$), P/S ($r = 0.319$, $P = 0.015$), and Total QLI ($r = 0.332$, $p = 0.012$). The H&F subscale score was positively associated with MSLT scores ($r = 0.278$, $p = 0.030$) and polysomnographic measures of nocturnal sleep latency ($r = 0.249$, $p = 0.48$), indicating higher life quality with lower sleepiness levels; overall QLI scores were also positively correlated with MSLT scores ($r = 0.263$, $p = 0.038$). H&F ($r = -0.326$, $p = 0.013$) and F ($r = -0.298$, $p = 0.048$) subscales were negatively correlated with periodic limb movement index. There were no significant relationships noted between quality of life measures and respiratory disturbance/brief arousal indices, total sleep time, or sleep efficiency.
Conclusions: Numerous factors have been previously associated with the compromised quality of life experienced by many HD patients. Our results demonstrate for the first time that quality of life may also be adversely affected by sleep-related variables including difficulties in initiating and maintaining sleep, not feeling rested during the day, physiologic sleepiness, and periodic limb movements. Thus, the recognition and appropriate management of sleep complaints and disorders may help optimize quality of life in these patients and further research designed to examine the effects of treatment on quality of life-related outcomes is warranted.

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0920.P

Sleep Characteristics Of Women Diagnosed With Preterm Labor

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Introduction: Elevated cytokine levels, particularly interleukin-1b (Il-1b) and tumor necrosis factor alpha (TNF-a), are believed to play important roles in the initiation of preterm labor, the occurrence of regular uterine contractions prior to 38 weeks gestation. These cytokines are also known to induce changes in sleep, suggesting a possible, but previously unexplored, association between sleep pattern changes and preterm labor. Thus, in order to begin a systematic examination of this potentially important relationship, we studied the subjective nocturnal sleep quality and daytime sleepiness in women experiencing preterm labor.
Methods: A convenience sample of 50 women hospitalized in an acute care medical center for preterm labor symptoms completed the Pittsburgh Sleep Quality Index (PSQI) and the Epworth Sleep Scale (ESS). Because hospitalization may adversely affect sleep, subjects were specifically asked to complete the instruments after reflecting upon their sleep during the 30 day period prior to their admission.
Results: The mean global PSQI score was 8.5 ($\pm$ 4.65), indicating poor subjective sleep quality, with overall sleep quality being reported as either "fairly bad" or "very bad" by 30% (n=15) of the sample. The average nocturnal sleep latency was 43 minutes ($\pm$ 64.25); 22% (n=11) of women reported sleep latencies ranging between 31-60 minutes with 14% (n=7) reporting sleep onset of greater than 60 minutes. The average sleep efficiency (SE) and total sleep time (TST) were 73.7% ($\pm$ 21.23) and 6.57 hours ($\pm$ 1.75), respectively, values significantly lower when compared to the polysomnographic measures of SE and TST of women experiencing normal pregnancies that have been previously reported in the literature (SE = $p < .0005$; TST = $p < .007$). Reasons given for nocturnal sleep disruption included the need to go the bathroom, difficulty in getting in a comfortable position, fetal movement, and feeling hot. In addition, 70% (n=35) reported greater sleep disruption after beginning treatment with terbutaline, an oral tocolytic drug often associated with tachycardia and nervousness, typically taken at 2-3 hour intervals throughout the night. Although 68% (n = 34) of the subjects reported some degree of daytime dysfunction associated with sleepiness, the mean ESS score was 8.3 ($\pm$ 4.35), indicating a relatively normal chance of daytime dozing.
Conclusions: These preliminary data suggest that women with pre-term labor have poorer sleep quality than those women with normal pregnancies, and that sleep disturbances may precede the onset of early labor. While further studies examining the relationship between preterm labor and sleep are warranted, current standard of care for women with preterm labor should include sleep assessment in order to identify those individuals who may benefit from interventions aimed at improving sleep quality.

0921.P

Reliability of Clinical Impression in the Differential Diagnosis of Disorders of Excessive Daytime Sleepiness (EDS)

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Introduction: Clinical impression is the first step in the diagnosis of any illness and of any sleep disorder as well. It should always precede and direct the choice of diagnostic procedures. Our goal, based on a large sample of subjects with a primary complaint of EDS, was to evaluate the sensitivity and specificity of the clinical impression in the differential diagnosis of EDS.
Methods: The charts of 1553 patients, 1135 male and 419 female, referred to the Montpellier Sleep and Wake Disorders Center, from January 1st 1991 to December 31st 2000, with a primary complaint of EDS, were thoroughly reviewed. The clinical impression after the first outpatient clinic visit was compared with the final diagnosis after completion of relevant diagnostic procedures. All subjects underwent polysomnography (PSG) followed by a multiple sleep latency test (MSLT), except those with a suspicion of recurrent hypersomnia who underwent a 36 hour continuous PSG and no MSLT. Other diagnostic procedures were chosen according to the clinical impression. Among these were static charge sensitive bed recording in those subjects with suspicion of obstructive sleep apnea and no apnea on the PSG (before October 1995), PSG with monitoring of oesophageal pressure (from October 1995), 36 hour continuous PSG, psychological evaluation, HLA typing.Diagnostic categories included items listed in the International Classification of Sleep Disorders (ICSD), narcolepsy (N), recurrent hypersomnia (RH), idiopathic hypersomnia (IH), posttraumatic hypersomnia (PTH), obstructive sleep apnea syndrome (OSAS), periodic limb movement disorder (PLM), insufficient sleep syndrome (ISS), hypersomnia associated with mental disorders (HAMD), long sleeper (LS); items not listed, snoring with respiratory abnormalities (SRA) (before October 1995), upper airway resistance syndrome (UARS) (from October 1995), narcolepsy without cataplexy (NWC), overlap syndrome (OS), relative of narcoleptic with isolated EDS; other etiologies (neurologic, metabolic, infectious); and unclassified cases either at first and/or after diagnostic procedures.Sensibility and specificity were calculated at their 95% confidence interval
Results: Final diagnosis was OSAS in 782 patients (50.3%), N in 164 (10.5%), HAMD in 103 (6.6%), other etiologies in 91 (5.8%), UARS in 77 (4.9%) and SRA in 53 (3.4%), PLM in 42 (2.7%), IH in 34 (2.2%), RH in 16 (1.0%), NWC in 13 (0.8%), OS in 10 (0.6%), LS in 7 (0.4%), ISS in 5 (0.3%), PTH in 4 (0.2%) and relative of narcoleptic with isolated EDS in 2 patients (0.1%). 150 patients (9.6%) remained unclassified.The sensitivity of the clinical impression was high in N (95.73) and OSAS (88.49), average in NWC (69.23) and IH (50.00) and low in HAMD (25.24), UARS (22.08), PLM (14.29) and the specificity was high in PLM (99.67), HAMD (99.04), N (98.42), NWC (97.22), IH (96.99) and average in OSAS.
Conclusions: The sensitivity and specificity of the clinical impression vary widely according to the various etiologies of EDS. These results are a preliminary step before discussing the type of error(s) in each etiology and improving the clinical interview.

0922.P

Sleep Patterns during Candida albicans-Induced Renal Disease in Mice

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Introduction: Various strains of mice demonstrate clear differences in susceptibility to infection with the fungal organism Candida albicans. After intravenous administration to mice, Candida typically colonizes the kidney, producing acute pyelonephritis. Human patients with end stage renal failure often develop disturbed sleep and severe fatigue, often in relation to hemodialysis. We characterized the sleep patterns of two relatively resistant strains of mice, C57BL/6J and BALB/cByJ, after acute challenge with Candida albicans to assess their suitability as a model for investigating the relationships between renal failure and alterations in somnolence.
Methods: Adult male BALB/cByJ and C57BL/6J mice (n = 4 and 5, respectively) were surgically instrumented for monitoring EEG and EMG, and were permitted at least 2 weeks for recovery and acclimation. Mice were housed in individual cages placed in sound-attenuating chambers on a 12:12 hour light:dark cycle at 21-22°C. Beginning at light

onset, sleep was monitored for 24 hours before and 72 hours after intravenous inoculation with 1x106 colony-forming units (CFU) of Candida albicans. At the time of euthanasia, serum was analyzed for creatinine, blood urea nitrogen (BUN), and glucose, and kidneys were cultured for fungal titers. Sleep was scored using standard methods.

Results: After intravenous inoculation with Candida albicans at light onset, both C57BL/6J and BALB/cByJ mice spent more time in slow-wave sleep (SWS), particularly during the dark phase. The SWS enhancement was somewhat greater in magnitude in C57BL/6J mice, which showed dark-phase SWS enhancement for the entire 72-hour post-inoculation recording period. In contrast, BALB/cByJ mice showed only marginal dark-phase increases in SWS time, and SWS time had normalized by day 4 post-inoculation. Both strains also demonstrated a marked suppression of REMS. The reduction in REMS time was less robust in BALB/cByJ mice than in C57BL/6J mice, but was reduced in both strains during the light phase and the initial 4 to 6 hours of the dark phase. Renal titers of Candida albicans were 11.7 ± 2.3 x104 CFU/g and 72.6 ± 29.1 x104 CFU/g for C57BL/6J and BALB/cByJ mice, respectively. Serum concentrations (mg/dl) of creatinine, BUN, and glucose were 2.5, 26, and 171, respectively, in mice treated with heat-killed Candida (n = 2); 3.5 ± 0.3, 56 ± 6, and 157 ± 13, respectively, in infected C57BL/6J mice; and 3.1 ± 0.5, 50 ± 9, and 99 ± 3, respectively, in infected BALB/cByJ mice.

Conclusions: Mice undergoing acute pyelonephritis induced by Candida albicans demonstrated reduced REMS and enhanced SWS. After recovery from the acute infection, these mice could provide a model system for the study of altered somnolence during chronic renal failure.

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0923.P

Hours of Sleep and Glycosylated Proteins: Investigating the Potential Role of Short Sleep Duration in Metabolic Dysfunction

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Introduction: Laboratory studies have shown a decrease in glucose clearance after acute sleep deprivation in normal subjects, leading to the hypothesis that chronic sleep deprivation may result in ustained metabolic dysfunction, possibly increasing the risk of glucose intolerance and diabetes mellitus. To test this hypothesis, we examined the relationship between habitual sleep length and levels of glycosylated protein in blood, an integrative measure of glucose regulation, in a population-based sample.

Methods: We used data from the Kuopio Ischemic Heart Disease Risk Factor Study, a prospective, population-based study implemented in Kuopio, Finland in the mid-1980s. The study population is a random, age-stratified sample of 42, 48, 54 and 60 year old men at the time of baseline data collection (n=2,682), who were reexamined 4 and 11 years later. The sample size was reduced to 2,426 after limiting the analysis to non-diabetics and respondents with non-missing responses for the variables of interest. Sleep-habit data was collected by questionnaire at all three waves of data collection, and glycosylated proteins were measured from blood drawn after a 12-hour fast within 2 days of administration of the questionnaire. The relationship between sleep hours and glycosylated protein was assessed using a generalized linear models (GLM) procedure in SAS v.8.02.

Results: The study population was categorized according to exposure groups based on usual sleep time, with 19.8% reporting 6 or less hours of sleep, 40.7% from 7 to 8 hours, 32.6% from 8 to 9 hours, and 6.9% 9 or more hours of sleep per night. The outcome variable, glycosylated protein, had a mean value of 267.5 and standard deviation of 37.1 mmol/l. Results from the GLM models found no difference in the mean level of glycosylated protein in the group reporting 6 or less hours of sleep (269.1 mmol/l), compared to those sleeping from 7 to 8 hours (267.3 mmol/l, p=.38), 8 to 9 hours (266.9 mmol/l, p=.30) and 9 or more hours (266.8 mmol/l, p=.49). Controlling for age and body mass index (BMI) in the analysis did not change the results. Further analysis assessing the age- and BMI-adjusted relationship between mean level of glycosylated proteins and a cumulative score of short sleep duration over the three waves of data collection did not find any relationship consistent with the hypothesis. Repeating the analysis using a measure of self-reported sleep need as the exposure resulted in similar findings.

Conclusions: These results do not support the hypothesis that chronic sleep deprivation, measured by short as well as inadequate sleep duration, leads to sustained glucose regulatory derangement. Limitations of this analysis include the absence of data on women and the use of self-reported hours and adequacy of sleep time, which may provide an imprecise index of sleep deprivation. Further work should address the potential role of loss to follow-up due to incident diabetes or mortality in influencing the results of these analyses.

0924.P

Impact of Kidney Transplantation on Sleep in Chronic Kidney Disease

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Introduction: While the association of advanced renal insufficiency with sleep complaints is well-recognized, few have pursued the underlying cause of these complaints. Some believe that the poor sleep and high rate of sleep apnea in those with ESRD is related to poor kidney function and that these sleep disorders should improve with kidney transplantation. However, weight gain and immunosuppressant medications may cause disturbed sleep architecture and an increased tendency for sleep apnea. Therefore, we are prospectively characterizing sleep in kidney transplant recipients.

Methods: Patients undergoing living donor kidney transplantation at NEMC were assessed by polysomnography, self-reported sleep quality and quality of life, and genioglossal EMG (GG-EMG) one month prior to transplant and 6 months following transplantation. The studies were performed at the Sleep Laboratory of NEMC and the sleep records were scored according to standard criteria independently of any knowledge of the experimental conditions. Patients were administered the Epworth Sleepiness Score and other sleep and HRQOL outcome measures. GG-EMG activity was measured using unipolar electrodes in the oral appliance referenced to a single ground, thus producing a bipolar recording. The EMG signal was amplified, rectified, and integrated on a moving-time-average basis, with a time constant of 100 ms. The intra-oral electrode appliance was inserted and the three-genioglossal maximal EMG maneuvers were performed. The subsequent EMG moving-time-average signal was scaled between 0 and 100% of maximum. The GG-EMG was subsequently recorded during the wake-sleep transition and during spontaneous obstructive events. The data are presented as mean (standard deviation).

Results: To date, 9 subjects have been enrolled. The demographic data is as follows: 89% men, 100% Caucasian, age 50 ± 11 years, and BMI 26.1 ± 3.6 kg/ m2. Five patients received a pre-emptive kidney transplant and had an estimated GFR of 11 ± 7 ml/min/1.73 m2. The baseline sleep architecture was as follows: total sleep time 344 ± 73 minutes, sleep efficiency 82 ± 13%, stage 1 sleep 29 ± 13%, stage 2 sleep 40 ± 7%, slow-wave sleep 20 ± 11%, REM sleep 14 ± 7%. The arousal index was 34 ± 23 , the apnea-hypopnea index 15 ± 8, and GG-EMG 2.2 ± 1.5%. The self-assessed outcomes were as follows: Epworth

sleepiness score 10.0 ± 4.8, hours of sleep 6.7 ± 2.8 h/day, and sleep quality score 5.4 ± 2.5 (range 1-10, higher better). There were no significant differences in sleep parameters between those on dialysis and those receiving a preemptive kidney transplant. The two subjects who have completed the study have similar sleep architecture to their baseline studies. However, the AHI increased in one subject (from 6 to 18), but decreased in the second (from 28 to 13).
Conclusions: While the follow up data are only preliminary, the baseline data demonstrate a high prevalence of sleep apnea, reduced amounts of slow wave sleep, frequent arousals, and a high rate of self-reported daytime sleepiness among patients with advanced kidney disease and kidney failure.

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0925.P

Sleep Complaints In A Group Of Patients With Fibromyalgia
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Introduction: Fibromyalgia (FM) is commonly associated with sleep complaints, daytime sleepiness, insomnia, and nonrestorative sleep. This is supported by altered polysomnographic findings such as increased arousals, decreased total sleep time and delta frequency sleep. The spectrum of sleep complaints has not been systematically studied in a large population of fibromyalgia. We are reporting sleep-related symptomotology in 79 patients with FM, who were diagnosed by rheumatology specialists and were referred to our sleep clinic.
Methods: We retrospectively reviewed all sleep questionnaires (CCF Sleep-Disorders Questionnaire) of patients with FM who underwent polysomnography between 1999-2002. All subjects met the criteria for FM. The questionnaire pertains to symptoms of excessive daytime sleepiness (EDS), insomnia, sleep-related breathing disturbances (snoring and apnea), sleep-related periodic limb movements, parasomnias, narcolepsy, and morning headaches. Objective data included the Epworth Sleepiness Scale (ESS), body mass index (BMI) and Beck Depression Inventory scale (BDI). An abnormal ESS was defined as > than 10. A BMI value of >27.3 Kg/M2 was considered abnormal. A BDI scale was defined as abnormal if the value was > 11.
Results: There were 79 patients with FM (71 females, 8 males) with a mean age of 48 years (range 25-77). Sleep complaints included EDS (81%), snoring (63%), insomnia (59%), morning headaches (26%), witnessed apneas (24%), restless legs symptoms prior to sleep (18%), periodic limb movements during sleep (13%), hypnogogic hallucinations (13%), sleep paralysis (11%), acting out dreams (9%), bruxism (5%), and cataplexy (4%). Patients had a mean ESS of 12 (range of 1-22), mean BMI of 33 (range of 18-73), and mean BDI of 16 (range of 1-37).
Conclusions: These patients with FM have a wide range of sleep complaints that extends beyond what is commonly reported. This may help explain their symptomotology of daytime fatigue and generalized pain. The disproportionate number of females, compared to males with FM, in our study is consistent with the higher prevalence of females in FM. Larger population studies of FM patients are needed to further elucidate the role of sleep disturbance in the symptomotology of FM.

0926.P

Characterization of Patients Undergoing Routine Polysomnography Prior to Bariatric Surgery
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Introduction: Bariatric surgery is increasingly being recognized as an effective treatment for patients with morbid obesity. Such patients are at increased risk for obstructive sleep apnea (OSA) and often undergo polysomnography during their pre-operative assessment. However, there presently is no consensus as to which patients should undergo pre-operative polysomnography. At our institution we have routinely performed polysomnography prior to bariatric surgery. The following summarizes our experience.
Methods: We reviewed the records of all patients referred for routine polysomnography prior to bariatric surgery from September 2001 to November 2002. Demographic data including sex, age, height, weight, BMI and neck circumference were recorded. Historical features recorded included: history of hypertension, history of witnessed apneas, history of snoring, Epworth Sleepiness Scale(ESS) and history of tobacco use(>10 pack-years). Polysomnographic data analyzed included: RDI, RDI-REM, RDI-supine and minimum SaO2. The occurence of post-operative respiratory complications was noted. Patients were grouped into severe (RDI>40) and non-severe (RDI<40) categories based upon the RDI; univariate t-test and chi-square analyses were used to compare the groups.
Results: There were 17 patients. 10(59%) were female and 7(41%) were male. Average BMI was 46.4; average height was 67.6"; average weight was 340.8 lbs.; average age was 44.9 years. Neck circumference averaged 19.75"(n=8). 11 patients(64%) had histories of hypertension. 6 patients(35%) had histories of witnessed apneic episodes; 15(88%) had histories of snoring. Average ESS was 8.4(n=16). 8 patients(47%) had histories of tobacco use. Polysomnography documented OSA (RDI>5) in 14 patients(82%). Severe OSA (RDI>40) was present in 4(23%) patients; 1 patient had moderate OSA (RDI 20-39); 9 patients had mild OSA (RDI 5-19); 3 patients had normal studies (RDI<5). Patients with severe OSA had ESS scores significantly greater than those without severe OSA (13 vs. 6.8; p=.0007) and tended to be taller (70.75 inches vs. 66.6 inches; p=.0536). Patients with RDI<40 tended to have greater REM-RDI than those patients with severe OSA (22.8 vs. 10.2; p=.08); there was no significant difference in minimum SaO2. Demographic and historical features, except as noted, were not significantly different between groups. Immediate post-operative respiratory complications (prolonged intubation, need for re-intubation or non-invasive ventilation) did not occur in any of the patients.
Conclusions: Patients undergoing routine polysomnography prior to bariatric surgery have an extremely high incidence of OSA. Patients with severe OSA had significantly greater ESS scores than those without severe OSA and tended to be taller. Although most patients had relatively mild disease the REM-RDI tended to be greater in these patients than in those with severe OSA; further, the severity of oxyhemoglobin desaturation was comparable. Thus, we consider that the potential for airway obstruction is present even in those patients with milder degrees of OSA. Although all patients in this series underwent surgery without respiratory compromise extreme vigilance in peri-operative airway management is appropriate. Further studies to determine which, if any, polysomnographic parameters are predictive of adverse outcomes are warranted.

0927.P

Sleep Disturbances And Excessive Daytime Sleepiness In Cirrhosis: A Case-Control Study
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Introduction: Sleep disruption and excessive daytime sleepiness (EDS) have been reported in patients with liver cirrhosis. We performed a case-control study to evaluate daytime sleepiness and sleep complaints in patients with cirrhosis compared to healthy subjects.
Methods: We compared 178 patients with cirrhosis (115 M and 63 F, mean age 52.12 yrs, SD 9.65) to a healthy sex and age-matched popula-

tion. The etiology of cirrhosis was viral hepatitis in 78.6% (HBV 18.5%; HCV 53.4%; HBV+HCV 6.7%), autoimmune diseases in 9%, other causes in 11.4%. Patients with alcoholic cirrhosis were excluded. Sleep features and EDS were evaluated by the BNSQ (a subjective questionnaire) modified. We considered "Sleepy (S)" those who reported "daytime sleepiness occurring at any time during the day, at least 3-5 times per week" and as "pts with PostPrandial Sleepiness (PPS)" those who complained of "daytime sleepiness only after lunch at least 3-5 times per week".We considered insomniacs" patients who reported sleeping "badly or very badly". Data were analyzed by the McNemar test.

Results: Patients with cirrhosis complained significantly more of EDS than controls ($p<0.005$): 18.5% were Sleepy (vs. 3.9% of controls), 30.9% reported PostPrandial Sleepiness (vs. 18.5% of controls) and 50.6% were Not Sleepy (vs. 77.5% of controls). Among patients with cirrhosis, 55% reported habitual postprandial naps (vs. 23% of controls). Moreover, 26% of patients with cirrhosis reported insomnia (vs. 7.9% of controls) ($p<0.005$). In particular, patients with cirrhosis complained more of difficulty falling asleep ($p<0.01$) and night awakenings ($p<0.005$). We did not find any difference between patients and healthy subjects concerning early awakenings and snoring

Conclusions: Our results confirm previous literature reports suggesting a high prevalence of sleep disturbances in patients with cirrhosis. Insomnia and daytime sleepiness are the main complaints

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0928.P

Behavioral Insomnia Therapy for Patients with Fibromyalgia: An Update

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Introduction: Fibromyalgia (FM) is a prevalent, debilitating, and poorly understood condition that contributes to impaired occupational/social functioning and increased health care utilization among affected individuals. The vast majority of FM patients complain of unrelenting sleep disturbances (delayed onset, extended awakenings and/ or nonrestorative sleep). Pharmacotherapies have shown some efficacy in reducing sleep disturbances among a subset of these patients, but a substantial proportion of those with FM-related sleep complaints fail to respond to such treatments. Our clinical observations suggest that factors common among other insomnia subtypes likely perpetuate the sleep problems of these medication-refractory FM patients. Thus, nonpharmacologic interventions which directly address these perpetuating mechanisms are likely needed to remedy the sleep difficulties of these patients.

Methods: This randomized clinical trial is designed to test if behavioral insomnia therapy would reduce subjective sleep disturbances among FM patients who do not show sleep improvements with conventional pharmacotherapy. Prior to randomization to treatment, subjects were screened for psychiatric, medical (other than FM) and sleep disorders. In addition subjects were required to have a nightly average of 60 minutes of total wake time (TWT) during the week prior to their lab visit. Subjects were diagnosed with FM by a collaborating rheumatologist using tenderpoint criteria. Subjects were then assigned to one of three conditions: standard care (SC;n=9), sleep hygiene (SH;n=14), and cognitive-behavioral therapy (CB;n=16). Subjects in SC receive ongoing standard medical care for fibromyalgia, but no behavioral intervention. Subjects in SH receive sleep related information and recommendations for reducing caffeine and alcohol, engaging in moderate exercising, and making sure the sleep environment is comfortable. Subjects in CB receive sleep related information as well as stimulus control and sleep restriction therapies. All therapy took place over 6 weeks. At baseline and post-treatment subjects completed several questionnaires including the Dysfunctional Beliefs and Attitudes about Sleep (DBAS), the Insomnia Symptom Questionnaire (ISQ) and the Sleep Self-Efficacy Scale (SES).

Results: Our present results from 39 randomized subjects (37 female, Mean Age=48) reiterate our findings from last year. Both total wake time (TWT) and sleep efficiency (SE%) from sleep logs were significantly improved for those receiving behavioral therapy (TWT & SE%, $p< .005$). In terms of improvement, CBT performed significantly better than both SH and SC; also, SH performed significantly better than SC. Reductions for TWT in minutes for CBT, SH and SC were 44, 19, and 5, respectively and in percentage were 45%, 19%, and 5%, respectively. Pre-post improvements in SE% for CBT, SH, and SC were 8%, 3% and 1%, respectively. In addition to subjective sleep improvement, paper and pencil questionnaires provided evidence of the efficacy of the behavioral treatments. Both CBT and SH significantly reduced insomnia symptoms as measured by the ISQ, but SC did not ($p.<.004$). All three treatment conditions improved on the SES, but there was no differential treatment effect. No treatment effects were observed for the DBAS.

Conclusions: The results provide preliminary evidence that stimulus control, sleep restriction and sleep hygiene therapies can improve the sleep of individuals suffering from fibromyalgia. In addition, insomnia symptoms appear to be reduced with both CBT and SH, but dysfunctional beliefs about sleep may require additional intervention to improve.

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0929.P

Impact of Chronic Angina Pain Characteristics on Self-Reported Sleep Quality in Patients with Coronary Artery Disease

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Introduction: The presence of chronic angina pectoris, the chest pain or discomfort associated with myocardial ischemia, has been linked to sleep disturbances. Chronic angina episodes are multidimensional pain experiences with characteristics such as frequency, duration, and severity but few studies have examined the relationship between angina pain characteristics and sleep quality. The purpose of this study was to examine which angina pain characteristics were most predictive of sleep quality in patients with documented coronary artery disease and chronic stable angina.

Methods: Seventy-three subjects (24.7% women, 90.4% Caucasian), mean age 61.6 years (SD 10.3), mean BMI 29.4 (SD 5.9) with medically documented coronary artery disease (CAD) and angina were recruited from cardiac catheterization laboratories at a large academic medical center in the Southeast. All subjects read and spoke English and had experienced an episode of angina within the previous 7 days. Demographic and clinical information were obtained from subjects' medical records and subjects completed the Chest Discomfort Diary-Revised, a reliable and valid instrument to measure chronic angina and the Pittsburgh Sleep Quality Index (PSQI). Multiple regression analysis was used to examine the impact of chronic angina on sleep quality. The global sleep quality index and subscale scores of the PSQI were used as the dependent variables in the models with the following variables used as predictors: age, gender, number of years diagnosed with CAD, BMI, history of acute myocardial infarction, angina frequency, duration of angina episodes, angina pain intensity, emotional upset associated with angina, and perceptions of angina as a health problem.

Results: The mean score for the Pittsburgh Global Sleep Quality Index was 9.18 (SD 4.78) suggesting overall, the sample had poor sleep quality. The model of predictor variables was associated with a significant amount of the variance in the global sleep quality index (R2 34.1, $F=2.74, p=.009$). Significant models were also obtained in predicting habitual sleep efficiency (R2 34.1, $F=2.04, p=.044$) and sleep quality (R2 31.3, $F=2.82$, $p=.006$). Models predicting other PSQI subscales were not significant. Greater angina pain severity was an independent predictor of

global sleep quality (t =2.6,p =.012), poorer habitual sleep efficiency (t=2.7,p=.009) and poorer sleep quality (t =3.5,p=.001). Greater angina pain duration was an independent predictor of poorer habitual sleep efficiency (t= 2.05,p=.045).
Conclusions: Among the multiple angina chest pain characteristics examined, angina pain severity was a key predictor of sleep quality. Assessing angina pain from a multidimensional perspective has the potential to inform the relationship between angina and sleep, by focusing on the specific aspects of angina that are most disruptive to patients' sleep.

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0930.P

The Effect of Depressive Symptoms on Objective and Subjective Sleep Quality, Quality of Life, and Gastrointestinal Symptoms in Irritable Bowel Syndrome (IBS)

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Introduction: Sleep disturbances, such as insomnia and early morning awakenings, are commonly reported in depressed patients and considered a substantial risk factor for depression. Affective disorders are very prevalent in patients with IBS and are considered to be important comorbid conditions. A recent study determined that IBS patients with severe illness were more likely to have greater psychosocial disturbance specifically depression, and diminished quality of life. The primary aim of this study was to investigate the role of depressive symptoms in IBS patients on objective and subjective sleep quality. Our secondary aim was to determine how depressive symptoms impact the quality of life and gastrointestinal symptoms in IBS patients.
Methods: A community sample of 43 IBS patients participated in an overnight sleep study. The diagnosis was determined utilizing Rome II criteria and verified by a gastroenterologist. IBS patients were stratified into two groups based on their Beck Depression Inventory (BDI) scores. Eighteen IBS patients had BDI scores < 11 and were classified as IBS-DS (IBS patients without depressive symptoms). Twenty-five IBS patients were classified as IBS+DS (IBS patients with depressive symptoms) as their BDI scores were > 11. The Pittsburgh Sleep Quality Index was utilized to measure subjective sleep quality and standard polysomnography was utilized to determine sleep architecture. Quality of Life for IBS was assessed using the IBSQOL questionnaire. In addition, each participant completed a questionnaire assessing the symptom frequency of 18 gastrointestinal symptoms during the past three months.
Results: The IBS+DS patients had significantly (p<.05) higher global PSQI scores (Mean = 10.96) than the IBS-DS patients (Mean = 8.06). The PSQI composite scores revealed that the IBS+DS patients reported significantly (p<.05) poorer daytime functioning, longer sleep onset latencies, and more sleep disturbances than the IBS-DS patients. The IBS+DS patients had (p<.05) significantly more arousals (mean = 35.83) than the IBS-DS patients (mean = 14.64). No other significant differences in sleep architecture were detected. The IBS+DS patients also reported (p<.05) significantly more frequent (occurrence within the past month) gastrointestinal symptoms, specifically feeling overly full and bloated, feeling an incomplete bowel movement more than 25% of the time, and a reaction to food including milk products. The IBS+DS patients also reported significantly (p<.05) diminished quality of life than the IBS-DS patients on the following dimensions: mental and emotional well-being, energy, social and physical role in life, and sexual relations.
Conclusions: In contrast to previous published results, objective sleep abnormalities are present in a subset of IBS patients. 2. Depressive symptoms exacerbate subjective sleep complaints in IBS patients. 3. Depressive symptoms in IBS patients contribute to an increased frequency in gastrointestinal symptoms, support a significant brain-gut interaction.

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0931.P

The Impact Of Nasal CPAP/Bi-level In Stage III And IV Cardiac Failure

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Introduction: Nasal ventilatory support (CPAP/Bi-level) has been reported helpful in the treatment of congestive heart failure (CHF). Patients in stages III/IV CHF are often on a transplant list and may die before having an appropriate donor. Despite medical treatment advances, quality of life is poor. We investigated the impact of nasal ventilatory support on short term mortality, left ventricular ejection fraction, daytime sleepiness, and perceived energy level.
Methods: Nineteen patients classified as stage II and IV CHF, under standard and stable medical treatment participated in the study. Subjects were subdivided in Controls who signed informed consent but did not want to undergo CPAP/Bi-level treatment (n=6), Nasal CPAP (n=7) and Bi-level (n=6) subjects. All subjects had an ambulatory monitoring with Stardust TM to diagnose Sleep Disordered Breathing (Cheyne-Stokes respiration) and a nocturnal polysomnographic recording with equipment titration.Subjects filled a visual analogue scale (VAS) (0: very poor,-10: very good) for daytime sleepiness, and daytime energy with treatment for the active subjects. Left Ventricular Ejection fraction (LVEF) was also determined at baseline and 3 months follow-upResults were analyzed by Mann Whitney U test considering controls vs nasal ventilatory treated patients. Two way ANOVA considering CPAP vs Bi-level group effect on baseline condition and 3-month follow-up.
Results: This is a severe patient population with a LVEF below 40% and poor quality of life despite improvement in medical management. There was no difference at entry between patients who refused nasal ventilation compared to those who accepted it as far as age, gender, medical treatment, LVEF, and severity of disease. Rejection happened after the nasal ventilation titration night. Mortality: three patients (50%) died in the control group compared to none in the ventilatory treated patients. LVEF: There was no difference in the baseline vs the 3 month follow-up measurements. VAS scores: there was a significant improvement in the daytime sleepiness and daytime energy scores (P=0.04) at 3 months compared to baseline for the total ventilation group.Effect of CPAP vs Bi-level: Two-ways ANOVA showed no significant difference between the 2 modes of treatment. But there was a non-significant higher score for satisfaction with treatment with Bi-level machine (9.4 ± 0.9) than with CPAP (7.0 ± 2.7)
Conclusions: In this severe population often waiting for a heart transplant, nasal ventilation reduces mortality in the short term. LVEF does not significantly change during that short period but there is a significant improvement in perceived energy level and daytime alertness compared to baseline in the treated patients. Bi-level despite only a trend due to the small groups, gave higher satisfaction than CPAP. Considering the difficulties for cardiac patients with severe disease to accept one more demand on them, this should be taken into consideration when prescribing nasal ventilation during sleep.

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0932.P

Autonomic Activity During REM Sleep is Associated with the Symptom Profile of Irritable Bowel Syndrome Patients

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Introduction: Our laboratory has detected an autonomic abnormality, sympatho-vagal dominance during REM sleep, in irritable bowel syndrome (IBS) patients. This same pattern was detected in IBS diarrhea-predominant patients when compared to other symptom subgroups (constipation, alternating) after the ingestion of a meal. It has been suggested that subtle abnormalities in the autonomic nervous system may be an underlying factor in the visceral sensitivity detected in IBS patients. Yet, little is known regarding differences in autonomic activity during sleep in symptom subgroups. The aim of this study was to determine if diarrhea predominant (D) patients demonstrate an autonomic abnormality (i.e. sympatho-vagal dominance) during sleep when compared to constipation predominant (C) and alternating (A) IBS patients.
Methods: A community sample of 41 IBS patients participated in an overnight sleep study (15 C, 11 D, 15 A). Several questionnaires were filled out by each patient, the Pittsburgh Sleep Quality Index, Beck Depression Inventory (BDI), and Spielberger State Anxiety questionnaire. Standard polysomnography was utilized and electrocardiography provided beat-to-beat intervals that were subjected to spectral analysis. Fifteen-min. segments were selected from a 30-min. pre-sleep period, stage 2, stage 4, and REM sleep. Spectral analysis of heart rate variability determined percent of low frequency (LF) band power (sympathetic activity), percent of high frequency (HF) band power (vagal tone), and the ratio of low frequency/high frequency band power (LF/HF), indicating sympatho-vagal balance.
Results: Sleep architecture and subjective sleep quality were similar for each group. D patients exhibited significantly ($p<.05$) greater sympatho-vagal dominance (mean = 1.77) during REM sleep than the C patients (mean = 1.11) and A patients (mean = 1.03). There were no significant differences between the C and A groups. The sympatho-vagal dominance was due significantly ($p<.05$) increased LF band power and significantly ($p<.05$) decreased HF band power, indicating both sympathetic and vagal influences. The LF/HF ratio during stage 2 and REM sleep were significantly correlated with sleep onset latency ($r = .31$, $p<.05$; $r = .47$, $p<.01$). There were no differences in symptom subgroups for depression symptoms or anxiety.
Conclusions: 1. Autonomic alterations during REM sleep agree with previous postprandial data and provide support for the notion that IBS patients with D predominant symptoms are a group physiologically distinct from those with C or A symptoms. 2. Sympatho-vagal dominance during REM sleep does not appear to be related to depressive symptoms or anxiety. 3. But rather, sleep onset latency may be associated with sympatho-vagal dominance in all IBS patients irrespective of the dominant symptom.

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0933.P

Sleep Assessment in a Population-Based Study of Chronic Fatigue Syndrome

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Introduction: Sleep physiology may be central to understanding chronic fatigue syndrome (CFS). Postulated etiologies of CFS affect sleep and conversely primary sleep disorders can present with symptoms of CFS. Accurately describing the relationship of sleep abnormalities to CFS requires characterizing sleep in subjects representative of the CFS population rather than CFS patients from referral centers. We used two self-administered questionnaires, the Epworth Sleepiness Scale and the Centre for Sleep and Chronobiology's Sleep Assessment Questionnaire© (SAQ©) to profile sleep abnormalities in persons with CFS identified in the general population of Wichita.
Methods: The study included 339 subjects (24 classified as active CFS, 18 as CFS in remission, 90 with insufficient symptoms or fatigue for CFS, 145 with medical or psychiatric conditions explaining fatigue, and 62 non-fatigued). Subjects were identified by a random digit-dialing telephone screening of 56,146 adult residents of Wichita and detailed interviews of the 3,528 who reported fatigue of at least 1-month's duration, and 3,634 randomly selected non-fatigued people. At baseline, all subjects meeting criteria for CFS on the telephone and randomly selected non-fatigued subjects were invited to clinic for medical and psychiatric evaluation and classified as CFS, chronic fatigue not CFS, medical or psychiatric exclusion, or not fatigued. In accordance with CFS case definition, subjects endorsing sleep apnea or narcolepsy during the clinical evaluation were excluded but other primary sleep disorders were not queried. In the second year all subjects previously evaluated at clinic, and newly identified CFS-like subjects were invited to clinic and all clinic participants completed the SAQ© and Epworth Sleepiness Scale. Scores for insomnia/hypersomnia, non-restorative sleep, excessive daytime somnolence, sleep apnea, and parasomnia/restlessness in SAQ© were dichotomized based on cut-offs. The Epworth Sleepiness Scale score was used as a continuous variable. We used F-tests, t-tests, or Kruskal-Wallis tests to compare groups with respect to continuous variables and chi square or Fisher-exact tests for categorical data. Pair wise comparisons were performed using the Bonferroni adjustment. Logistic regression models were used to estimate odds ratios and 95% confidence intervals between abnormalities in sleep factors and potential predictors.
Results: 81.4% of subjects had an abnormality in at least one SAQ© sleep factor. Subjects with sleep factor abnormalities had significantly lower wellness scores compared to those without SAQ© abnormality. Fatigue severity scores did not differ statistically. CFS subjects had significantly increased risk of abnormal scores in the non-restorative (adjusted odds ratio [OR] = 28.1; 95% confidence interval [CI]= 7.4-107.0) and restlessness (OR = 16.0; 95% CI = 4.2-61.6) SAQ© factors compared to non-fatigued, but not for sleep apnea or excessive daytime somnolence (consistent with previous findings that, while fatigued, CFS subjects are not sleepy). A strong correlation (0.78) of Epworth score was found only for the excessive daytime somnolence factor.
Conclusions: The SAQ© was developed for screening and this is its first use in a population-based study of fatigued subjects. The SAQ© found sleep abnormalities associated with CFS and provided more information than the Epworth. Validation of these promising results will require formal sleep studies.

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0934.P

Subjective and Objective Correlates of Sleep Quality in HIV Infected Persons

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Introduction: Caring for persons with HIV/AIDS presents challenges in both physical and emotional care. Both the quality and the quantity of sleep are influenced by such parameters as age, circadian rhythms, medications and pathological alterations. Sleep disturbances in HIV+ per-

sons are the third cause for seeking medical care even in the era of HAART therapy. Enhancing the quality of life or functional status of individuals requires continuous evaluations and opportunities to develop new strategies for improvement of care. Therefore, the broad purpose of the study was to compare the patient's subjective experience of sleep with the objective measure of a computerized measurement device and hormone production.

Methods: A descriptive, repeated measures design was used. Repeated measures were used for observations made over four-24 hour periods. Time series observations were used to determine serial correlations of periods and phases of circadian rhythms. HIV subjects were studied from an inpatient AIDS facility in Southwest Texas over a three-year period. Male and female subjects were studied (n=45). Subjects were given the Sleep Disturbance Scale and wore the Actiwatch for 48 consecutive hours. A second 48 hours were used to collect salivary melatonin and cortisol, and core temperature data.

Results: The measure of sleep efficiency was inversely correlated with the sleep disturbance scale (-.85, p= <.001). Sleep efficiency scores ranged from 36% to 81%, indicating disturbed sleep. Sleep latency periods ranged from 17 minutes to 4 hours. Temperature data supported previous research with a hectic pattern of the temperature and with a temperature nadir of 99.1°F. The temperature cycle demonstrated advanced phase shifts of 6-12 hours within a 21.3-22.6 hour rhythm. Subjects were found to have two oscillators. Melatonin peaks occurred 4-14 hours (m= 8.7 hours) with advanced shifting with suppression of 39% (range of 19-49%). Melatonin was at its highest during the latemorning or early afternoon. Secretory bursts of cortisol were found at different points within the measured time, however a predictable pattern was not identified. Each subject demonstrated advanced phase shifting of 2.1-10.2 hours with a mean of 5.5 hours. Cortisol was reduced by 51% (range 37-69%).

Conclusions: Subjects with HIV perceive their sleep to be disturbed and is supported by objective measures. These findings could be related to the circulating cytokines or to the use of continuous light that suppresses melatonin from inducing sleep. The lack of temperature decline in the early evening has a disturbing effect on the circadian function of the body's feedback system. Sleep has profound effects on both the quality of life and functional status. Fatigue interferes with the activities of daily living. Intervention studies are needed to determine if there is sufficient melatonin in the body to maintain a normal sleep pattern.

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0935.P

Sleep Disorders In End-Stage Renal Failure On Dialysis

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Introduction: Patients on dialysis therapy due to end-stage renal failure report a high prevalence of sleep disorders, among which restless legs syndrome, insomnia, excessive daytime sleepiness and respiratory disorders during sleep.Uraemia and iron deficiency have been presumed to play an important role in the pathogenesis of these disorders in such chronic disease, even if no clear evidence has been found yet.

Methods: To study the incidence of the different sleep disturbances in a large population of dialysis patients, a questionnaire was administered, in the dialysis units of the "Triveneto" geographical area (North-Eastern Italy), to all the patients who accepted to take part in the study.

Results: The present data refer to the first 601 patients [61.5 % males and 38.5 females; age 64y.o. ± 13 (range 17-95); time on dialysis 64.6 months ± 71.3 (range 1-396)] coming from 20 centers.The prevalence of patients unsatisfied with their sleep was 43.3 %; 59.7 % presented nocturnal awakenings every night; 22.1 % used hypnotics every night; 33.3 % complained of mood disorders due to sleep deprivation; 7.3 % of excessive daytime somnolence (Epworth Sleepiness Scale >9); 27.8 % of habitual snoring; 48% of patients answered positively to at least one of the questions in the RLS questionnaire (IRLSSG, 1995).Applying the international criteria for RLS, the percentage of patients in our sample decreased to 21%. An additional 14% of patients answered positively to at least 3 questions of the IRLSSG questionnaire (questionable RLS patients?).Comparing patients who are definitively affected by RLS (n = 127) with patients who are not affected by RLS (n = 280), we found that RLS is not correlated to use of coffee, alcohol or smoke, nor to evening physical activity, while the two groups differ significantly as to time on dialysis treatment (years of dialysis dependence) and consequences on daytime quality of life. Patients who result RLS positive report a very fragmented and not restful night-time sleep and are more affected by daytime somnolence.

Conclusions: Differently from other studies, coming from one single or from very few dialysis units, our results were obtained from a large sample without possible biases due to the dialysis strategies applied or to the psychological problems resulting from peculiar relationships between patients and unit personnel.Our findings can be useful to analyze the differences compared to those obtained from clinical series gathered during the years prior to the improvements in dialysis techniques and pharmacological therapies.The study and knowledge of the prevalence and of the pathophysiology of these frequent disorders may help to find out the right therapy to improve the quality of life of our patients.Sleep fragmentation and sleep deprivation may have a role in the cardiovascular complications and infections, often with bad prognosis, presented by dialysis patients.

0936.P

Spindle, Not Delta, Waveforms are Altered in Midlife Women With Fibromyalgia

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Introduction: We have shown previously that midlife women with fibromyalgia (FM) and pain have fewer sleep spindles and spindle frequency activity in NREM stage 2 sleep compared to control women without pain. Reduced spindles could reflect abnormal sensory processing in the thalamus as a result of a chronic hyperalgesic state. To further explore this hypothesis, we quantified spindle and delta waveforms by time domain analysis during the first 2 NREM cycles in women with FM and pain and control women.

Methods: Thirty-three medication free women with FM and pain (mean age, 44.9 ± 7.9 years) and 30 control women (mean age, 44.2 ± 7.8 years) with self-reported good sleep and no pain were studied. All women had low levels of physical activity, did not have a current diagnosis of depression, and had sleep recorded in a laboratory for 2 consecutive nights. Spindle and delta waveforms were identified by the SACS automated computer software system based on zero crossing combined with period amplitude and pattern recognition methods. A NREM cycle was defined as more than 15 minutes stages 2,3 and 4 and terminated by either 5 minutes of wake or stage REM. Between group comparisons for the data from night 2 were made using the Mann-Whitney U test.

Results: Compared to controls, women with FM had fewer spindle waveforms in stages 2, 3, 4 (s/min) in the first (FM 3.0 ± 0.4, controls 4.8 ± 0.8, P =.07, mean ± SEM) and the second (FM 2.9±0.4, controls 5.4±0.8, P =.009) NREM cycle. Delta waveforms (s/min) among women with FM and controls in the first (FM 13.6 ± 1.2, controls 15.4 ± 1.1) and second NREM cycle (FM 11.8 ± 1.1, controls 11.7 ± 0.7) were similar.

Conclusions: These data suggest that in women with FM, thalamocortical mechanisms of sleep spindle generation are impaired more than those involved with delta wave generation. In this model, an inability to keep the 'sensory gate closed' in the thalamus during sleep compromis-

es sleep integrity. In women with FM, sleep may be more easily disturbed both by internal and external stimuli and any benefits associated with spindle activity also would be reduced.

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0937.P

Sleep-wake Disturbances in Patients with Advanced Lung and Colorectal Cancer

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Introduction: Nocturnal sleep disturbance and daytime sleepiness, problems that may adversely affect quality of life, are common complaints of patients with cancer. While there is evidence that sleep-wake disturbances are present across the disease trajectory, patients in the advanced stages of cancer may be particularly vulnerable. Few studies, however, have specifically focused on describing the sleep of this population. Therefore, in order to begin a systematic examination of the sleep-wake patterns of patients with advanced cancer, we studied a sample of patients with late-stage lung and colorectal cancer and examined variables related to subjective nocturnal sleep quality and daytime sleepiness.
Methods: The sample included ten oncology outpatients (5 men and 5 women) with a mean age of 52.1 (SD 12.48, range 28-68) who had a diagnosis of stage IV colorectal (n = 4) or either stage IV non-small cell or extensive small cell lung cancer (n = 6). All were cognitively intact (Mini-Mental State Examination >24), had no previous history of PSG diagnosed sleep disorder, no known cerebral metastases or other neurologic disease, or DSM IV mood, anxiety or psychotic disorder. Nine subjects were undergoing chemotherapy. Subjects were independent in activities of daily living, seven reported working at least part-time, and all had a Karnofsky Performance Status (KPS) of 80 or greater (mean 88,SD 4.22). Subjects completed the Pittsburgh Sleep Quality Index (PSQI) and the Epworth Sleepiness Scale (ESS) and were interviewed regarding their sleep history.
Results: Seven patients reported a history of sleep disturbance; two had difficulty prior to the diagnosis of cancer while the remaining subjects had onset at the time of cancer diagnosis or initiation of cancer treatments. Although most subjects rated their overall sleep quality as “Very good” or “Fairly good” (n=9), seven subjects had PSQI global scores of >5 (mean 7.8, SD 4.26, range 2-15), indicating moderate to severe sleep disturbances. Mean (SD) habitual sleep parameters from the PSQI included: sleep onset latency, 31 (28.85) minutes; total sleep time, 7.1 (.88) hours; and sleep efficiency, 86.89% (11.92). In addition to increased sleep onset latency, the most frequently reported disturbances included nocturnal awakenings, nocturia, and cough. Five subjects reported regular use (at least once a week) of sleep enhancing medications. Subjects reported no daytime sleepiness and minimal daytime dysfunction on the PSQI. Mean ESS score was 6.2 (SD 2.86, range 2-10). However, two subjects had scores of 10, suggesting the presence of significant subjective daytime sleepiness.
Conclusions: These preliminary results suggest that sleep-wake disturbances are prevalent in patients with advanced cancer. As we enroll additional subjects, examination of associations between sleep-related variables and demographic, disease- and treatment-related factors will provide a basis for understanding the factors that contribute to sleep-wake disturbances in this population.

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0938.P

Sleep patterns in Patients attending Primary Care Units in Santiago

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Introduction: Different studies shows frecuently consultation to General Physitian due to sleep problems.In Chile the Sleep Medicine is just develping and included in the General Hospital.We studied the Sleep patterns and sleep problems in a population attending Primary Care units in Santiago, Chile.
Methods: We studied 700 adult persons attending the Primary Care Unit.The patients attendend the Primary Care units due to chronic or acute deseases like Blood Hypertention or other diseases.The population belongs to a City District of about 500.000 people, in charge of the Primary Care Units.We studied the patients in an standarized interview, focusing on age, gender, social and labor status.The Sleep History was studied using sleep questionnaire.The results were analysed using the SPSC statistics.
Results: The population was 700 patients, 60% female and 40 $ males.The mean age was 55 years, withs sd $\pm$ 1560 % of the patients were working at the time of the study.52% have some kind of sleep complain, more frecuent in females.Isomnia was the most common complain, in some cases very severe. Short sleep and sleep deprivation is also frecuent.Hypersomnia was refered in 15% of the polulation, most of them males over 40.Periodic Limb movement was only refered in 2% of the sample.There was a correlation between insomnia and anxiety. A psychiatric history, depression, was present in 3% of the polulation.Therre was a correlation between BH , snoring and hypersomnia.45% of all consultats were under some benzodiacepine treatment.Only 5 % of all sample had consult due to sleep problems. In the Hospital History was not mentioned Sleep as part of the genral examination.
Conclusions: Sleep Disorders are very frecuent in the population consultig a Primary Care Unit.Insomnia was very frecuent, but assumed by the patients, to be not a medical disease.Hypersomnia was less frecuent, more in males , after 40. Associated to Blood Hypertention and snoring.An important number of patients were under madication, mos of then trinquilizers.The Sleep Disorder was not propialy studied in the previous consultations. Neither the clinical history or the examination report about sleep disorders.general physician or the specialist pay much attention to Sleep.

0939.P

Subjective Sleep Quality and Psychological Status in Patients with Carpal Tunnel Syndrome

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Introduction: Carpal tunnel syndrome (CTS) is a common compressive neuropathy in which the median nerve is compressed in the space formed by the wrist bones and the carpal ligament, causing pain. In the general population an estimated 9.2% of women and 0.6% of men suffer from CTS. Patients with CTS commonly complain of increased pain severity during the night, which is associated with fragmentary sleep. Patients with CTS may also experience mood disturbances associated with the pain. The extent to which sleep and psychological status are disturbed in patients with CTS, however, is unknown. We therefore investigated the relationship between pain, psychological status, and sleep quality, based on subjective assessments, in 33 patients with CTS (14 males and 19 females; age: 41±10 years).
Methods: Patients attending a Neurophysiology Clinic in Johannesburg, South Africa, for clinical examination and nerve conduction tests for CTS, participated in the study. The distal motor (4.7±1ms) and palmar

distal sensory (3.0±0.3ms) conduction latencies of the median nerve were significantly slower in these patients than normal, confirming a diagnosis of CTS. The patients completed a questionnaire about their day and night-time pain severity, sleep and psychological status over the past few weeks.
Results: The patients rated their pain intensity on a 100mm visual analogue scale (VAS) anchored from "no pain at all" to "unbearable pain", as being significantly greater (paired t test, $p<0.03$) during the night (70±24mm), than during the day (46±24mmSD). Night-time pain ratings were similar to those of patients with severe postoperative pain. The majority of patients (91%) reported that their sleep was disturbed by pain. Patients reported that they had trouble falling asleep (94%), that they awoke during the night (88%), and that they experienced a restless sleep (94%) at least sometimes, because of CTS pain. Only nine patients (27%), however, were excessively sleepy during the day, as indicated by a score of greater than 10 on the Epworth Sleepiness Scale. Scores on the Epworth Sleepiness Scale were not significantly correlated with VAS pain ratings (Pearson correlation, $r = 0.2$, $p = 0.3$). CTS was not only associated with disturbed sleep, but also with altered psychological status. A quarter of the patients had very high scores on the General Health Questionnaire (GHQ) and the mean score for all the patients (7±7 mean±SD) was higher than that for a normal population, indicating disturbed mental health. Pain severity, however, was not significantly correlated with psychological status, as measured on either the GHQ or the Profile of Mood States ($r = 0.2$, $P>0.05$).
Conclusions: Patients with CTS have trouble falling asleep and maintaining sleep because of severe nocturnal pain. Most patients, however, do not report an associated increase in daytime sleepiness. Patients with CTS also have disturbed mental health, although apparently independent of pain severity. Similar to other pain-related diseases, therefore, neuropathic pain, in patients with carpal tunnel syndrome, is associated with disturbed sleep and psychological status.

0940.Q

Is there a "First-Night Effect" in Drug-Naive, Acutely Ill Patients with Schizophrenia? Results on Sleep Organisation and REM Sleep qEEG Activity

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Introduction: The first night effect is a well known phenomenon in healthy participants. The present study aim at verifying whether a first night effect exists in drug-naive patients with schizophrenia.
Methods: The sleep of six acute patients never exposed to neuroleptics (4 M, 2 F, mean age = 35.0 ± 19.3) was recorded for two consecutive nights in the sleep laboratory during the first week of their hospitalization. According to DSM-IV-R criteria, the final diagnosis was confirmed within six months. All participants had a 10-electrodes EEG setup (C3, C4, Fp1, Fp2, F7, F8, T3, T4, O1 and O2) referenced to linked earlobes. Both nights were visually scored according to Rechtschaffen and Kales (1968) using 20 sec. epochs. Fifteen four-seconds epochs of artefact-free EEG were selected from the first three REM sleep periods and submitted to Fast Fourier Transform with a cosine window smoothing and a resolution of 0.25 Hz. Power amplitude was computed and absolute and relative ([Band power/total power] * 100) EEG activity of five bands were extracted: Delta (0.75-3.74Hz), Theta (4.00-7.75Hz), Alpha (8.00-12.75Hz), Beta1 (13.00-19.75Hz) and Beta2 (20.00-30.00Hz). Sleep and EEG variables were compared between night 1 and night 2 using Wilkoxon matched pairs tests.
Results: Compared to night 2, night 1 showed more stage 3 percentage ($p=.05$) and less REM sleep percentage ($p=.05$) during the first third of the night. Compared to night 2, night 1 showed less relative Alpha activity on F8 ($p=.05$) and more relative Beta1 activity on C3 electrodes ($p=.05$).
Conclusions: The present results show that an atypical FNE is present in drug-naive patients with schizophrenia. The fact that we observed more Stage 3 percentage on night 1 could be attributed to sleep deprivation associated with the acute condition of patients before coming to the laboratory. However it has been reported that patients with schizophrenia do not show post-deprivation sleep rebounds (Luby & Caldwell, 1967). Similarly to depressed inpatients (Toussaint et al., 2000), we found less REM sleep percentage on night 1 and short REM sleep latencies on both nights. On the other hand, and contrary to depressed inpatients and healthy participants (Gingras et al., 2000), we found that qEEG measures shown to be correlated to schizophrenia clinical states (Poulin et al., 2001) are sensitive to FNE. On the whole, the present results suggest that FNE in schizophrenia could be a useful tool to investigate the pathophysiology of this disease and thus needs to be further investigated.

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0941.Q

Prediction Of Remission From Untreated Depression

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Introduction: Fewer than half of those experiencing major mood disorders ever seek treatment, yet 60-70% will be in remission within one year. Little is known of the mechanisms responsible for this change. REM sleep has been hypothesized to have a mood regulatory function. This sleep stage has several abnormal features in depressed persons including a reduced latency to the first REM and poor dream recall. Manipulations which reduce REM sleep have been associated with improvement in waking mood in depressed persons but not in normals.
Methods: Thirty subjects all going through a first marital separation with intent to divorce were recruited for a five month study of their sleep, dreams and waking functioning. Twenty met SCID, Hamilton Depression>18 and Beck Depression >14 criteria as depressed and ten were not depressed on any of these measures. All were untreated. All had sleep studies of 420 minutes for two nights on three occasions. Night 1 was a sleep through and Night 2 was a REM Interruption night for dream collection. POMS tests were completed before and after each night. Remission was predicted to be associated with overnight down-regulation of depressed mood on the POMS on the REM Interruption nights, and the production of dreams with high Dream-like fantasy scores.
Results: Thirteen of the depressed (65%) were in remission at Month 5. There was a significant difference in overnight mood change following REM Interruption nights between the two groups. Non-depressed controls had an increase and depressed a decrease in POMS Depression scores. There was a significant negative correlation between the total overnight reduction on POMS Depression and the final Beck score $r=-.65$ $p<.003$ and with the final Hamilton score $r=-.50$ $p<.02$ when the initial level of each score was held constant. A regression analysis with the final Adjustment score as the dependent variable and four predictors (length of time separated, number of nights with reduced REM latency, total reduction in overnight mood scores on REM Interruption nights, and per cent of dream reports rated as high on the Dream-like Fantasy Scale) yielded an r=835 and r square =.697.
Conclusions: REM interruptions on three nights over a five month period improved overnight mood in untreated depressed but not in controls. Seventy per cent of the variance in remission from an untreated, divorce-related depression, could be accounted for by four variables: an increased time since separating, few sleep signs of a biological component (reduced REML), more positive mood following REM Interruption, and ability to produce elaborate dreams.

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0942.Q

Gamma Activity During Sleep in Schizophrenia and Depression

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Introduction: Despite the evidence relating fast-frequency EEG abnormalities to the clinical symptoms of schizophrenia, few studies have quantified gamma activity in this psychiatric disorder. Four studies demonstrate that medicated patients with schizophrenia exhibit reduced power (based on power spectral analysis) in induced gamma compared to healthy controls. One study by Kwon, et al also exhibited delayed onset of synchronization at 40Hz. Yet in EEGs obtained at rest, Begic and colleagues reported increased power in spontaneous beta 2 (18.5-30Hz) in unmedicated schizophrenic patients. We report a post-hoc analysis of spontaneous gamma activity during sleep in healthy controls, and in unmedicated patients with schizophrenia and depression.
Methods: Forty-nine participants 23-44 years of age were chosen from an archival database collected under identical conditions during the past 10 years. Inclusion in the study required complete digital records of sleep EEG recorded from frontal, central and parietal electrodes over two consecutive nights in the laboratory, and complete psychiatric data. Seventeen patients with schizophrenia (SZ) were chosen first, followed by 15 outpatients with unipolar major depressive disorder (MDD) and 17 healthy normal controls (NCs). All patients were symptomatic and unmedicated at the time of study. All-night gamma (35-45 Hz) and beta (20-35 Hz) were quantified with power spectral analysis following standardized procedures. The resultant power values were then averaged within stage of sleep. Data were coded for group (SZ vs MDD vs NC) and for sleep stage. Repeated-measures, factorial ANOVAs evaluated group differences.
Results: Gamma power was significantly higher in unmedicated schizophrenic patients than in either healthy controls ($p<.0001$) or depressed patients ($p<.02$) in all sleep stages. Those with MDD also had higher gamma than NCs ($p<.05$). Beta power was greater in wakefulness and in REM sleep than in NREM Stages 1-4 in all groups. Those with SZ also had higher beta power than the MDD group for all sleep stages but not in wakefulness ($p<.05$) and both clinical groups had higher beta power than NCs in sleep and in wakefulness.
Conclusions: These findings suggest that gamma activity differentiates patients with schizophrenia from those with depression and from healthy controls. It remains to be determined whether this spontaneous gamma activity relates to the clinical features of either psychiatric illness. Taken together with previous research, these results suggest that schizophrenic patients have increased gamma (34-45 Hz) and beta (20-35 Hz) during sleep. Abnormalities in thalamocortical oscillations and recurrent inhibition may underlie these findings. Further studies exploring the state/trait characteristics of fast-frequency activity in schizophrenia are indicated.

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0943.Q

Delta Sleep Response to Metyrapone in Posttraumatic Stress Disorder

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Introduction: Metyrapone blocks cortisol synthesis leading to a stimulation of cortiocotropin releasing factor (CRF) and a reduction in delta sleep. We examined the effect of metyrapone administration on endocrine and sleep measures in male subjects with and without chronic PTSD. We hypothesized that metyrapone would result in a decrease in delta sleep and that the magnitude of this decrease would be correlated with the endocrine response (rise in 11-deoxycortisol and adrenocorticotropic hormone: (ACTH)). We utilized the delta sleep response to metyrapone as an indirect measure of hypothalamic CRF activity and hypothesized that PTSD subjects would have a greater decrease in delta sleep induced by metyrapone.
Methods: Three nights of polysomnography were obtained in 24 male subjects with combat-related PTSD and 18 male combat-exposed normal controls. All were medically healthy without sleep apnea and free of psychotropic medication. On day 3 metyrapone was administered during normal waking hours until habitual sleep onset preceding night 3. Endocrine responses to metyrapone were measured in plasma obtained the morning following sleep recordings the day before and after administration. Repeated measures ANOVAs were conducted to compare the endocrine and sleep response to metyrapone in PTSD and controls.
Results: PTSD subjects had significantly less delta sleep as indexed by stages 3 & 4 (group effect- $F= 9.2$, $p <.01$), and total delta integrated amplitude by period amplitude analysis (group effect- $F= 6.5$, $p < .01$) prior to metyrapone administration. Metyrapone caused an increase in awakenings and marked decrease in quantitative measures of delta sleep (condition effect- $F= 9.6$, $p < .01$). Unexpectedly, the decrease was significantly greater in controls compared to PTSD (group x condition effect- $F= 5.2$, $p = .03$). Metyrapone produced a robust increase in ACTH that was significantly greater in controls compared to PTSD (group x condition effect- $F= 7.0$, $p < .01$).. The decline in total delta integrated amplitude was significantly associated with the magnitude of increase in 11- deoxycortisol ($r= -.56$, $p < .01$) and ACTH ($r = -.42$, $p = .03$).
Conclusions: The effect of metyrapone on delta sleep is predicted both by the rise in 11-deoxycortisol, which is most proximal to the adrenal blockade of cortisol synthesis, and by the magnitude of rise in ACTH, which presumably is stimulated by an increase in CRF release secondary to the reduction of feedback regulation by cortisol. These correlations are strong evidence that the effect of metyrapone on sleep is mediated by the response of the HPA axis as opposed to a possible non-endocrine effect of metyrapone. The results suggest that the delta sleep response to metyrapone is a measure of the brain response to an indirect CRF challenge. Compared to controls, PTSD was associated with a diminished endocrine and delta sleep response to metyrapone, suggesting that PTSD subjects are less sensitive to an indirect CRF challenge.

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0944.Q

Evening Preference Predicts High Excitability in Schizophrenic Patients

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Introduction: Disturbed sleep-wake patterns are pervasive in those afflicted with schizophrenia. Whereas most well persons have robust and somewhat rigid sleep-wake cycles, many patients with schizophrenia seem to have spare and irregular sleep-wake cycles, and increased activity at night. The purpose of this study was to test the hypothesis that chronotype (when the peak of one's activity occurs in a 24 hour day) influences symptoms and measures of cognitive function in patients with schizophrenia.
Methods: Subjects were enrolled from the VA Hospital Day Treatment program. To enter the study we required that subjects have a SCID confirmed diagnosis of schizophrenia or schizoaffective disorder and be in

outpatient treatment. They also were clinically stable, defined as having no hospitalizations or changes in housing or medication in the last three months. Excluded were those with a history or presence of seizure disorder, stroke, mental retardation, and/or traumatic brain injury. All subjects signed an IRB-approved informed-consent contract.All subjects had had an extensive assessment battery that included an interview and the Positive and Negative Syndrome Scale, The Scale to Assess Unawareness of Mental Disorder; the Beck Hopelessness Scale; the Heinrichs Quality of Life Scale; the Ways of Coping Questionnaire; the Wisconsin Card Sort Test; Gorhams Proverbs Test; Hopkins Verbal Memory Test; and the Continuous Performance Test.Sleep and Sleep-wake cycle assessment consisted of a brief structured interview to assess sleep, the Horne-Ostberg Morningness-eveningness Scale, and the Pittsburg Sleep Quality Index.

Results: There was a significant correlation between the Horne-Ostberg morningness/eveningness scale and the PANSS category assessing excitement and hostility. Patients with owl-like preference had high excitibility/hostility. The sleep interview had a high correlation with the responses given to the Pittsburgh Sleep Quality Index. The sleep interview responses were also correlated with the Horne-Ostberg morningness/eveningness scale. Those reporting very poor sleep tended to be those with an owl-like chronotype.

Conclusions: The most difficult to manage patients may be those with the owl-like chronotype. These patients are also among those that report highly disturbed sleep. It is possible that the abnormally-phased chronotype may be contributing to poor sleep and that exacerbates the excititibility/hostility part of the symptom spectrum. An alternative explanation is that unsuccessful social interactions of the hostile patients may make partitioning their daily activity into the night a way of avoiding social contact. We will use actigraphy as the next stage of the study to assess if the self-reported sleep/wake cycle agrees with the atigraphic records.

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0945.Q

Insomnia And Heart Rate Variability In Depression

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Introduction: Research suggests that aberrations in autonomic nervous system activity might play a role both in Primary Insomnia and in Major Depression. Specifically, lower levels of heart rate variability have been observed in all stages of sleep in individuals with Primary Insomnia compared with controls. Similarly, lower levels of resting heart rate variability (influenced by both sympathetic and parasympathetic branches) and resting high frequency heart rate variability (respiratory sinus arrhythmia; predominantly parasympathetic) have been found in depressed patients compared to controls. We hypothesized that a relationship between depression and heart rate variability might be mediated by disturbed sleep, a very common symptom of Major Depression. To test this hypothesis we examined the relationship between daytime resting heart rate variability, disturbed sleep, and depression severity in a sample of patients with major depressive disorder.

Methods: The present study uses data from 129 (out of 151) participants, enrolled in a 16-week randomized controlled treatment study, who provided heart rate and sleep data at intake. All participants met DMS-IV criteria for Major Depression. The mean severity score, measured by the 17-item HRSD (Hamilton Rating Scale for Depression) was 22.4 (sd=4.8). The gender distribution was 70% female and the average age was 42 years (sd=11 years). At intake, midpoint, and post treatment assessment an electrocardiogram (ECG) at rest was recorded for 5 minutes followed by an HRSD interview assessing depression severity. Participants completed a sleep diary for seven days during the week preceding each assessment of heart rate.

Results: Early morning awakening (EMA), defined as the difference between planned and actual rise time indicated in the sleep log, was associated with lower levels of both total heart rate variability ($r = -0.27$, $p<.01$) and parasympathetically-mediated heart-rate variability (respiratory sinus arrhythmia; $r = -0.26$, $p<.01$). These relationships existed at intake but at no other time point. Lower levels of heart rate variability were also related to self reports of poorer quality of sleep ($r= -0.20$). A decrease in EMA from pre to post treatment was related to an increase in respiratory sinus arrhythmia ($r= -0.27$, $p<.05$). The relationships between the heart rate variability measures were unrelated to the severity of depression at any time-point ($p>.1$).

Conclusions: The observed relationship between decreased vagal tone and early morning awakening in depression suggests that previously reported association between vagal tone and depression severity might be mediated by the severity of early morning awakening, a common symptom of major depression. Our findings, together with previous findings of an association between decreased depressive symptoms severity and increased respiratory sinus arrhythmia, suggest that low vagally-mediated heart-rate variability is a state-dependent characteristic of depressive episodes involving disturbed sleep.

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0946.Q

Functional Neuroanatomical Correlates of REMs In Depression

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Introduction: Increased REM density characterizes sleep in depression. Observations derived from polysomnographic (PSG) studies indicate that REM density parallels depression severity and predicts treatment outcomes in depressed patients. These findings suggest that REM density may be a correlate of emotional or arousal regulation in depressed patients. The goal of the present study was to investigate the functional neuroanatomical correlates of average REM count (RC), an automated analog of REM density, in a group of depressed patients. We predicted that average RC would positively correlate with glucose metabolism in areas involved in emotion (amygdala) and arousal regulation (brainstem, thalamus, midline cortical attentional system) including components of the visual attention system (cortical eye fields).

Methods: Fourteen medication-free depressed patients (8 women, 6 men, mean age 38.1/pm 9.8 years) underwent all night PSG and [18F] FDG PET scans during REM sleep. Regression analyses were conducted with Statistical Parametric Mapping (SPM-99), with relative cerebral metabolic rate of glucose (rCMRglu) during REM sleep as the dependent variable (after correcting for the effects of inter-subject differences in global metabolism), and average RC (the number of automatically-detected REMs divided by the number of REM minutes) as the independent variable. Statistical significance was set at $p<.05$ after corrections for multiple comparisons. The relationships between average RC and a priori determined regions of interest (ROIs) were investigated using ROI analyses, which limit statistical procedures to discrete ROIs and require less stringent statistical corrections.

Results: Average RC significantly and positively correlated with rCMRglu in a large area that included bilaterally the lingual gyrus and the striate cortex, the right precuneus, areas corresponding to the midline attentional system in the right hemisphere, and right medial prefrontal cortex. Regions of interest (ROI) analyses defined by a priori hypotheses indicated significant positive correlations between average RC and rCMRglu in areas corresponding to the frontal and supplemental eye fields, and right caudal thalamus. Average RC were negatively correlated with rCMRglu in areas corresponding to the cuneus bilaterally, left superior occipital gyrus, and left inferior and superior parietal lobules. Average RC was also negatively correlated with rCMRglu in a priori

ROIs in the left parietal eye field, bilateral anterior cingulate, and left parahippocampal gyrus.
Conclusions: The areas where average RC was positively correlated with rCMRglu appear to constitute a diffuse cortical system involved in the regulation of emotion-induced arousal. The present study bridges prior observations that both lower baseline activity in the anterior cingulate cortex and elevated average RC in depressed predict poor treatment response in depressed patients by demonstrating that average RC (or elevated REM density) is a direct albeit inverse correlate of anterior cingulate metabolic activity in depressed patients.

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0947.Q

Delta Sleep Changes in Untreated Depression
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Introduction: Although the function(s) of sleep remain unknown, subjective complaints of insomnia, difficulties maintaining sleep, early morning awakening and objective findings in depressed subjects show marked variation from the normal sleep in healthy subjects. The reported EEG abnormalities include, increased sleep onset latency, a shortened REM onset latency, prolonged first REM period, increased amount of REM sleep period in the first half of the night, increased REM density, decreased sleep maintenance, diminished SWS production as compared with age- and sex-matched controls, and increased arousals with intermittent wakefulness. This study aims to investigate these sleep abnormalities in untreated depressed versus a control group. The group included both those who remitted (n=13) and who did not (n=7) and control (n=10) subjects studied over five months.
Methods: Thirty subjects (10 males; 20 females) participated in a study approved by the IRB. All signed informed consent. Subjects were recruited by various means inviting those "feeling blue following separation or divorce". Following initial telephone screening; all potential subjects were evaluated to be free of major illness. All experimental subjects were diagnosed as depressed using the Structured Clinical Interview (SCID-NP). These remained untreated by psychoactive medication during the study, and agreed to refrain from alcohol for the 12 hr prior to the laboratory sessions. Subjects agreed to have 3 nights of sleep studies on the first month; and 2 overnight sleep studies on the 2nd and 4th month respectively. The first night sleep study was a clinical evaluation night to rule out major sleep disorders and 'first night effect".Following the initial sleep screening all subjects had two nights of sleep, one a baseline and the second for dream collections on three occasions: months 1, 2 and 4 and were scored according to Rechtschaffen and Kales. All subjects were asked to maintain a normal rest/activity cycle and allowed to go to bed at their usual time, for 420 minutes of PSG recording. Subjects were classed as remitted or not remitted at Month 5 on clinical criteria and as socially adjusted on a ten point scale.
Results: The three groups Remitted, Not Remitted and Controls did not differ on delta % on the baseline sleep night but did at Month 5 with Remitted having significantly higher delta % (24.3) than non-remitted (14.9%). Delta % at Month 4 was correlated negatively significant with BDI at screening r=-.473;p=.03 and positively with the final Adjustment score r=.469; p=.03.
Conclusions: Among those meeting clinical criteria for depression, volunteers who are most disturbed on a self reported depression measure will continue to have a low delta sleep %. Those with an increase in delta % at Month 4 were more likely to have a high score on an independent rating of social adjustment.

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0948.Q

Determinants Of The Severity Of Sleep Disturbances In PTSD Patients
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Introduction: Severe sleep and dreaming disturbances (SDD) characterize posttraumatic stress disorder (PTSD). SDD severity, however, has been assessed in PTSD patients volunteering for sleep studies of seeking SDD-focused treatments. The influence of determinants such patient characteristics, disorder-related characteristics, and psychiatric comorbidity on SDD severity in a more general PTSD population remains undetermined. The goals of the present study were to assess SDD severity in a large sample of PTSD patients, and to determine the influence of patient-related characteristics (i.e., sex and age), disorder-related characteristics (trauma type, PTSD chronicity, and PTSD severity), and psychiatric comorbidity on SDD severity.
Methods: A group of 368 patients with a primary diagnosis of PTSD (177M; mean age = 36.5/pm 9.9 yrs.; 191W, mean age = 45.4/pm 10.8 yrs.) participated in a baseline assessment prior to randomization in two sertraline PTSD treatment studies. The studies did not bear a specific focus on reduction in SDD. All patients completed the Pittsburgh Sleep Quality Index (PSQI) and the PSQI Addendum for PTSD (PSQI-A) at baseline. The PSQI assesses global sleep quality in the month preceding the questionnaire completion. The PSQI includes 7 components of sleep quality. The PSQI-A consists of 7 additional items to assess the frequency of seven disruptive nocturnal behaviors often reported by PTSD patients (e.g., nightmares, bad dreams, panic attacks, sleep terrors). Types of trauma, PTSD severity, PTSD chronicity, and psychiatric comorbidity were assessed using two structured interviews (CAPS and SCID). ANOVAs were conducted on global PSQI and PSQI-A scores to determine whether SDD severity varied across groups based on sex, age, type of trauma, PTSD chronicity, PTSD severity, and psychiatric comorbidity.
Results: SDD severity did not differ between men and women (p=.66), or across age groups (p=.11), type of trauma (p =.46), PTSD chronicity groups (p=.74), or psychiatric comorbidity (p=.29). SDD severity differed across groups of PTSD severity (PSQI = F(2,636) = 25.88, p <.001; PSQI-A = F (2, 364) = 34.17, p<.001). Patients with extremely severe PTSD (CAPS score > 80) endorsed significant higher PSQI and PSQI-A scores (i.e., poorer sleep quality and more disruptive nocturnal behaviors) than severe (CAPS score = 60-79) and moderate PTSD groups (CAPS score = 50-59).
Conclusions: The generalizability and validity of the findings are reinforced by the inclusion of PTSD patients not enrolled in sleep studies or not seeking SDD-focused intervention. SDD severity in PTSD is independent from gender and age. Trauma type and PTSD chronicity did not influence SDD severity, indicating the SDD are a stable feature of PTSD. Consistent with previous studies, SDD severity parallels PTSD severity. The findings support the notion that sleep disturbance is a core dysfunction of PTSD.

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0949.Q

BDI Items as Predictors of Remission for Untreated Depression
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Introduction: Research suggests that depression is associated with abnormalities in REM sleep. REM sleep has been associated with affect

regulation. Studies show that depressed mood is improved following REM reductions. However, it is possible that improvement is greater for psychological symptoms than for those with a more biological component.Hypotheses are as follows: 1)There will be a significant decrease in total scores on the BDI for all subjects between screening and month 5.2)All subjects will show a significant decrease on 17 psychosocial symptom items. 3)Subjects whose Hamilton is still > 18 and who meet major depression criteria on SCID-NP will not show a decrease on the vegetative items at month 5.

Methods: 20 volunteers (13 female and 7 males, age range 24-49 years) were recruited. Criteria included having been divorced or separated with intent to divorce from a marriage lasting more than 3 years. A structured clinical interview (SCID-NP) ruled out other psychiatric disorders. Subjects with a BDI score > 14 and an HRD score >18 were included. Participants slept in the lab for 2 nights at month 1, 2 and 4 for 420 minutes. Night 1 was a sleep through night and night 2 was a REM interruption night. A BDI was administered on each morning 2 immediately after waking. On month 3 and month 5 subjects completed the BDI, HDR and final SCID.

Results: There was a significant difference found in BDI scores for all subjects from the screening to month 5. Item analysis showed remitters having a significant reduction on all items except items 6 (punishment) and 7 (self-confidence.) Non-remitters demonstrated significant improvements on only items 19 (concentration), 20 (fatigue) and 21 (sex).To distinguish further the change between remitters and non-remitters, items were grouped as vegetative or psychosocial sub-scales. All subjects showed a significant decrease on psychosocial scores [t=4.890 p=0.000<0.05.] from screening to month 5. Remitted subjects had a significant decrease on both psychosocial score [t=5.066 p=0.000<0.005] and vegetative sub-scale [t=4.956 p=0.000< 0.05]. Non-remitters had no significant differences from screening to month 5 on either subscale.Non-remitters had a higher initial and month 5 score on the psychosocial and vegetative sub-scales than remitters.

Conclusions: Results confirmed that all depressed subjects show a significant decrease in the total BDI score and a significant decrease on the 17 psychosocial items without treatment over a 5month periodNon-remitters showed no significant decrease on the vegetative sub-scale. These appear more resistant to change in the absence of treatment.Individuals who score high on the vegetative items on the BDI should be recommended for more conventional treatments. Those with lower scores may respond well to REM interruption.

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0950.Q

Evaluation Of Sleep Disturbance In Posttraumatic Stress Disorder

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Introduction: The character of sleep structures in PTSD are controversial. In several previous polysomnographic studies in PTSD subjects, there is general agreement that total sleep time and sleep efficiency are reduced, however, there are disagreements as to REM sleep and slow-wave sleep (SWS). Those subjects in several previous studies were mainly chronic subjects whose PTSD had been present for more than 20 years, therefore there is a possibility that those studies can not demonstrate typical features of PTSD. Therefore we investigated relatively acute PTSD subjects.

Methods: The subjects were 7 patients with relatively acute PTSD. The average age was 25.7±9.0 years old, and average time since trauma was 18.7±19.9 months. Three subjects were sea disaster survivors, two were traffic accident survivors, one was a rape survivor and one was witness to the struck accident by lightning. All subjects were assessed by Clinician-Administered PTSD Scale (CAPS), and the average CAPS score was 85.9±14.5, well above the suggested cutoff value of 50. All subjects underwent 2 nights of polysomnographic study before treatment in the sleep laboratory. All subjects went to bed at their own chosen time, and all woke up naturally without an alarm. Informed consent was obtained from all subjects after the objective and procedures of this study had been fully explained to them. Polysomnographic data was analyzed, using the procedures described by Rechtschaffen and Kales. Only data from sleep night 2 were used for formal analysis in the present report. We compared with previous healthy control subjects of average 21 years old in our sleep laboratory.

Results: Total sleep time and sleep latency for PTSD subjects (respectively 446.9±50.2 and 14.3±13.7) were almost normal, while those for control subjects was respectively 447.5±15.5 and 21.4±17.0. Sleep efficiency for PTSD subjects (87.4±5.2) was reduced, compared with control subjects (94.3±2.9). Wake time after sleep onset for PTSD subjects (32.3±27.8) was prolonged, compared with control subjects (5.1±4.2). Number of arousals for PTSD subjects (20.7±13.7) was remarkably increased and this was one of the notable features in present study. Another feature for PTSD subjects was decreased percent slow-wave sleep (4.9±5.3), while that for control subjects was 14.8±3.9. In two patients (patients 1 and 7) who reported frequent nightmare, REM interruption of more than 10 minutes was recognized. REM latency for PTSD subjects (128.2±44.5) was prolonged, compared with control subjects (61.9±7.1).

Conclusions: Reduced sleep efficiency in the present study agreed with several previous studies in PTSD subjects. There is disagreement as to number of arousals, REM interruption, REM latency, and percent SWS in previous studies. However, our findings demonstrated increased number of arousals, frequent REM interruption, prolonged REM latency, and reduced percent SWS. This may be because subjects in this study were relatively acute PTSD patients and they had frequent nightmare and hyperarousal state for more intensive memory of trauma, compared with chronic PTSD patients in previous studies.

0951.Q

Burnout Syndrome is Associated with Markedly Reduced Sleep Efficiency and SWS

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Introduction: Burnout has become very prevalent in western society and accounts for a large part of the costs of sickness absence in Sweden. Its main characteristic is extreme fatigue despite apparently adequate sleep duration, although subjective sleep quality is greatly impaired. However, as yet there has been no published reports of polysomnography in burnout patients. The present study sought to provide this.

Methods: 32 patients were recruited from the patient register of an insurance company. All approached had been on sick leave for a minimum of three months with a diagnoses of burnout, stress-related disorder or exhaustion/depression. A control group of 16 normals of the same gender and age were recruited through advertisments and contacts. All subjects had a polysomnographical recording in their home (after habituation) and had a 24h ambulatory blood pressure recording carried out the next day. Actigraphy was carried throughout the week of measurement and sleep quality ratings were given each day. Also blood samples were obtained in the morning and saliva samples for cortisol every two hours during one day. Sleep was scored according to Rechschaffen and Kales (1968) and arousals were scored according to the consensus established by the American Sleep Disorders Association. The data were analysed with t-tests or ANOVAs depending on the type of data.

Results: The results showed that the patients slept as long as the normals (TST = 372±19 vs 419±18 minutes; ns) but had a lower sleep efficiency (76±4% vs 90±5%; p<.01), a higher number of arousals (17±2 vs 14±2 per hour; p<.05), a longer sleep latency (42±12 vs 12±3 minutes; p<.01), a longer latency to stage 3 sleep (26±5 vs 13±2 minutes;

p<.05), less slow wave sleep (stage 3+4: 8±3% vs 18±4%; p<.01)) and more stage 2 sleep (59±3% vs 45±2%; p<.001). REM% did not differ between groups. Most measures of subjective sleep quality showed more disturbances in the patient group.
Conclusions: The results indicate that sleep is severly disturbed in burnout patients, although total sleep time may show relatively normal values.

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0952.Q

Sleep Difficulties and Attention Deficit Hyperactivity Disorder: Children's Perspectives

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Introduction: Introduction: It has often been assumed, by parents as well as clinicians, that sleep problems are prevalent in children with Attention Deficit Hyperactivity Disorder (ADHD). Surprisingly, little systematic research has been directed towards exploring the relationship between ADHD in children and the prevalence of sleep problems. Further, in both research and clinical practice, children's reports of their sleep difficulties are often unsolicited; a review of the literature reveals little information about the prevalence of children's sleep difficulties from the child's perspective. The purpose of the present study was to explore self-reported sleep problems among children with ADHD. Since stimulant medications are the most common form of treatment for ADHD, and have been linked to certain sleep problems, the incidence of sleep problems among ADHD children who are being treated with stimulant medications was also examined.
Methods: Method: Ninety-nine 7-17year old (Mean=10 years, 0 months) children, diagnosed with ADHD following a comprehensive evaluation at an ADHD clinic, participated. Thirty-six percent of participants were taking stimulant medication at the time of the data collection. As part of the ADHD evaluation, children completed a self-report questionnaire, developed by the authors, designed to assess children's sleep habits and sleep problems.
Results: Results: Children with ADHD report experiencing various sleep difficulties on a frequent basis. Among the most prevalent sleep difficulties endorsed by these children were the following: delayed sleep onset (74%); not being tired at bedtime (73%); nighttime awakening (66%); nightmares (64%); and daytime fatigue (58%). Whereas 69% of the entire sample reported experiencing sleep difficulties, 100% of those on stimulant medication reported experiencing such problems (X2=10.39, p<.001). Overall, the ADHD children on stimulant medication reported a greater number of sleep problems on a frequent basis than did the ADHD sample as a whole. Of the ADHD children taking stimulant medication, 100% reported experiencing delayed sleep onset on a frequent basis. Other prevalent sleep difficulties endorsed by the ADHD children taking stimulant medication included the following: not being tired at bedtime (78%); nighttime awakening (78%); nightmares (78%); headbanging (75%); daytime fatigue (67%); and napping (63%).
Conclusions: Conclusions: Taken together, these results highlight the importance of obtaining children's reports of their sleep difficulties and suggest that children with ADHD. experience a variety of sleep difficulties on a frequent basis. Further, the present study highlights the impact that stimulant medications have on sleep, as it suggests that utilizing stimulant medications dramatically increases the likelihood that an ADHD child will experience sleep problems. Future research attention should be directed towards elucidating the relationships between stimulant type and dose on sleep. These preliminary findings speak to the importance of evaluating and treating sleep problems in children with ADHD.

0953.Q

Comparison of In-Lab Polysomnography in Night Eating Syndrome Patients and Overweight Controls

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Introduction: Night eating syndrome (NES) is a disorder of sleep, eating and mood, characterized by morning anorexia, evening hyperphagia, nocturnal ingestions and depressed mood. This is the first study to date to examine the sleep of these patients using more than one night of polysomnography, and to compare their sleep patterns with those of weight matched control subjects. This is the first study to include an adaptation night in the sleep laboratory in order to control for first night effects.
Methods: Twelve NES patients and 15 overweight control subjects completed a 3-day laboratory protocol in the GCRC, consisting of 2 nights of polysomnographic (PSG) recordings, followed by a 24-hour blood collection period. Subjects were allowed to eat ad lib in their rooms, and were encouraged to bring in favorite foods to be available for snacking purposes overnight. The first night of PSG recording included clinical assessments to screen subjects for occult sleep disorders (OSAS, PLMS, RLS). The second night of PSG recording assessed sleep variables including sleep latency, sleep efficiency, wake after sleep onset, number of awakenings and sleep stages, scored using standard criteria. Video recordings were collected on a subset of subjects.
Results: The results were analyzed on TEMEC's CASA analysis system software on computers in the Sleep and Chronobiology Laboratory. Traditional sleep stage scoring was performed using standardized criteria. No subjects were excluded due to the presence of occult sleep disorders on night one. On the second night of PSG, NES patients had a significantly lower sleep efficiency compared to the control subjects (65.5%±5.1 vs. 82.0%±2.2, p<0.01), with less stage 2 (118.9m+22.2 vs. 227.7m+20.9, p=0.01) and stage 3 sleep (23.8+3.2 vs. 38.2+3.3), p<0.05). There was no significant difference in total sleep time, sleep onset latency, REM onset latency, REM sleep, or the number of awakenings between the two groups. There was a significant difference in the timing of awakenings, however, with the NES patients waking earlier in the sleep period than control subjects. In addition, in the NES patients, significantly more of these awakenings were associated with ingestion of food than in the control subjects (80.8% vs. 5.7%, p< .0001).
Conclusions: It is likely given these results that the decreased sleep efficiency was associated with increased duration of awakenings (WASO). This may be due to an increased incidence of food consumption during awakenings by the NES patients compared to the control subjects. Further analysis of the awakenings is continuing. This supports both self-report and diary records in NES subjects of frequent nocturnal arousals with getting up out of bed to eat.

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0954.Q

Sleep-Disordered Breathing Prevalence In Non-Treatment Seeking Crime Victims

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Introduction: Research suggests Sleep-Disordered Breathing (SDB) is prevalent in 80-90% of trauma survivors and appears to exacerbate Post-traumatic Stress Disorder (PTSD). However, these studies may have been limited by selection bias due to samples of patients seeking sleep treatment. To address this bias, we investigated SDB in non-treatment seeking crime victims.

Methods: We recruited 254 consecutive crime victims seeking reparation from a state agency, a majority (80%) of whom were not seeking sleep or mental health treatment. Of 254, 162 participated and had high rates of PTSD (88%), insomnia (85%), and nightmares (60%). SDB was presumptively diagnosed with AASM research criteria and was classified into four SDB presentation types: No SDB, SDB Type-A (*criterion A only: sleepiness*), SDB Type-B (*criterion B only: insomnia type*), and SDB Type-AB (*criteria A and B*). To compare levels of PTSD, insomnia, quality of life impairment, and traumatic nightmares (TN) between SDB presentation groups, we used three validated scales: PSS, ISI, and Q-LES-Q. Cohen's d effect sizes were calculated to compare groups.
Results: Of 162 participants, 144 (89%) were presumptively diagnosed with SDB, and only 18 (11%) had no SDB symptoms. Of 144 with SDB, 64 (44%) presented SDB Type-B, and a majority, 79 (55%), presented SDB Type-AB. Compared to the No SDB group reporting mild or no symptoms of PTSD, insomnia, and quality of life impairment, SDB Type-B and SDB Type-AB groups reported significantly (all p<.01) worse PTSD [Type-B (d=2.15); Type-AB (d=2.60)], insomnia [Type-B (d=2.14); Type-AB (d=2.93)], and quality of life impairment [Type-B (d=1.13); Type-AB (d=1.90)]. SDB Type-AB patients also had significantly (all p<.01) worse PTSD (d=0.45), insomnia (d=0.74), and quality of life impairment (d=0.64) compared to SDB Type-B. Last, a majority of SDB Type-AB patients reported a high frequency of TN (62%), whereas, a majority of No SDB (100%) and SDB Type-B (63%) patients reported a low frequency of TN.
Conclusions: This is the first study to document a high rate of SDB in non-treatment seeking trauma survivors. These findings coupled with findings in treatment seeking samples suggest that SDB in trauma survivors functions as an important component of posttraumatic sleep disturbance, which is likely to exacerbate PTSD. Furthermore, the mechanism by which SDB might fuel greater PTSD appears to be complex. This complexity was most evident in those reporting paradoxical symptoms of sleepiness and insomnia (SDB Type-AB), who had significantly worse PTSD, insomnia, impairment, and TN frequency compared to those who indicated insomnia-type only (SDB Type-B). We speculate that the combination of insomnia and sleepiness thwarts psychological and physiological coping abilities, which in turn undermines the trauma recovery process. We are currently enhancing the validation of this study with a general population control group. Notwithstanding, research is needed to determine whether treatment of SDB, which may alleviate insomnia and sleepiness, would enhance other PTSD treatments and subsequent recovery.

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0955.Q

Cortisol Reactivity to Social Stress in High-Functioning Autistic Spectrum Disorders \bold

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Introduction: Previous studies have shown various types of neuroendocrinological abnormalities in autism, including at the level of the hypothalamic-pituitary-adrenal (HPA) axis. Additionally to core deficits, persons with autism frequently develop emotional disturbance including anxiety. The aim of the present study was to analyze anxiety and stress levels in persons with high-functioning Autistic Spectrum Disorders (ASD).
Methods: Fourteen participants diagnosed with high-functioning ASD (mean age: 21,7 y.o. ± 3,89) and 5 healthy controls (mean age: 22,6 y.o. ± 3,05) came to our laboratory for two successive nights for sleep recordings. On both occasions, samples of saliva were obtained in the evening (5 samples) and morning (2 samples); cortisol levels were determined using radioimmunoassays. The State-Trait Anxiety Inventory was administered on the evening of night 2. Statistical comparisons were made using Mann-Whitney U-test for independant groups on salivary cortisol secretion and T-test for independant groups on the state-trait anxiety Inventory global scores.
Results: The high-functioning ASD group showed a lower mean level of salivary cortisol for night one first measure only ($p < .042$) compared with controls. The analysis of the state-trait inventory showed no difference between group for state-anxiety score but a significantly higher trait-anxiety score for high-functioning ASD compared to controls ($p < .046$).
Conclusions: The results obtained on the STAI questionnaire shows that persons with high-functioning ASD are characterized with chronic high levels of anxiety. The fact that Trait Anxiety was not different from controls needs replication since results were obtained upon night 2 so that habituation might have blunted the acute effects of stress. On the other hand we found a cortisol decrease in participants with ASD only upon the first measurement of night one, which could reflect an atypical response to acute social stress. The present results suggest that persons with ASD may be characterized by an atypical regulation of anxiety and stress processes. We suggest that sleep disorders in persons with ASD may be explained in part by limited abilities to react adequately to perturbating factors such as psychosocial stress and reflect a cascade of biochemical events leading to atypical cortisol regulation.

0956.Q

Sleep Quality Deteriorates Over a Simulated Binge-Abstinence Cycle in Chronic Cocaine Users: A Combined Nightcap and Polysomnographic Study

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Introduction: Abstinent cocaine abusers report poor sleep, sometimes developing an insomnia-like condition with extended sleep latency and poor sleep efficiency.
Methods: Participants, 5 non-treatment-seeking crack users (4 male, mean age 36.4, range 30-41) with DSM IV diagnoses of Cocaine Dependence, signed consent. They lacked other DSM-IV Axis I disorders or medical illness. They resided at the Columbia-Presbyterian Medical Center's CRC. During the 22-day (D) protocol, sleep was monitored with PSG (D2=adaptation, D4-D6, D9, D11-D13, D16, D20-D21) and Nightcap (NC, all days). Three days abstinence/washout ("WA," D1-D3) was followed by 3 days binge ("BI," D4-D6) and 16 days abstinence ("AB," D7-D21, subdivided: i. early, "ABE_NC"=D7-D8, "ABE_PSG" =D9+D11-D13; ii. late, "ABL_NC"=D9-D21, "ABL_PSG"=D16+D20-D21; iii. last week, "AB7," NC=D15-D21). Each BI day, participants completed 2 self-administration sessions under medical supervision smoking six 50 mg, NIDA-supplied doses every 14 min. PSG (Grass Colleague) with bilateral EMG, EOG, and EEG (C3/A2, C4/A1, O1/A2, O2/A1) was scored by R&K criteria. Analyses were: i. regressing daily variable means of 5 subjects against experimental day; ii. repeated measures ANOVA of subject (N=5), study phase (WA, BI, AB), Bonferroni-corrected variable means.
Results: NC sleep duration (SD) decreased across WA+BI+AB ($p<.0001$, $r=.768$), BI+AB ($p<.01$, $r=.693$), and AB ($p<.05$, $r=.528$). PSG SD decreased across BI+AB ($p<.05$, $r=.697$). ANOVA showed NC SD phase differences (AB< WA or BI $p<.0167$; ABL_NC<WA or BI $p<.0083$). NC sleep efficiency (SE) decreased across WA+BI+AB ($p<.05$; $r=.509$) and BI+AB ($p<.05$; $r=.508$). PSG SE decreased over BI+AB ($p<.05$, $r=.643$). ANOVA showed PSG SE difference between BI and PSG_ABL ($p<.0167$). NC sleep latency (SOL) increased across

WA+BI+AB (p< .01; r=.580) and BI+AB (p<.05; r=.525). PSG SOL to the first 10 min of sleep (SOL10) increased over BI+AB (p<.05., r=.650). ANOVA showed SOL10 increase from BI to AB (p<.05). PSG REM latency (REML) decreased over BI+AB (p<.05, r=.738; ANOVA mean BI>AB, p<.05).

Conclusions: Using NC or PSG, SD, SE and SOL declined from binge to abstinence. Mean NC SD, SE and SOL fell from 6.4 hr, 83% and 24 min respectively during BI to an insomnia-like 5.6 hr, 75%, 48 min during AB7 suggesting possible allostatic sleep quality maintenance by cocaine. REML declined from 66 min to 48 min from BI to ABL suggesting depressive symptoms.

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0957.Q

Cognitive Performance in Chronic Cocaine Users over Binge-Abstinence is Temporally Associated with Sleep Quality Declines

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Introduction: Cognitive impairments of chronic cocaine users have been documented during sustained abstinence. We investigate cognitive changes temporally associated with sleep quality declines.

Methods: Five non-treatment-seeking crack users (4 male, mean age 36.4, range 30-41) with DSM IV diagnoses of Cocaine Dependence but no other Axis I disorders or medical illness signed consent. In this 22-day (D) protocol at Columbia-Presbyterian Medical Center's CRC, three days abstinence/washout ("WA," D1-D3) was followed by 3 days binge ("BI," D4-D6) and 16 days abstinence ("AB," D7-D21). Each BI day, participants completed 2 self-administration sessions under medical supervision smoking six 50 mg, NIDA-supplied doses every 14 min. Every day (except D9-D10 and D16-D17), subjects completed a multiply repeatable battery developed by CDR, Ltd. shortly after awakening (am tests) and again in late afternoon (pm tests). Tasks included simple reaction time (SRT), choice reaction time (CRT), digit vigilance (DV), numeric (NWM) and spatial working memory (SWM), immediate (IR) and delayed word recognition (DR). Simple regression preliminarily analyzed principal CDR output variable changes over experimental days using all-subject daily means in the 4 (of 5) subjects analyzed to date.

Results: Daily mean IR original stimuli accuracy (IROAC) and sensitivity index (IRSI) declined over all experimental days (both p<.0001). IROAC and IRSI declined over AB (D7-D21) alone (both p<.05) and in am (p<.05 and p<.01 respectively) and pm (both p<.0001) tests. DROAC and DRSI declined over all days (p<.01, p<.05). DROAC and DRSI did not change over AB or am tests but declined in pm tests (p<.001, p=.05). Daily mean SRT increased over all days (p<.0001), AB alone (p<.01) and am and pm tests (p<.01 each). DV speed of detection (DRRT) but not accuracy (DRACC) increased over all days (p<.01), AB alone (p<.05) and pm (p<.001) but not am tests. CRT reaction time CRTRT (but again not CRTACC) increased over all days (p<.01), AB alone (p<.05), and am and pm tests (p<.05, p<.01). In contrast, Spatial Working Memory SWMOACC and SWMSI improved over all days and for SWMOACC in pm tests (p<.05 each) but not during AB alone. No changes were seen for NWM.

Conclusions: Over the WA-BI-AB cycle and AB alone, preliminary results suggest declining recognition memory, vigilance reaction time and psychomotor speed. Greater pm declines suggest circadian and/or homeostatic components in declines. Abstinence declines suggest allostatic maintenance of performance by cocaine in chronic users. Cognitive declines were temporally associated with sleep quality declines we also report in this volume.

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0958.Q

PTSD: Posttraumatic Stress Disorder or Posttraumatic Sleep Disorders?

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Introduction: In psychiatric nosology, insomnia and nightmares that occur after traumatic exposure are generally understood as symptoms of PTSD, which may inadvertently limit the treatment of posttraumatic sleep disturbances to psychological or psychiatric interventions. Few studies have addressed the potential for PTSD sleep problems to manifest as diagnosable, intrinsic sleep disorders that would benefit from sleep medicine interventions. When sleep medicine diagnostic criteria have been applied to sleep disturbances in trauma survivors, psychophysiological insomnia (PPI), chronic nightmare disorder (CND), and sleep-disordered breathing (SDB) have been highly prevalent. To examine these sleep and PTSD relationships, we tested whether symptoms of PPI, CND, and SDB predicted PTSD symptom severity in a group of disaster survivors.

Methods: The sample comprised 78 individuals reporting insomnia and/or nightmares allegedly caused or exacerbated by the Cerro Grande National Forest Fire (May, 2000), evacuation, or related events. Fifty women and 28 men (Age M=51.5, SD=13.0) participated. Based on AASM nosology (1997) and research criteria for SDB (1999), 99% were presumptively diagnosed with PPI, 33% with CND, and 95% with SDB. The Insomnia Severity Index (ISI), Disturbing Dream and Nightmare Severity Index (DDNSI), and Functional Outcomes of Sleep Questionnaire (FOSQ) measured symptoms of PPI, CND, and SDB respectively. Multiple linear regression (MLR) analyses were conducted to predict PTSD severity from these sleep disorders scales.

Results: Multiple linear regression showed that ISI (b = .33, p < .01), DDNSI (b = .29, p < .01), and FOSQ (b = -.22, p < .05) were each significant predictors of overall PTSD severity, accounting for 39% of the variance (R2 = .39, F = 11.17; p < .0001). Follow-up analyses with PTSD subscales showed that ISI (b = .38, p < .01) and DDNSI (b = .30, p < .01) were positively associated with intrusion symptoms; FOSQ was the sole significant predictor of avoidance symptoms (b = -.27, p < .05); and all three measures individually predicted PTSD arousal (ISI, b = .33, p < .01; DDNSI, b = .24, p < .05; FOSQ, b = -.24, p < .05).

Conclusions: In fire disaster evacuees, 39% of PTSD distress was explained by symptoms of PPI, CND, and SDB. Nightmares and insomnia each predicted PTSD intrusion and arousal; SDB also predicted arousal. Unexpectedly, SDB-related sleepiness (FOSQ measurements) was the sole predictor of PTSD avoidance behaviors. These findings raise important treatment implications. Independent treatment of intrinsic sleep disorders in PTSD may directly reduce posttraumatic sleep disturbance complaints not addressed by standard psychiatric/psychological interventions. In particular, future studies are needed to test whether treatment of SDB-related sleepiness decreases PTSD avoidance behaviors—the symptom cluster described as a highly reliable indicator for development and entrenchment of chronic PTSD..

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0959.Q

Mood and PTSD symptom Correlates with Polysomnography and Actigraphy

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Introduction: Polysomnography (PSG) is the "gold standard" for measurement of sleep, however few studies have compared its efficacy to actigraphy in the measurement of sleep in the PTSD population. We hypothesized that both actigraphy and polysomnographic measures of sleep would be correlated with mood states, particularly depression, and PTSD symptoms Vietnam War Veterans with Post Traumatic Stress Disorder (PTSD).
Methods: Twenty-seven (78% Caucasian, 11% African-American, 7% Hispanic and 4%Asian) subjects (age 45.7, SD±10.4) underwent full night PSG for three consecutive nights in addition to wearing a wrist actigraphy monitor on the nondominant wrist. Sleep variables were scored from the automatic sleep scoring form the Action 4® software program for actigraphy and standard criteria for PSG. Self-report state measures of mood including the Beck Depression Index (BDI), Profile of Mood States, and Impact of Event Scale-Revised (IES-R) were obtained the morning after each sleep recording.
Results: Results: The actigraphic and polysomnographic measures: total sleep time (TST), wake after sleep onset (WASO) and sleep maintenance (SM) means, standard deviations and ranges are presented in Table 1.

Table 1.	Actigraphy TST	WASO	SM	Night 1
355.67±86.2	73.5±65.2	82.9±14.9	Night 2	352.26±102
79.48±65.8	81.4±16.65	PSG		Night 1
323.23±81.8	108.62±79.36	75.2±16.4	Night 2	
347.98±60.8	82.30±59.1	82.1±12.0		

A visual examination of Table1 reveals reasonable agreement between PSG and actigraphy, however Pearson Correlations between PSG and actigraphy findings reveal no significant correlations for night 1 (adaptation night). On night 2 the Pearson Correlations between PSG and actigraphy was r = .75 (p = .01, 2 tailed) for WASO and r = .61 (p = .01, 2 tailed) for SM. On night 2, there was no significant correlation between between PSG and actigraphy for TST.BDI correlations:There was a modest positive relationship between actigraphy TST night 1 and the BDI for day 1 (r = .37), however the PSG variables, WASO and SM findings were more robust, r = .68 (p = .01, 2 tailed) and r = .63 (p = .01, 2 tailed) respectively in predicting depression for day 1. Neither PSG or actigraphy measures were significantly correlated with depression on night 2.POMS correlations:Actigraphic TST for night 1 was modestly correlated with the POMS total mood score (r = .34) for day 1, however the PSG variables, WASO and SM for night 1 were more strongly correlated, r = .64 (p = .01, 2 tailed) and r = -.57 (p = .01 2 tailed) respectively. Neither PSG or actigraphy measures were significantly correlated with mood states on night 2.IES-R correlations:Only the actigraphic TST measure on night 1 was significantly correlated with the IES-R total score r = .50 (p = .01, 2 tailed). PSG variables on night 1 and the IES-R score were significantly correlated with WASO (r = .62, p = .01, 2 tailed) and SM (r = -.58, p = .01, 2 tailed). Neither PSG or actigraphy measures were significantly correlated with PTSD symptoms on night 2.
Conclusions: In contrast to the more robust measures for PSG, actigraphic measures of sleep were not significantly correlated with many of the state measures of mood and PTSD symptoms. Further, actigraph measures are not strongly correlated with PSG on the first night of recording. It is possible that the standard algorithm used to estimate sleep from actigraphy is not sensitive in a PTSD population particularly on adaptation nights.

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0960.Q

ADHD and Sleep Problems in Adults

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Introduction: Research on the relationship between sleep problems and Attendion Deficit/Hyperactivity Disorder (ADHD) has revealed several interesting associations in children and adolescents. The dimensions of inattention and hyperactivity have been associated with snoring, sleep disordered breathing, daytime sleepiness, and periodic limb movement in clinical and nonclinical populations. It is unknown at the present time, however, whether sleep problems act as a vulnerability factor in the development of ADHD or whether the relationship operates in the opposite direction. The relationship between sleep problems and adult ADHD has received very little attention compared to the research on children and adolescents. Adult research has focused on a very narrow range of sleep disturbances and has failed to take into account lifestyle issues related to sleep hygiene that are known to be associated with adult ADHD. The present study examined the relationship between ADHD symptoms and sleep symptomatology in a community-based sample of adults.
Methods: 125 men and 448 women participated in the study. The mean age for men was 21.2 (sd = 3.79) years and for women was 21.3 (sd = 5.30) years. Participants completed the two DSM-IV ADHD scales from the Conners Adult ADHD Rating Scale (CAARS), as well as all items from the Sleep Problems Inventory (SPI). The SPI is a 52-item self-report measure developed to assess symptoms associated with common sleep disorders (nightmares, circadian rhythms, sleep walking, insomnia and excessive sleepiness) and behaviors associated with poor sleep hygiene (substance abuse and disrupted routine).
Results: A series of hierarchical multiple regression analyses were conducted with each of 5 sleep disorder scales as a dependent variable. In each regression analysis, the two ADHD variables were entered first, followed by the two sleep hygiene variables in a second step (ADHD was entered first, since it has been linked with substance abuse and lifestyle issues, as well as sleep problems in adults). With insomnia problems as the dependent variable, ADHD symptomatology produced an R2 of .08 ($p < .01$); when the two sleep hygiene scales were entered in a second step the R2 change was 0.10 ($p < .01$). For nightmares, ADHD symptomatology produced an R2 of .02 ($p < .05$); the two sleep hygiene scales produced an R2 change of 0.04 ($p < .05$). For circadian rhythm problems, ADHD symptomatology produced an R2 of .07 ($p < .01$); the two sleep hygiene scales produced an R2 change of 0.30 ($p < .01$). For sleepwalking problems, ADHD symptomatology produced an R2 of .03 ($p < .05$); the two sleep hygiene scales did not produce a significant R2 change. For excessive sleepiness, ADHD symptomatology produced an R2 of .16 ($p < .01$); the two sleep hygiene scales produced an R2 change of 0.11 ($p < .01$).
Conclusions: The overall results suggest that there is a modest association between several types of sleep problems (particularly insomnia, circadian rhythm problems, and excessive sleepiness) and ADHD symptomatology in adults.

0961.Q

First Night Effects in Posttraumatic Stress Disorder and Control Participants in Home and Hospital Environments

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Introduction: The first-night effect (FNE) is a well-known phenomenon in sleep research, mainly characterized by lower sleep efficiency, increased wakefulness, reduced rapid eye movement (REM) sleep time and prolonged latency to the first REM sleep period. To date, only a few

studies have been conducted in posttraumatic stress disorder (PTSD) to assess whether first-night effects occur in these participants. The aim of this study was to evaluate first-night effects on sleep architecture in participants with posttraumatic stress disorder (PTSD) and normal controls, by using polysomnography (PSG) recordings obtained in participants homes and again in a hospital observation unit.

Methods: This study's main comparisons were between outpatient participants with PTSD (N= 33) normal controls (N= 15). All were free of psychotropic medication at the time of the sleep recordings. Potential participants were screened and excluded for the following: sleep apnea, systemic illness affecting CNS function, neurological disorder, bipolar disorder, psychosis, drug/alcohol abuse/dependence in the past 5 years. Normal controls met the same exclusion criteria and had no lifetime history of PTSD and/or Major depression.Sleep-wake activity was monitored over eight consecutive nights. The study involved 5 nights of ambulatory polysomnography, 2 at home and 3 in a hospital research unit. The home PSG and hospital PSG are separated by 3 nights. The order of home vs. hospital sleep studies were counterbalanced in order to study order effects in adaptation to recording equipment and hospitalization. Each morning participants filled out self-report measures of mood, PTSD symptoms and subjective sleep quality on a 10cm visual analog scale.

Results: No first night effects were found in the home environment in either the PTSD or control groups.FNE were found in the Hospital environment in both groups. PTSD subjects had lower sleep efficiency, REM sleep time, REM percent, and lower subjective sleep quality on night 1 compared to night 2. Controls had less total sleep time, sleep efficiency, REM sleep time, and lower subjective sleep quality on night 1 compared to night 2.Relative to subjects with chronic PTSD, control subjects had a greater first night effect adapting to hospital admission as evidenced by significantly greater decrease in total sleep time (group x time F= 6.4, p <.015), REM time (group x time F= 4.4, p = .04), and subject sleep quality ratings (group x time F= 4.6, p = .04) on hospital night 1 relative to night 2.

Conclusions: First night effects are absent in home polysomnography in both PTSD and controls. Both PTSD and controls demonstrated FNEs to being admitted to a hospital clinical research unit. Control subjects demonstrated a significantly greater decrease in total sleep time, REM sleep time, and subjective sleep quality on night 1 versus night 2 relative to PTSD subjects.

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0962.Q

Sleep and Psychiatric Disorders in Alcoholics

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Introduction: Alcohol has adverse effects on sleep, and sleep complaints are common in alcoholics. Alcoholics also have high rates of psychiatric comorbidity, and psychiatric disorders are strongly correlated with sleep disorders in the general population. Thus sleep problems in alcoholics may be secondary to alcohol use, related to coexisting psychiatric disorders, or represent a primary premorbid characteristic of this population. We assessed the association between sleep complaints and psychiatric disorders in an alcoholic population.

Methods: Subjects were 96 veterans who had entered a substance treatment program at the William S Middleton Veterans Hospital in Madison, Wisconsin. Charts of consecutive admissions were reviewed and the following data extracted: demographic information, Beck Depression Inventory-II scores (including overall scores, scores for sleep items only, and overall scores minus sleep items), psychiatric diagnoses, and substance treatment program involvement over the 6 months after entry.

Results: Of 96 subjects total, 57 of 75 (76%) with comorbid psychiatric diagnoses reported a complaint of sleep change, while only 7 of 21 subjects (33%) with no psychiatric diagnosis other than alcohol abuse or dependence reported a sleep disturbance. All of these 7 subjects scored their level of sleep disturbance as a 1 (on the 0-3 scale) on the BeckD-II, whereas the average score for the 57 patients with comorbid psychiatric illness was 1.8. There were no obvious differences in alcohol use history in patients with or without comorbid psychiatric disorders. Nineteen of the 96 subjects had a diagnosis of an anxiety disorder, 26 had a mood disorder, and 6 a thought disorder, with some overlap. 63% and 58% of those with a diagnoses of anxiety or mood disorders, respectively, complained of decreased sleep, 21% and 27% complained of increased sleep, with only 15% of each of these groups reporting no change in sleep symptoms. In contrast, of those with a thought disorder (n=6), 1/3 reported a decrease in sleep, while 2/3 reported an increase in overall sleep. Subjects with PTSD had the most severe complaints of sleep disturbance, which were correlated with unemployment. Whether the severity of sleep difficulties affected employability, or if lack of structure from unemployment led to sleep disturbance is not known.

Conclusions: In this population of alcoholics in substance abuse treatment, two-thirds complained of sleep disturbance, which is consistent with previous studies. Patients with other comorbid psychiatric disorders had significantly higher rates of sleep complaints and rated them as more severe. Diagnoses of anxiety or mood disorders were primarily associated with complaints of decreased sleep, whereas those with thought disorders more often reported an increase in sleep. The latter group, however, were all on medications that are considered sedating, which likely impact on reported sleep complaints. These results suggest that even in a population with alcoholism, sleep disturbance is significantly correlated with psychiatric disorders, particularly mood and anxiety disorders.

0963.Q

Modafinil Improves Wakefulness and Reduces Fatigue in Patients with Seasonal Affective Disorder/Winter Depression: An Open-Label Study

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Introduction: Hypersomnia and fatigue are cardinal symptoms of seasonal affective disorder/winter depression. The novel wake-promoting agent modafinil works selectively through the sleep/wake centers of the brain to improve wakefulness in a number of clinical models, including narcolepsy, obstructive sleep apnea, and Parkinson's disease. Modafinil has also been shown to reduce fatigue in multiple sclerosis and major depressive disorder. This open-label study assessed modafinil as treatment for seasonal affective disorder/winter depression.

Methods: Patients with a diagnosis of seasonal affective disorder/winter depression were enrolled in this 8-week, open-label, single-center, pilot study conducted during winter months. All patients received oral modafinil 100 mg in the morning for week 1. For weeks 2-8, patients could continue on the 100 mg morning dose or take 200 mg/day of modafinil as a split dose (100 mg morning plus 100 mg midday). Modafinil could be taken as monotherapy or adjunct to ongoing, stable antidepressant therapy. Efficacy was assessed at weeks 1, 2, 5, and 8. The effects of modafinil on sleepiness and fatigue were quantified by changes in the Epworth Sleepiness Scale (ESS) and the Fatigue Severity Scale (FSS), respectively. Other efficacy measures included clinical ratings and depression scales. Adverse events were monitored.

Results: Thirteen patients (11 women, 2 men; mean age, 41 yr) were enrolled, 12 (92%) were evaluable for efficacy, and 9 (69%) completed treatment (8 weeks). Daily modafinil dose (weeks 2-8) was 100 mg for 5 (42%) and 200 mg for 7 (58%) patients. Six patients were taking only modafinil, while 6 were also taking antidepressants. Modafinil significantly improved wakefulness from mean (SD) ESS score of 13.3 (4.1) at baseline to 9.1 (2.8) at week 2 (P<0.01) to 8.0 (3.3) at week 8 (P<0.01). At week 8, only 5/12 (42%) of patients had moderate to excessive day-

time sleepiness (ESS score ≥ 10), compared with 10/12 (83%) at baseline. Modafinil also significantly reduced fatigue from mean (SD) FSS score of 5.3 (0.9) at baseline to 4.6 (0.8) at week 2 (P<0.01) to 3.9 (1.3) at week 8 (P<0.01). At week 8, only 5/12 (42%) of patients had moderate to severe fatigue (FSS score ≥ 4), compared with 11/12 (92%) at baseline. These significant improvements in wakefulness and reductions in fatigue were accompanied by significant improvements in overall clinical condition and depression scale ratings. Modafinil significantly improved mean CGI-C ratings from week 1 onward (P<0.001) and symptoms of winter depression assessed by mean SIGH-SAD and MADRS scores from weeks 1 and 2 onward (P<0.01), respectively. Modafinil was well tolerated. The most common adverse events were headache (38%), dry mouth (30%) and dyspepsia (23%).
Conclusions: Modafinil significantly improved wakefulness and reduced fatigue in patients with seasonal affective disorder/winter depression. Modafinil treatment was also associated with significant improvements in mood and overall clinical condition. Modafinil was well tolerated. Further controlled trials of modafinil in this population are warranted.

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0964.Q

Does Environmental Context Affect Sleep Measures in Posttraumatic Stress Disorder and Controls?

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Introduction: Subjects with Posttraumatic Stress Disorder (PTSD) report subjective feelings of hypervigilance particularly when exposed to novel environments. This has led to the speculation that out-of-home sleep recordings in PTSD are less valid than home studies. The aim of this study was to examine if environmental context affected objective and subjective sleep parameters with a particular focus on REM sleep.
Methods: This study's main comparisons were on the second night of sleep recordings (post-adaptation night) between outpatient participants with PTSD (N= 32) and normal controls (N= 15). All were free of psychotropic medication at the time of the sleep recordings. Potential participants were screened and excluded for the following: sleep apnea, systemic illness affecting CNS function, neurological disorder, bipolar disorder, psychosis, drug/alcohol abuse/dependence in the past 5 years. Normal controls met the same exclusion criteria and had no lifetime history of PTSD and/or Major depression. The larger study involved 5 nights of ambulatory polysomnography (PSG), 2 at home and 3 in a hospital research unit. The home PSG and hospital PSG were separated by 3 nights. The order of home vs. hospital sleep studies were counterbalanced in order to study order effects in adaptation to recording equipment and hospitalization. Each morning participants filled out self-report measures of mood, PTSD symptoms and subjective sleep quality on a 10cm visual analog scale. This study compared Home night 2 to Hospital night 2 in PTSD and controls.
Results: There were no home-hospital condition differences in either PTSD or controls in subjective sleep quality or state sensitive measures of mood, PTSD, and daytime vigor.Also, there were no home-hospital differences in total sleep time and sleep continuity measures. There was a significant group x condition interaction with REM activity (F=5.2, p=.03) and REM density (F= 6.3, p = .02). PTSD subjects exhibited a relative increase in REM activity and REM density in the hospital context.
Conclusions: Although there was no effect of environmental context on subjective sleep quality or objective sleep time and sleep continuity, there is subtle evidence that PTSD subjects are more aroused in the hospital context as indexed by the relative increase in phasic REM activity.

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0965.Q

Sleep Functioning in Treatment Seeking Female Rape Victims Diagnosed with PTSD

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Introduction: Previous research has suggested that there is a high degree of association between Posttraumatic Stress Disorder (PTSD) and sleep disturbances. However, there has been no study to date that has examined REM related sympathetic activation in a population of female rape victims with a diagnosis of PTSD. Further, if it is true that psychotherapy exposures serve the same function as dreaming in modulating affectively laden trauma memory networks, then a successful course of exposure-based psychotherapy should lead to a decrease in REM related sympathetic arousal. As a part of a larger treatment outcome study, pilot data was collected on a sample of 5 female rape victims to assess sleep disturbances at both pre- and post-therapy. The goal of this study was to: (1) Compare the REM related sympathetic activation to that for SWS at pre- and post-treatment; (2) To compare the REM related sympathetic activation at pre-treatment to post-treatment; (3) To compare the SWS related sympathetic activation a pre-treatment to post-treatment.
Methods: Five women who met diagnostic criteria for PTSD were offered either Prolonged Exposure (PE) or Cognitive Processing Therapy (CPT) to address their PTSD symptoms. Their pre- and post-therapy sleep functioning was assessed using polysomnography in conjunction with their subjective self-reports. Heart Rate Variability (HRV) was used as a measure of sympathetic nervous system activity and was digitally recorded using standard polysomnographic techniques. Because of the small sample size, non-parametric statistics (Wilcoxon Matched-Pairs Signed-Ranks Test, Wilcoxon-Z) were used to compare these within-group comparisons.
Results: The HRV data for REM were compared with the HRV data for SWS at both pre- and post-treatment. Results indicate greater sympathetic arousal in REM compared to SWS at pre-treatment (Wlicoxon Z = -2.02; p<.05) and post-treatment (Wlicoxon Z = -2.02; p<.05). The HRV data for REM at pre-treatment and post-treatment was also compared. Results indicate a significant decrease in sympathetic arousal from pre- to post-treatment (Wlicoxon Z = -2.02; p<.05). Lastly, The HRV data for SWS at pre- and post-treatment were compared. As anticipated, there was no significant change in sympathetic arousal from pre- to post-treatment (Wilcoxon Z = -.67, p>.05).
Conclusions: The results are intriguing in that they implicate REM sleep in PTSD associated sympathetic activation. REM sleep showed greater autonomic activation as compared to SWS, providing support to the suggestion that work with affectively laden trauma memory networks occurs in REM sleep. Further, results from this pilot data suggests that the sympathetic activation from pre- to post-treatment occurred for REM but not for SWS, thus, providing support that the information processing that occurs during REM, uses connections that are facilitated between trauma issues addressed in therapy, and affectively related memory networks.

0966.R

Effect of Ethnicity on Sleep: Complexities for Epidemiological Research

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Introduction: Given the growing interest in the effects of ethnicity on health, it is surprising that there have not been more studies on ethnic variation in sleep. Ethnicity may significantly impact perceived sleep quality as well as objectively recorded polysomnographic sleep measures. The goal of this study was to examine whether there were ethnic differences in polysomnographically-recorded sleep either in the controlled laboratory environment or in the home setting.
Methods: This was a prospective study of ethnic differences in stress physiology and sleep. Fifty-one employed healthy adult subjects, aged 15 to 50 years were studied. 24 self-identified as black (12W/12M), and 27 as white (8W, 19M). A total of 3 sleep nights were collected: two on consecutive nights in a hospital-based sleep laboratory, followed by a third 1 to 4 weeks later in the subject's home. The first night of sleep in the hospital was considered an adaptation night. All sleep recordings used a polysomnograph (Embla, Flaga Medical, Reykjavik, Iceland) that recorded central and occipital EEG derivations (C3, C4, O1, O2), bilateral electrooculogram (LOC and ROC), submental and anterior tibialis EMG, ECG, nasal/oral airflow using a thermistor and nasal canula, respiratory effort, and finger pulse oximetry. Sleep was scored according to standard criteria. Several variables that could confound the relationship between ethnicity and sleep were considered, including age, AHI, depressive symptoms, social class, and blood pressure level.
Results: The ethnicities did not differ in age, body mass index, blood pressure level, social class, or depression level. A repeated measures ANCOVA was performed entering the sleep stage variables measured in minutes as the repeated measures across location, ethnicity as the between subjects factor and age and AHI as the covariates. The omnibus multivariate test revealed a significant location by ethnicity interaction (Wilks' Lambda = .708; F (4, 44) = 4.54; p = .004). Univariate tests revealed the location by ethnicity interaction was significant for slow wave sleep (SWS) (F (1, 47) = 12.24; p = .001). Between subjects analysis showed that the ethnicities differed on amount of SWS (F (1,47) = 7.82; p = .007). Specifically, compared to whites, blacks had fewer minutes of SWS, both in the hospital (blacks: 15.3 ± 16.6; whites = 49.3 ± 35.1) and home setting (blacks: 23.1 ± 28.1; whites: 37.8 ± 28.4). Blacks had significantly more SWS at home compared to the hospital setting; while the reverse was true for whites. Depression ratings and social class could not account for this location-by-ethnicity interaction.
Conclusions: The home setting is generally considered to be more ecologically valid than the controlled hospital-based laboratory setting for the monitoring of sleep. These data suggest that ethnicities may respond differentially to the sleeping environment. This observation may need to be taken into account in future epidemiological studies of sleep.

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0967.R

Autoset T Titration for Fixed CPAP Pressure

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Introduction: Most patients with sleep apnea are treated with fixed CPAP determined by manual titration. Automatic titration could be used to determine the fixed CPAP(1), resulting in more efficient use of technician time. The AutoSet T system titration responds to snoring, apneas, and inspiratory airflow limitation (2). AutoSet T may, therefore, respond to events (airflow limitation) that are not recognized by technicians.We evaluated the use of attended automatic titration in 10 obstructive sleep apnea (OSA) patients to determine fixed pressure for treatment.
Methods: Ten patients with uncomplicated, moderate-to-severe OSA were assigned to receive titration using the AutoSet T device set in the automatic mode (APAP). The technician monitored the study and intervened for patient management. No manual pressure adjustments were made. Data acquisition was accomplished with the Alice 3 System and Alice Host software. Airflow was determined with either pressure transducer, thermistor, CFLO, or combination of two. Respiratory effort was determined by Piezo sensor. Apneas were scored conventionally. Hypopneas were scored if there was change in effort or flow for 10 seconds with arousal or desaturation. Optimal pressure was determined by scanning the scored study and by review of the table, which displays apneas and hypopneas versus pressure and time. The pressure that eliminated snoring and resulted in fewer than 5 apneas or hypopneas per hour (RDI) was chosen.
Results: Optimal pressure was achieved in 7 of 10 patients. Comparing APAP night to diagnostic night, arousal index improved in 8 of 10 and REM time increased in 8 of 10. In four patients who had reduced sleep efficiency index (less than 85%), three improved. There was no evidence that the frequent changes in pressure disturbed sleep continuity. Pressure always increased appropriately for obstructive and mixed apneas. On two occasions of apparent central apnea, there was appropriate lack of pressure increase. Pressure responded appropriately to snoring. The pressure increased inappropriately in 11 instances: eight - during stage wake; one – coughing; one - spontaneous arousal; and one – periodic leg movement arousal. On two occasions, hypopneas and snoring occurred without appropriate pressure increase. Pressure increased twice during REM sleep without obvious events. Unrecognized airflow limitation could have triggered the pressure increases. Hypopneas occurred once during REM sleep without pressure increases. These could have been central hypopneas for which absence of pressure response was appropriate.Technician intervention was required 10 times: ·; three - increase initial pressure for comfort. ·; three - reposition the patient. ·; two - add chinstrap. ·; one - adjust mask for comfort. ·; one - administer hypnotic.
Conclusions: Automatic pressure titration with the AutoSet T in an attended laboratory setting was effective in establishing fixed CPAP for treatment of OSA in 7 of 10 patients. The other three patients might have benefited from technician intervention with manual titration. APAP usually responded appropriately to snoring and apneas. Technician intervention unrelated to titration was frequently necessary to optimize the result. Occasional inappropriate increases in pressure did not adversely affect the ability to choose optimal pressure.(1) Practice Parameters for the use of Auto-Titrating Continuous Positive Airway Pressure Devices for Titrating Pressures and Treating Adult Patients with Obstructive Sleep Apnea Syndrome. Sleep 2002; 25 – 2:143-173.(2) Lloberes P, et al. Comparison of Manual and Automatic CPAP Titration in Patients with Sleep Apnea / Hypopnea Syndrome. AM J Respir Crit Care Med, 1996; 154: 1755-58.

0968.R

The Sleep Timing Questionnaire (STQ)

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Introduction: The timing of a sleep episode in relation to the individual's circadian system is one of the most important determinants of sleep duration and architecture. It is thus important to know a subject's or patient's habitual patterns of sleep and wakefulness. The aim of this study was to develop a single-administration instrument yielding equivalent measures of sleep to those obtained from a formal (2-week) sleep diary.
Methods: A single-administration Sleep Timing Questionnaire (STQ)

was developed and will be presented. Test-retest reliability was examined in 40 subjects who were given the STQ on two occasions separated by less than one year (Study 1). Convergent validity was measured both by comparing STQ derived measures with objective measures derived from wrist actigraphy (Study 2, n=23), and by comparing STQ derived measures with other subjective measures derived from a detailed 2-week sleep diary in two non-overlapping samples (Studies 3 & 4, n=101, 93). Correlations of STQ measures with age and morningness-eveningness were also examined. Both genders were included, ages ranged from 20y to 89y, most subjects were healthy volunteers; some Study 4 subjects were patients (enrolled in research protocols).
Results: Test-retest reliability for the STQ was demonstrated for estimates of bedtime ($r=0.705$, $p<0.001$) and waketime ($r=0.826$, $p<0.001$). Convergent validity using wrist actigraphy was demonstrated by correlations of 0.592 ($p<0.005$) for bedtime, and of 0.769 ($p<0.001$) for waketime. Diary studies indicated STQ bedtime and waketime data to be highly correlated (at about 0.8) with those obtained from a formal 2-week sleep diary. The STQ also provided data on estimated Sleep Latency (SL) and Wake After Sleep Onset (WASO) which correlated reliably (at about 0.7) with average nightly ratings of these variables from a 2-week sleep diary. Mean estimated values of SL and WASO from the two instruments were within one minute of each other. STQ-derived bedtimes and waketimes correlated with both age and morningness in the expected direction (older subjects earlier, morning types earlier).
Conclusions: The STQ may be a reliable, valid measure of sleep timing that could provide a time-efficient alternative to traditional sleep diaries.

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0969.R

Non-linear Time Series Analysis Of Arousals In Children
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Introduction: Traditional analysis of polysomnographic recordings of sleep, utilizing the visual scoring methods for sleep stages of Rechtschaffen and Kales often fail to characterize problems of excessive daytime somnolence and sleep fragmentation. This lack of sensitivity for these clinical problems prompts the search for new methods of analysis of sleep data. While arousals are easily characterized by visual inspection, The characteristics of arousals that produce fragmentation and clinical symptoms are not. Polysomnographic variables as recorded via digital polysomnography represent a group of interrelated time series. In this paper illustrate use of nonlinear time series analysis to characterize arousals in children.
Methods: Ten randomly selected EEG arousals from five normal pediatric patients were identified according to the rules set forth by the Atlas Task Force 1992. Three phases of the epoch were analyzed: 30 seconds pre-arousal, the arousal, and 30 seconds post-arousal. Each segment was scored via Rechtschaffen and Kales criteria and were subjected to nonlinear analysis. Epochs were chosen which included arousals including NREM stages (1, 2, 3, and 4) and REM sleep. The sampling rate for each epoch was 200 Hz per channel. Recording from chin, C3, O2, T3, T6, F2, and Cz electrodes subjected to nonlinear analysis. The nonlinear measures that were calculated were correlation dimension, Z-value, and Kolmogorov entropy (K/s, and K/c).
Results: Signifigant differences were noted at each electrode and state across non-linear measures. When all arrousal and all pre and post arousal states across all electrodes were combined, There were signifigant differences between pre arousal, arousal and post arousal states ($p<0.005$). There were no overlap of 95% confidence intervals across this combined analysis of the pre-arousal, arousal and post-arousal sleep state.
Conclusions: Non-linear times series analysis of the pre-arousal, arousal and post-arousal state demonstrate signifignt differences across state for multiple scalp recordings. These findings are robust and reproducable from subject to subject. The concept supports the notion of cyclic alternating patterns during sleep and arousal. Further work is ongoing to correlate these findings in children with polysomnographic evidence of sleep and arousal disorders.

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0970.R

Usefulness of Epworth Sleepiness Scale in Primary Snoring and Obstructive Sleep Apnea Syndrome Patients in South Korea
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Introduction: Excessive daytime sleepiness(EDS) is a frequent consequence of obstructive sleep apnea syndrome(OSAS). The mean sleep latency tests(MSLT) is often considered to be the gold standard assessment for EDS, but it is expensive and time consuming. On the other hand Epworth sleepiness scase(ESS) is considered to be a simple questionnaire measuring the general level of sleepiness. But there are many debates about the clinical usefulness of ESS. We observed whether ESS is related to the severity of OSAS and snoring. And we also observed which variables are related to OSAS severity and snoring.
Methods: All subjects had one night's diagnostic polysomnography with sleep staging according to the standard criteria. There were 120 patients who had primary snoring and 265 with OSAS. Among the patients with OSAS, those with 5 to 14.9 of RDI diagnosed as mild OSAS, 15 to 29.9 as moderate OSAS, and over 30 as severe OSAS. Four groups of patients compared with BMI, lowest O2 saturation level, age, RDI and ESS.
Results: There were 120 primary snorers, 90 mild OSA, 64 moderate, 111 severe OSA patients. BMI and RDI were significantly different between primary snorer and OSA patients, and between mild, moderate, severe OSA. Against my expectation, ESS was negatively related to the severity of OSAS. Linear regression test to remove bias from patient's age and sex, shows no significant differences among patients groups. Only BMI and lowest O2 level were significantly different between primary snores and OSAS, and between mild, moderate, and severe OSAS.
Conclusions: This results shows that ESS didn't distinguish primary snorers from patients with OSAS, nor different according to the severity of OSAS. Even the ESS widely used to test daytime sleepiness, this study raises questions about the validity of the ESS as a tool for sleepiness results from obstructive sleep apnea syndrome. But this study has some defects. Generally, these patients referred from other clinics and hospitals, and gender difference is significantly different according to the severity of OSAS, chances are that the patients groups are not well controlled. Further studies about the selection bias, gender differences, and cultural differences needed.

0971.R

Picking REM from the Finger: An Automatic Algorithm to Identify REM Sleep Based on Measurements of Pripheral Arterial Tone (PAT)
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Introduction: Traditionally the detection of REM sleep is based on monitoring rapid eye movements, EEG and EMG activities during sleep. Here we describe a novel methodology for REM detection which is based on monitoring peripheral arterial tonometry (PAT) as measured by variations in the pulse wave amplitude in the tip of the finger during

sleep. We developed an automatic REM detection algorithm (ARDA) that utilize data collected by the wrist device Watch-PAT100 for REM detection and describe its validation against polysomnographic (PSG) recordings.

Methods: A cohort of 57 subjects (43 OSAS patients, RDI: 24.6±19.6 and 14 normal volunteers, 48 male, age 44±14 years, BMI 28.1±5.6) underwent simultaneous PSG and WP100 recording. The WP100 signals (PAT signal, actigraphy, oxygen saturation)were analyzed automatically for REM and sleep-wake (SW) identification while the PSG recordings were scored blindly for sleep staging according to conventional criteria. To construct the automatic algorithm, first, two time-series were constructed from concatenations of PAT pulses: (i) the peak-to-peak amplitudes and (ii) the time-interval between two consecutive pulses. Next, four features are extracted for every 30 seconds using sliding window of 15 minutes: (a) mean PAT amplitude, (b) high-to-low-peak-spectral-ratio, (c) scaling exponent from the amplitude time-series, and (d) high-to-low-peak-spectral-ratio from the inter-pulse interval time-series (ii). Each feature was normalized using its whole sleep night average and standard deviation. Smoothing FIR filter was applied using boxcar window with 29-lags, with missing value consideration. When a linear combination of the normalized and smoothed features, determined by logistic regression, exceeded a given threshold – Automatic-REM was determined, for each sleep epoch. Sleep epochs were determined by the automatic sleep-wake algorithm of the WatchPAT100. Agreement between the WP100 and PSG scored epochs was calculated for each subject and then averaged for the entire group.

Results: The average value for agreement was 86±6%. The average duration of sleep based on WP100 and PSG was 318±60 and 330±62 minutes, respectively, from an average valid recording PSG time of 407±52 minutes. The correlation coefficient between WP100 and PSG REM time was 0.88 ($p<0.00001$). The sleep efficiency, as determined by the two methods, was 75±9% and 81±11% for WP100 and PSG, respectively.

Conclusions: The automatic detection of REM by the WP100 ARDA, which is based on a single channel of information and actigraphic monitoring of sleep-wake, has a good agreement with PSG based manual scoring for normal subjects and for OSAS patients with wide range of severities. Adding the ARDA to the Watch Pat will allow an ambulatory monitoring of REM sleep relying on the PAT signal.

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0972.R

The Effect of "End of Session" Information on the MSLT

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Introduction: In sleep deprivation studies, the performance decrement observed across increasing deprivation is reversed during the last test session when information is available to the subject identifying the session as the last. Such information presumably heightens anticipation and alertness, which results in improved test performance. Similarly, this "end of session" effect may influence MSLT scores when patients are aware that the last nap concludes their study. We tested this hypothesis under two different information conditions. Group I patients were scheduled for a one-night sleep study, followed by a daytime MSLT. After the fourth nap, these patients were free to go home. Group II patients were scheduled for two consecutive nights with an intervening daytime MSLT. Latencies on Nap 4 for both groups were predicted to be higher than other nap latencies since Nap 4 was the last nap of the day. Further, Nap 4 latencies would be higher in Group I than in Group II, since the last nap signaled the completion of the entire study for Group I, but only a mid-point in the study for Group II.

Methods: Group 1 (N=44, 19 males) had an average age of 44 and RDI of 9.5. Group II (N=40, 24 males) had an average age of 45 and RDI of 13.3. All patients knew whether they were staying for one or two nights at the time of their initial scheduling. Patients in both groups were informed of the number and timing of naps. A standard 4-nap MSLT protocol was used with sleep onset determined by the first epoch of any sleep stage.

Results: Latencies were shortest for Nap 1 and longest for Nap 4 for both groups. Latencies for naps one through four for Group I were 7.8, 9.9, 9.3 and 12.3 min. For Group II latencies were 6.6, 8.4, 7.7, and 10.0 min. Within comparisons revealed that the difference between Nap1 and Nap 2 was significant, $p<.01$ for both groups. The difference between Nap 1 and Nap 4 was also significant, $p<.01$ for both groups. Nap 2 vs. Nap 3 was not significant ($p>.01$) for either group. Between comparisons revealed that there were no significant differences between Group I and II for Naps 1, 2, or 3. However, as predicted, the difference between the groups on Nap 4 was significant, $p = .028$.

Conclusions: Information that Nap 4 was the last nap of the MSLT may have resulted in higher levels of cognitive and/or physiological arousal, explaining the longer latencies on Nap 4 for both groups. This process may have been heightened in Group I since the end of Nap 4 signaled completion of the entire study and their impending departure from the sleep center. These results suggest that a cognitive set of anticipation may increase arousal, thereby suppressing sleep and inflating sleep latencies on the MSLT.

0973.R

Effect Of Varying Recording Cable Weight And Flexibility On Sleep And Activity In Mice

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Introduction: Sleep in mice has typically been determined from EEG and EMG recordings obtained from cabled animals. However, the relatively small physical size of mice can produce technical concerns in recording sleep with cables that may not be seen in larger animals. There is the possibility that variations in weight and flexibility of recording cables across experimental settings could influence assessments of sleep in mice. In the present study, we examined how cable weight and stiffness could impact sleep using three cable configurations that varied in weight and flexibility. We also recorded home cage activity under each configuration. BALB/cJ mice were studied because they have been one of the most active strains we have examined.

Methods: Male BALB/cJ mice (n=6) were implanted with electrodes for recording EEG and EMG. Sleep and activity were recorded with the mice connected with a commercially available cable, 363-SL/6 (40 cm, PlasticsOne Inc.), in three configurations. Approximate cable resting weights were determined on a scale placed at head stage height (L: without vinyl or spring covering (1.5 g); M: vinyl and 2/3 spring covering with spring attached at swivel (2.2 g); and H: vinyl and 2/3 spring covering with spring attached at head plug (3.0 g)). After recovery, sleep and activity were recorded for 48 hrs under each configuration in a counterbalanced fashion. Behavioral state (wakefulness, NREM and REM) was visually scored (10 sec epochs) based on EEG and EMG. Home cage activity (calculated as travel distance (meters/24 hr)) was assessed with photobeams. Comparisons were also made to data previously collected in this strain (n=20) using telemetry (transmitter implanted IP, DataSciences ETA10-F20 (3.5 g); Tang & Sanford, SLEEP 25: 691-9, 2002).

Results: Total sleep (min) was greater ($p < .05$, Tukey HSD) with the H (762±51) and M (760±18.4) cables compared to with the L cable (595±30). With the L cable, the mice showed total sleep similar to that previously assessed with telemetry (631±11.6). Total REM (min) was greater ($p < .05$, Tukey HSD) with the M cable (75±5) compared to the L (53±3.4) and H (53±8.3) cables and to telemetry (61±2). Rankings on total travel distance were: unoperated baseline (250±22.6) > L (207±8.6) = telemetry (142±25.2) > M (82±17) > H (38±5.4).

Conclusions: Cable weight and stiffness can impact sleep and activity in mice. However, while progressively heavier and stiffer recording cables produced a graded decrease in activity, the influence on total sleep was not graded. Sleep with the L cable was similar to that we previously obtained using telemetry. The L cable also produced the least decrease in activity, though the difference compared to telemetry was not statistically significant. The results indicate that cable properties are an important factor to consider in conducting and/or evaluating sleep studies in mice.

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0974.R

High Inter-scorer Reliability For Sleep Stage Does Not Always Indicate Absence Of Rater Effects

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Introduction: Cohen's Kappa can be used to measure epoch-by-epoch agreement between sleep scorers and used to provide predictive information about the extent to which rater differences affect statistical tests. While low values of Kappa can represent either poor agreement or the effect of base rate, high values of Kappa indicate that good agreement between the raters exists and it is usually assumed that rater effects in any statistical analysis will be minimal. This study evaluates whether significant rater effects can be found, despite high epoch-by-epoch agreement, using a simple analysis of sleep continuity as an example.
Methods: Previously obtained nocturnal polysomnographic (NPSG) records, evaluated for inter-scorer agreement for sleep among 5 skilled scorers, were used in this analysis (Norman, Sleep 2000). 17 NPSGs from normal subjects and subjects ruled out for obstructive sleep apnea were selected. Sleep scores were recoded for each epoch as either sleep (any stage) or wake. Reliability was measured for each pair of scorers by cross tabulating the recoded stages and calculating percentage agreement and Cohen's Kappa statistic by standard formulae. Continuity of sleep (defined as the length of a run of contiguous sleep) was assessed from each rater's scores using a non-parametric survival curve analysis for recurrent events (Pena, JASA 2001) and the median run length calculated. Differences between the survival curves for the 5 raters were assessed using a log rank test.
Results: For discrimination of sleep vs wake the raters showed excellent agreement with an average percent agreement of 95% (ranging from 93% to 97%) and an average Kappa of 0.79 (ranging from 0.73 to 0.84). Despite this high level of agreement, there were statistically significant differences between the 5 survival curves for all scorers combined ($p < 0.001$) and for 6 of the 10 pairs of scorers. Median sleep run length varied from 9 to 15.5 minutes.
Conclusions: Inter-rater agreement for sleep versus wake scoring was high, yet both statistically and clinically significant differences in a simple sleep continuity measure were found. These data demonstrate that the assumption that the presence of high agreement precludes significant rater effects from occurring may be unwarranted and, furthermore, that epoch-by-epoch Kappa values, a rigorous and commonly used measure of agreement, may not be appropriate in all situations.

0975.R

Variations in Fatigue Sampled Repeatedly in Healthy Controls

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Introduction: The four objectives of this study were to test the ability of a single item fatigue scale to correlate with the fatigue subscale of the Profile of Mood States (POMS), to test the acceptability of recording hourly fatigue ratings, to examine the chronobiological variation in self-reports of fatigue, and finally, to examine the degree to which self-report of fatigue correlated with actigraphy findings.
Methods: Ten healthy normal volunteers participated (5 men; 5 women); all were asked to complete a pencil and paper version of the Profile of Mood States (POMS) fatigue subscale hourly during waking hours for 3 consecutive days. The POMS was designed for repeated assessments of subjects participating in psychopharmacological studies. The fatigue subscale consists of 7 items, of which one is in fact Afatigue.@ Other items are Aworn out, listless, exhausted, sluggish, weary, bushed.@ Each individual=s score on the 1-item Afatigue@ was compared with the 6 other subscale score items, using Pearson correlations. The same 10 healthy subjects wore an actigraph for 72 consecutive hours. The standard actigraph was modified to incorporate two event buttons which subjects were asked to push hourly to report their level of fatigue. To remind subjects to complete their subjective self-report hourly, subjects also wore a second watch with a timer set to ring every hour during waking hours. The actigraph data were analyzed using the Action-W (version 2, AW2) and Action4 programs (Ambulatory Monitoring, Inc). The primary activity mode used in this analysis was PIM (Proportional Integrating Measure), which provides an estimate of movement intensity and is most useful for assessing daytime activity levels and patterns. The records were edited to eliminate data segments representing periods when the devices were obviously not being worn (e.g. when subjects bathed).
Results: The one item fatigue rating correlated significantly (mean $r = 0.61$) with the rest of the POMS subscale for fatigue. Subjects had no difficulty using the event button on the actigraph in entering the 1-item fatigue ratings. Fatigue ratings revealed marked differences in how healthy subjects report fatigue. There was no consistent diurnal patterning of fatigue across all subjects; rather, some subjects manifested constant levels of fatigue throughout the day; others had highly variable fatigue levels unrelated to clock time, and yet others manifested a clear increase in fatigue as the day went on. The fatigue ratings in general were not correlated with actigraphic measures.
Conclusions: The study documents that fatigue can be repeatedly assessed with an ambulatory device and that self-reported fatigue levels vary enormously from hour to hour in a healthy normal sample. The relationship between fatigue and sleep characteristics continues to be examined.

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0976.R

Objective Evaluation Of Sleepiness In A Clinical Setting Using A Reaction Time Recorder

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Introduction: Outcome measures for daytime sleepiness have serious drawbacks for routine clinical use, namely excessive cost, prolonged patient time investment, or subjectivity. A quick to administer, easy to interpret, objective measure of daytime sleepiness would be invaluable for office assessment of sleep medicine patients. A reaction time test which requires the patient's active participation for a number of minutes might be the best objective outcome neasure. Such a machine is commercially available, but clinical evaluation is limited. For this reason, we embarked on this exploratory analysis of a reaction time task to assess daytime sleepiness during office visits.
Methods: We employed the PVT-192 marketed by Ambulatory Moni-

toring, Inc. We decided that a 10-minute test was the longest practical duration for office use. We tested 25 normal controls in the same age range as most sleep patients. The normal group excluded individuals with Epworth Sleepiness Scale (ESS) scores greater than 9. Some of the normal controls were retested to determine stability of results in the absence of therapy. We administered the reaction time test to all sleep disorders patients seen from July 2002 to March 2003. We compared ESS and reaction time statistics using scatterplots. We observed what comorbidities might confound reaction time testing.
Results: Most of the statistics report by the software were highly correlated with one another. The percentage decline in reaction time between minute one and minute ten of the test was the most useful single indicator, but lapses were also useful. The performance decline correlated with ESS, but absolute values of reaction times had no correlation with daytime sleepiness on ESS. Test-retest data revealed no significant performance change in untreated subjects. In contrast, mean and standard deviation of reaction times improved substantially in patients treated with CPAP or stimulants. Major depression is the most common confounding condition for interpretation of reaction time performance.
Conclusions: Reaction time decline is a practical, objective measure of daytime sleepiness in an office setting. Reaction times can be used to determine if CPAP or stimulants improve daytime sleepiness. Slow reaction times from depression are independent of sleepiness, so reaction times before and after treatment with CPAP or stimulants can demonstrate improved alertness.

0977.R

The Portable Device Watch-PAT 100 Is Accurate In Detection Of Respiratory Disturbances In Stable CPAP Users

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Introduction: The Watch_PAT100 (WP100) is a portable device for diagnosis of breathing disorders in sleep, which is based on peripheral arterial tone (PAT), actigraphy and oximetry. Its automatic algorithm is based on detecting the sympathetic activation occurring in the termination of SDB events. We have recently validated the WP100 against polysomnographic monitoring in patients evaluated for suspected sleep apnea. Patients on CPAP may have difficulties dealing with the air pressure which may result in altered sympathetic activation. The purpose of this study was, therefore, to examine whether the WP100 is accurate in detecting SDB events in patients on CPAP treatment.
Methods: Twenty-one patients (19 males) with a previous diagnosis of obstructive sleep apnea (OSA) participated (mean age 57±12years, mean BMI 31±7Kg/m2). All were treated with CPAP for at least 3 months in their home (range 4-140 months). All underwent in-lab full polysomnography (PSG) simultaneously with WP100 recording, while sleeping with their own CPAP. The PSG recordings were blindly scored for apnea/hypopnea according to the American Academy of Sleep Medicine criteria (1999), and the PSG-respiratory disturbance index (PSG-RDI) was calculated. The WP100 data was analyzed automatically for PAT-RDI (PRDI) by an algorithm developed and validated in patients not on CPAP.
Results: Although chronically on CPAP, some of the patients had substantial SDB (mean PSG-RDI: 14±12 events/h, range 1-43). Across this wide range of RDI levels, the PRDI was highly correlated with the PSG–RDI ($R=0.87$, $p<0.001$). The white-Westbrook agreement between RDI based on the PSG and the WP100 was 85%. Clinical decision of a need to change CPAP pressure was similar in 90% of the patients based on PSG or WP100.
Conclusions: Some of the patients on CPAP treatment still suffer from substantial apnea. This raises the need for follow-up studies. The WP100 device may offer an accurate and useful tool for follow-up of patients with OSA treated with CPAP.

0978.R

Technical Note: The Use of Miniature, Wireless Data Recorders to Study Ankle and Ambient Temperatures as a Means of Enhancing Actigraphic Sleep Onset Assessment in Humans

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Introduction: The purpose of this study was to demonstrate the feasibility of assessing ankle skin temperature in conjunction with an actigraphic home study of sleep. Previous reports have shown (1,2) a precipitous rise in peripheral skin temperature that precedes the regulated drop in core temperature prior to sleep onset in normal subjects. This added information would be valuable in assessing sleep latency in actigraphic sleep studies. The inaccuracy of sleep latency has long been noted (3) as a primary weakness of the actigraphic technique, since subjects/patients may lie perfectly still for long periods before actually falling asleep.
Methods: Miniature (approximately 1"D by .5"H) and wireless, the MicroMini Family of sensors enable ambulatory subjects to wear multiple recorders and monitor the environment for up to 22 days. In a typical ambulatory setting, environmental parameters are desirable descriptors as well, since they may provide clues to causes for awakenings. Seven (7) self-contained sensors were employed in this study including: one (1) on the wrist of the non-dominant arm for movements/activity; one (1) attached to the non-dominant ankle for distal skin temperature; one (1) similarly attached to measure bed temperature; others placed on the nightstand recorded ambient light, sound and temperature. Additionally, one (1) motion sensor was positioned underneath the bed mattress to help discern time in bed. All sensors were time-synchronized to commence recording on the same time scale. The recording took place for a period of approximately 40 hours.
Results: A rise in ankle skin temperature was consistently observed prior to the fall-out of activity. The mean temperature rise on the ankle from the time the subject entered the bed (based on the mattress data) to the maximum nighttime ankle temperature was 3.95-degrees C.
Conclusions: Prior studies (1,2) have demonstrated a 2-degree C, precipitous rise in ankle skin temperature that ends with PSG sleep onset and precedes total activity fall-out by approximately 10 minutes. The absence of a convenient means for performing this measurement in an unattended, ambulatory environment has prevented a field/clinical application of this research. The development of small, wireless data recorders for temperature and environmental conditions should enhance unattended, actigraphic sleep studies.

0979.R

The Maintenance of Wakefulness Test (MWT) and Epworth Sleepiness Scale (ESS) in Railway Transportation: Reference Values and Connection to Dozing-off at Work

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Introduction: The MWT and ESS are used widely to measure excessive daytime sleepiness (EDS) and especially the ability to maintain wakefulness in soporific circumstances. Our objective was to define the distribution of MWT and ESS values in a random sample of workers with irregular shifts and to study the connection of MWT and ESS values to dozing-off at work.
Methods: 275 randomly selected train drivers and traffic controllers with irregular work hours participated in a combined sleep laboratory and sleep diary study. The subjects filled in a sleep diary for 21 consec-

utive days prior to laboratory testing. Nodding-off, sleep and working hours were reported. After at least two days with no night shifts, a polysomnography and MWT the following day were performed according to Doghramji et al. (1997). The subjects were asked to fill in ESS for the last 3 weeks.

Results: The mean sleep onset latency (SUSMWT40) was 35.9 ± 7.2 min. If the trial duration of 20 minutes would have been used, the mean S1 latency (MWT20) would have been 19.0 ± 3.0 min. Based on a definition of normality of 2SDs lower than the mean, the normal limits for the SUSMWT40 and MWT20 were 21.5 and 13.0 min, respectively. The mean ESS score was 5.5 ± 3.1 for the last 3 weeks. To exclude major sleep disorders, a subgroup of 159 subjects was formed based on the polysomnography with the following criteria: TST > 6 hours, AHI < 10 /hour and no signs of periodic leg movements in sleep. The mean MWT sleep latencies of the subgroup did not differ from the whole group and TST and sleep efficiency correlated negatively with sleep latencies in both groups. Workers with a mean latency in the SUSMWT40 of at least 1SD below average dozed off more often (16.7%) during the day shifts than the rest of the group (5.7%) while there were no significant differences during the other shifts. Similarly, the ESS scores were associated with dozing-off during the evening and night shifts and especially during the days off. The MWT sleep latencies were not related to age or the number of preceding work shifts.

Conclusions: The results show that the MWT and ESS are valid and feasible methods for the estimation of the ability to maintain wakefulness among shiftworkers. The lower reference limits for MWT became higher than in the data of Doghramji et al. (1997) even though our sample included habitual nappers. One explanation is that high requirements for maintaining wakefulness at work can be associated with longer sleep latencies in the MWT. Although ESS is a subjective measure, it seems to predict self-reports of dozing-off at work better than the MWT.

0980.R

A Method for Measuring Sleep Latency Using EEG Alpha Power

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Introduction: The Multiple Sleep Latency Test (MSLT) is considered the 'gold standard' objective measure of sleepiness in research and diagnostic clinical practice. In order to measure sleep latency the time of sleep onset is typically determined according to Rechtschaffen and Kales' conventional sleep-scoring criteria using raw EEG, EMG, and EOG activity. However, for many experimental purposes, it would be useful to have a more quantifiable and repeatable measure of sleep latency than is provided by conventional scoring. This is particularly important if the subject needs to be awoken as soon as sleep onset is determined. This requires an instantaneous judgement about the time of sleep onset which is not always easy or extremely consistent between different observers. The typical inter-rater reliability of visually scored sleep latencies is not perfect (r=+0.83). Since validity may improve as a function of increased reliability, we investigated a highly reliable method of determining sleep onset in an attempt to improve the validity of the MSLT.

Methods: Our MSLT protocol determined sleep latency using power spectral analysis (PSA) of EEG. Customised computer software (LabVIEW 5; National Instruments Corporation, Austin, TX, USA) was used to quantify and display EEG alpha (8-12 Hz) power for every 30-second epoch of each sleep latency trial. A 50-percent alpha baseline was calculated for each sleep latency trial by averaging the alpha power of the two epochs with the highest amount of alpha power and dividing by two. Sleep latency was defined as the latency (in minutes) from the termination of delta wave movement artefact (associated with adjusting to the sleeping position) to the first of three consecutive 30-second epochs below the 50-percent alpha baseline. In our laboratory, we have found this method of determining sleep latency to have very high inter-rater reliability (r=+0.99). MSLTs were also measured using a portable polysomnography (PSG) recording system and were scored retrospectively by an experienced PSG technician using the conventional criteria. Sleep latency measurements from 439 sleep latency trials were available for data analysis.

Results: The Pearson correlation between sleep latency scores derived using the PSA criteria and using the conventional criteria was highly significant, $r(439) = +0.90$, $p < .001$. The mean sleep latency derived from conventional criteria (M = 8.58 min, SD = 7.11) was slightly but significantly longer ($t(438) = 5.03$, $p < .001$) than the mean latency derived from PSA (M = 7.82 min, SD = 6.76).

Conclusions: The essentially perfect reliability of the PSA criteria plus the high correlation between the two sleep latency measures supports the validity of the PSA determination of sleep latency. The PSA determination of sleep latency is not dependent on complex perceptual judgements of raw EEG activity and, therefore, does not require extensive technical PSG training. This method promises to be an easy, perfectly reliable, and valid measure of sleep latency that allows sleep onset to be determined instantaneously.

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0981.R

Computer Assisted Scoring and Interobserver Agreement of Classification of Sleep Stages of NPSG's Obtained from Different Centers

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Introduction: The scoring rules for sleep staging by R&K are used for manual classification of sleep stages. The rules are subjective and are of fuzzy-nature (Kumar,1977). The inter-rater agreement between different scorers varies between 50-70%. The low amount of disagreement is a result of the high degree of variance in the interpretation of these rules. The variance is caused by divergence in the implementation of the rules, variance in visual recognition of signals on page, application of rules over many epochs, and inapplicability of these rules to certain epochs (Schultz 1980). Even the expectation of how the hypnogram should be can result in errors and low agreement between scorers from different institutions (Kumar et al.,1981).Computer asssited sleep stage scoring methods have been available since the early 1970s, but their use has been very limited. The lack of convincingly presented validation against an expert human scorer is one of the reasons not to use these tools. However, the present state of technology offers more possibilities. Such tools do not need to be used as fully automatic scorers. Computer assisted scoring can also be used as an aid in supporting expert human scoring to reduce the variance between human scorers.The present study evaluated the effectiveness of a methodology to use computer tools as an aid in increasing the consistency and reliability of sleep staging. For this purpose, standardized display and scaling was used for the computer screen.Three dimensional spectral analysis was used as an aid in supporting manual scoring.

Methods: Digital sleep recordings from two type of data-sets were collected. One dataset consisted of 35 NPSG's of patients referred to different sleep clinics (in different non-European countries) for diagnosis of OSAS. These recordings were not from a controlled protocol, however EEG, EOG and EMG were collected to satisfy R&K guidelines.The other dataset consisted of 70 recordings from a controlled trial of study on insomnia. These recordings were selected from a pool of 4 nights each of 156 patients from 21 clinics (from different European countries). The recordings were performed according to standardized operating procedures. The EEG, EOG and EMG were collected to satisfy R&K guidelines.The privacy of patients and volunteers was protected by randomizing any patient data stored with the study. The randomization was performed by another indpendent technician who has no access to the orig-

inal information.Manual scoring of all recordings was performed by one independent scorer by using a computerized system Rembrandt for sleep scoring. For all recordings, the human scorer used the same screen-layout, sensitivity and time scale. Epoch by epoch scoring was done only on the basis of visual interpretation of the computer screen. For quality control, all recordings were scored independtly by another expert scorer (Ph.D, 29 years of experience in different sleep laboratories).Spectrum analysis was used to check the quality of signals and to identify episodes of artifacts and sleep stage transitions. The scorers were blind to the source of data, the protocol, clinical or experimental condition and the patient.

Results: The overall inter-rater agreement was between 85% and 90%. A detailed analysis of the disagreement revealed that higher disagreement is caused by the transition- and artifact- episodes. Spectral analysis was a useful aid in identifying these episodes that helped to reduce the time and draw attention to difficult areas.Post-hoc analysis also showed that the computer assisted reduces time by atleast 30%.

Conclusions: Contrary to common belief, computer assisted scoring provides benefits of consistency and reduced variability in the quality. In addition, a simple tool like three dimensional spectral analysis reveals problems and issues in signals that are a great help in clarifying transitional episodes of sleep. This is not surprising, because the three dimensional spectral calculations are objective and not biased by visual patterns of signals in an epoch.More elaborates methods for automatic sleep scoring exist. Detailed evaluation and validation of these methods is needed and should be encouraged. Clinical and experimental research could benefit more from bias-free computer assisted methods with less sensitivity than from bias-prone methods with high sensitivity.

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0982.R

Evaluation of Home Versus Hospital Full Polysomnography In The Diagnosis Of Sleep-Disordered Breathing

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Introduction: The diagnosis of most sleep disorders is dependent on full polysomnography that are usually performed in hospital or specialized clinics. The role of new technology that allows full polysomnography at home is not completely understood. The objective of this study is to compare home (HM) versus hospital polysomnography (HP) in terms of: (1) Recordings' quality, (2) Sleep study average cost, and (3) Sleep quality.

Methods: We compared 65 consecutive HM studies, average age 56±13 years (51 males) to 65 consecutive HP studies, average age 50±13 years (44 males) done in the same period at our institution. All overnight polysomnograms were performed using the same equipment (EMBLA, 17 channels) and were scored based on the guidelines for sleep studies. In HM the technician goes to the patient's home twice (to hook and unhook), within 30 km distance from hospital. The quality of the tracing was assured at the beginning of the recording by a on line recording on a lap top that is left at the patient's home. Daytime sleepiness was assessed by a subjective rating (Epworth Sleepiness Scale). Significant differences between groups were analyzed by t test ($p<0.05$ was considered significant).

Results: The 2 groups (HM vs HP) were similar in respect to the Body Mass Index (30±5 vs 29±6 kg/m2); Epworth Scale (11±6 vs 10±6); Respiratory Disturbance Index 27±22 vs 29±25 events/hour; Sat O2 mean (93±3 vs 93±3 %); Sat O2 min (82±7 vs 81±14%). Five (7,7%) HM and no HP recordings had to be repeated due to technical problems. The cost of a full polysomnography at HM was about US$ 320 and about US$ 200 at HP. The following parameters were analyzed and presented statistical differences (HM vs HP): Total sleep time (min) = 368 ± 87 vs 336 ± 87 ($p= 0.04$); REM latency (min) = 113 ± 76 vs 157 ± 91 ($p=0.006$). The following parameters did not present statistical differences: Total time recorded (min) = 446 ± 66 vs 431 ± 41; Sleep efficiency (%) = 83±15 vs 78±18; Sleep latency (min) = 19±31 vs 16 ± 22; S1(%) = 4±3 vs 4 ± 3; S2(%) = 68 ±11 vs 65 ± 15; S3(%) = 2±3 vs 7± 5; S4(%) = 11±8 vs 9 ± 7; REM(%) = 16±7 vs 14 ± 8; Awakenings index = 39±30 vs 35±25 events per hour.

Conclusions: In our study the recording quality was similar in both groups. However, 7,7% of home full polysomnography had to be repeated due to technical problems. Home studies were 60% more expensive as compared to hospital studies. Patients studied at home had a higher TST, lower REM latency and lower number of arousals, suggesting a better sleep quality at home.

0983.R

Near-Infrared Spectroscopy for the Assessment of Vascular Responsiveness of the Brain: A Screening Method for Cerebrovascular Morbidity in Obstructive Sleep Apnea

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Introduction: Obstructive Sleep Apnea Syndrome (OSAS) is an important risk factor for the development of cardiovascular morbidity and mortality. Compromised cerebral blood flow (CBF) has been postulated to account for the cerebrovascular morbidity associated with OSAS. Near-infrared Spectroscopy (NIRS), a non-invasive, portable, cost-effective methodology that allows transcranial and continuous real-time measurements of brain tissue oxygenation and hemodynamics is the only modality that provides information on brain oxygenation. Hence, NIRS is an important tool for the assessment of cerebrovascular health.

Methods: A. Subjects: Twenty subjects (25-74yrs) participated in the study. Eight (29-74yrs) had OSAS (AHI>20), while twelve healthy non-snorers (25-54yrs) constituted the control group.B. Instrumentation and Monitoring: Arterial blood oxygen saturation (SaO2) and heart rate (HR) were monitored via pulse oximetry (N-200, Nellcor Inc., Pleasanton, CA), and the breathing rate with a respiratory strain gauge (Resp-EZ, Sleepmate, New-Life Technologies, Midlothian, VA). The NIRS parameters, such as oxy-([O2Hb]), deoxy-([HHb]), total hemoglobin ([tHb]) concentrations, and tissue hemoglobin oxygen saturation (SO2) were monitored by a frequency-domain tissue oximeter (OxiplexTS, ISS Inc., Champaign, IL).C. Experimental protocol: All subjects were instructed to perform breath-holding exercises while vascular reactivity and cerebral hemodynamic responses to hypoxia and consequent hypercapnia (carbon dioxide is a vasodilator in the brain) was determined. The protocol consisted of: 5-7 minutes normal breathing; 10-30 seconds of breath holding (at FRC); Resumption of normal breathing and repetition of breath holding (3-5 times).

Results: Appropriate analysis schemes have been applied to differentiate cerebrovascular reactivity between the two groups and characterize the subjects. In healthy subjects, the brain responds to hypoxia and hypercapnia by vasodilation and opening of the capillary bed. Normals in our study showed a prompt decrease in [HHb] and an increase in [O2Hb] and [tHb]. These changes correlated with an increase in CBF to meet the oxygen demands of the brain. The decrease in [HHb] represents the wash-out effect from the increased CBF. In subjects with OSAS, the hemodynamic response to hypoxia was significantly delayed, reduced or even absent ($p<0.040$).

Conclusions: Using simple breath holding exercises and a novel methodology, we showed that cerebrovascular reactivity to hypoxia and hypercapnia is compromised in OSAS sufferers. Our results suggest that

compromised brain microvasculature in OSAS may lead to structural and functional impairment and diminished or loss of ability to vasodilate. This finding may explain the increased cerebrovascular morbidity seen in OSAS. NIRS provides non-invasive, transcranial, real-time measurements of cerebral oxygenation and hemodynamics. It gives direct information on cerebrovascular health by monitoring the response of the brain to hypoxic insults. NIRS can provide a cost-effective screening method for individuals at risk for the cerebrovascular consequences of OSAS.

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0984.R

A Short Cognitive Test as a Measure of Alertness, and its Relationship With Sleep Disorders in a Population of Professional Drivers

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Introduction: Sleep disordered breathing, insomnia, and sleep deprivation may lead to low cognitive performance and accidents. The risk of accidents is even more important in a population of professional drivers. Objective: We sought to examine the ability of a population of professional male drivers to perform in a modified Trail Making Test part A (MTMT) before their regular trips, and its association with sleep disorders. MTMT may be an useful and simple tool to assess alertness impairment.
Methods: 330 male, BMI < 35 Kg/m2, mean age of 39,1± 6,59 were randomly selected to: a) perform MTMT, b) fulfill a standard sleep disorders questionnaire, and c) undergo to a polysomnographic recording (PSG). . MTMT is a test of higher executive function involving visuospatial organization and visuomotor processing at speed. The tests were always performed before drivers' regular journey, and after the off-work period. PSGs were recorded a week after MTMT completion.48 drivers also performed MTMTs in 3 different occasions (once a week). To avoid possible learning effect 3 different types of numbers' spatial distribution in the test answer sheet were offered to subjects. Statistics: ANOVA considering 3 levels for MTMT, and 6 levels for educational degree effects on time test performance. Individual measures of chart control and individual moving range were performed according to the following formulas: Higher threshold of Control (HTC)= = 40.0 seg. Central threshold of Control (CTC)= = 27. 5 seg. Lower threshold of Control (LTC)= = 15.0 seg.
Results: All individual values were plotted in a normal distribution curve. It was established the range in with the drivers had responded in a normal time, short time, and very long time (response considered as "not recommended to drive"), by establishing the longest and shortest time response for MTMT. Among HTC all had sleep complaints, and 59% had snoring and/or OSAS. Among CTC, only 6% had snoring and/or mild OSAS. Finally, among LTC 38% had insomnia. Subjects included in the range of HTC were "not recommended to drive".Nor the different types of numbers' spatial distribution neither educational degree or the repetition of the tests influenced the time response to MTMT for all subjects tested (p >0.05).
Conclusions: MTMT may be an useful tool to assess alertness, concentration and diffuse attention in an adult male drivers population before their professional driving tasks. Individual control measures were also associated with presence of sleep complaints and sleep breathing disorders.

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0985.R

A Primate Model of Sleep Regulation

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Introduction: The rhesus monkey (*Macaca mulatta*) was determined to be the best sleep model among thirteen non-human primate species (Balzamo et al, 1977) due to well-defined, human-like, sleep organization and for relative ease of husbandry. However, physiological monitoring of sleep via EEG, EOG and EMG measurements has typically required the use of restraint chairs or collars, preventing animals from sleeping in their natural postures. Recording sessions longer than 24 hours have also been difficult. Here we report on a sleep model using rhesus monkeys with fully implantable biotelemetry transmitters, allowing us to measure EEG, EMG, EOG and brain temperature continuously in unrestrained animals during long-term studies.
Methods: The sleep telemetry system consists of an implantable transmitter and computer-based FM receivers and demodulators (Konigsberg Instruments Inc., Pasadena, CA). The transmitter provides two channels of EEG, EOG, and EMG. Deep brain temperature is measured with a thermistor (Thermometrics Inc. Edison, NJ), implanted stereotaxically. An attached battery pack allows operation for up to a year. All surgeries are performed by veterinary surgeons (California National Primate Research Center, Davis, CA). Programs for data logging, polygraph emulation and visual scoring, and spectral analysis were developed in LabVIEW 6.0 (National Instruments Inc., Austin, TX). Data were sampled at 256 samples per second in 30 sec epochs. An automated scoring program was developed in Matlab 5.0 (Mathworks Inc., Natick, MA) using neural network algorithms. The automated scoring program is trained to recognize sleep stages by associating EEG/EMG patterns with hand scored records. An average agreement of 83% with visual scoring is obtained with novel data. Animals are housed individually in isolated chambers with controlled lighting and ambient temperature. The monkeys are trained to perform video-based tasks (Psychomotor Test System, Dr. David Washburn, Georgia State University, which provide a nutritionally complete food reward, as well as performance measurements. Animal husbandry is performed daily on an alternating AM/PM schedule to avoid providing social cues for circadian entrainment.
Results: Data are presented here for six days of continuous recording from six adult male rhesus monkeys in a light-dark cycle of 16 hours dim light (< 20 lx) and 8 hours dark (LD 16:8). In these conditions, monkeys spent 52+6% (Mean+S.D.) awake, 24+3% in SWS1-2, 11+3% in SWS3-4, and 13+5% in REM sleep in an average 24-hour period, similar to percentages reported for restrained animals. During the light period, 22+9% of epochs show sleep, mainly in the first and last two hours of the light period. Short naps also occur throughout the day. Waking occupies 11+5% of the dark period, much less than the 20-45% reported for animals in restraint chairs.
Conclusions: By eliminating potentially stressful handling or restraint, and by allowing long-term sleep monitoring, this primate model is an excellent biomedical model for human sleep disturbances.

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0986.R

Validation Of A Simple Sleep-Wake Scoring Algorithm In Rats

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Introduction: Most automated sleep-scoring systems rely on medially-placed electrodes to record cortical EEG activity, especially in the theta frequency band (; 6-10 Hz). In our studies, midline instrumentation dictated the use of frontal and lateral (parietal) electrodes only, and we found that EEG amplitude is unreliable for assignment of behavioural

state. We therefore devised and validated a computer-based sleep scoring system for real time scoring of sleep-wake state using an algorithm that does not involve the EEG band.
Methods: Ten 300-350g male Wistar rats were used. Two cortical EEG electrodes were implanted into the skull (coordinates relative to bregma (mm); frontal, AP 2.0; L 2.0 left; parietal, AP -4.0; L 4.0 right). EMG amplitude (m Vrms, bandpass 10-100Hz with 60Hz notch) was recorded bilaterally from the nuchal muscle (3 rats had additional electrodes in the temporalis and shoulder muscles). Rats were connected to a freely rotating counterbalanced tether via a headpiece. Additional rats were studied using implanted radiotransmitters to explore the merits of a wireless system.A LabVIEWTM program was used for acquisition and analysis of data. Animal behaviour was recorded on videotape to aid visual scoring. EEG amplitude (m Vrms) was measured in the following frequency bands: delta (d; 1.5-6Hz), alpha (a; 10.5-15Hz), beta (b; 22-30Hz), and gamma (g; 35-45 Hz). Epoch duration was 5s and all recording sessions were > 1000 epochs in duration. We developed a simple two-step algorithm:STEP 1: EMG amplitude greater than threshold? Yes = wake, no = sleep.STEP 2: EEG amplitude ratio [(d*a)/(b*g)] greater than threshold? Yes = NREM, no= REM.
Results: The algorithm had an overall accuracy of 93.3 $\pm$ 4.6% when compared to unequivocally-defined epochs as scored by two experienced raters. Inter-rater agreement was over 95%. An analysis using EMG alone yielded a mean accuracy of 86.3 $\pm$ 13.1% in correctly identifying wake and a mean accuracy of 98.8 $\pm$ 1.8% in correctly identifying sleep. Nuchal muscle yielded greater accuracy than temporalis or shoulder muscle (p=0.009; ANOVA). A comparison of day versus night recordings in 3 rats showed no significant effect of circadian time on the accuracy of scoring (p=0.76; t-test). Preliminary results from rats examined using radiotransmitters indicate that signal quality is improved when transmitters are used, due largely to a decrease in movement-related contamination of the delta band.
Conclusions: These results show that measurement of is not necessary in order to develop a sleep scoring algorithm with a high degree of accuracy. This algorithm is useful when measurements are impractical or when lateral EEG recording sites must be used. EMG alone is useful for a simple discrimination of wakefulness and sleep.

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0987.R

Change in PVT Alertness Levels Pre and Post MSLT Sessions

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Introduction: The Psychomotor Vigilance Task (PVT) has been used extensively to test alertness levels in subjects for many years. No data has been presented showing a change in PVT levels pre and post MSLT nap sessions.
Methods: As part of an ongoing long-term actigraphic project a subject, ER, has been wearing a Mini-Mitter® Actiwatch-64 for 4 months. Biweekly MSLT's are also being recorded. We recently had the opportunity to have the subject complete a 10-minute PVT pre and post MSLT nap sessions recorded at 10:00 am, 12:00, and 2:00 pm. Standard PVT parameters were used with a random stimulus presentation set between 1000 ms and 7000 ms. A total of 130 to 150 stimuli were presented in each PVT. All PVT's were performed under supervision with minimal distractions.A standard research MSLT protocol was used with a 20-minute nap opportunity. Naps were terminated after 60 consecutive seconds of any clearly identifiable stage of sleep.
Results: In nap session 1, at 10:00 am, the subject had a sleep latency of 17 minutes. In nap session 2, at noon, the subject had a sleep latency 18.5 minutes. In nap session 3 at 2:00 pm the subject had a latency of 20 minutes, no sleep being recorded. There were microsleeps lasting from 3 to 15 seconds in each MSLT trial.The mean PVT reaction time showed a marked reduction in mean values for each nap session. In nap 1 the mean PVT reaction time decreased from 302.36 ms (SD=65.72) to 287.61 ms (SD=58.00). In nap 2 the mean reaction time decreased from 326.49 ms (SD=91.6) to 262.70 ms (SD=42.45). In nap 3 the mean reaction time decreased from 316.33 ms (SD=75.57) to 278.53 ms (SD=53.89). All results were statistically significant at p<.001.
Conclusions: The fact that no sleep occurred on nap 3 and that only 1 minute of sleep occurred on naps 1 and 2 raises the question of whether quiet resting results in an increase in alertness levels as measured by the PVT. Another possibility is that repetitive microsleeps have some restorative value.We are planning to record PVT's pre and post MSLT naps on a series of future patients in order to develop a wider data set.

0988.R

The Alpha Attenuation Test is not Affected by Occipital Electrode Site

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Introduction: The Alpha Attenuation Test (ATT) is an objective measure of sleepiness that uses power spectral analysis and Fast Fourier transformation of EEG alpha activity to calculate EEG alpha power. The alpha attenuation coefficient (AAC) is the ratio of mean alpha power with eyes closed to mean alpha power with eyes open. It is standard practice to record alpha rhythm from the occipital region using a single EEG electrode placement at O2 (Stampi C. et al 1995). However, EEG alpha activity is known to vary between cerebral hemispheres, independently of cerebral dominance. Here, we compared the AAC recorded from O2 with that recorded with electrodes at Oz and O1 to establish whether electrode placement affects the results of the AAT.
Methods: We studied 20 healthy right-handed volunteers (10 men and 10 women; mean age 27.6 years, range 18 – 44 years). All subjects were screened for covert sleep disorders using the Liverpool Sleep Questionnaire (LSQ1) and two-week sleep diaries. Subjects abstained from caffeine for 24 hours prior to testing.All recordings were performed under controlled conditions. The AAT was performed a total of 4 times at 2 hour intervals in each individual, starting no later than 2 hours after waking. Alpha activity was recorded from the 01, Oz, and O2 electrode sites during each recording. Quantitative EEG software (Persyst Inc.) was used to calculate the AAC at each electrode site for each individual, and statistical software used to compare the results (MINITAB).
Results: For each subject, the AAC score from each of the 4 trials was averaged to produce a mean AAC score at each electrode site, O1, Oz, and O2. A total mean AAC score for each electrode site was then generated, by averaging the AAC score from each subject. The AAC score at each electrode site was compared using one-way ANOVA (F=2.55, p=0.132). Thus there was no significant difference between the AAC recorded from each of the three sites.In addition, Tukey pairwise comparison was performed. There was a confidence interval (CI) of –1.308 to 9.06 for O2 compared with OZ, a CI of –1.856 to 8.512 for O2 compared with O1, and a CI of –5.733 to 4.638 for OZ compared with O1. Again, there was no significant difference between the AAC from each the electrode site as the CI for all comparisons included zero.
Conclusions: Our findings suggest that there is no difference in the AAC recorded from electrode sites O1, Oz, and O2. Thus, interhemispheric alpha asymmetries have no effect on AAC, at least in right handed individuals, and the current practice of performing the ATT using the O2 electrode site is valid.

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0989.R

Muscle Activity During Sleep:A Quantitative Electromyography Analysis During Standard Polysomnography

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Introduction: Muscle activity changes during sleep: tonus is maximal during wakefulness, decreases in NREM sleep and is markedly reduced to absent during REM. The change in muscle activity characteristic of normal REM, is a prerequisite for REM scoring (R&K criteria are based solely on signal amplitude), and makes EMG recording necessary during sleep studies. To evaluate sleep EMG, which represents the temporal and spatial summation of all active motor units within the recording electrodes' area, we investigated a set of variables based on the temporal and spectral properties of the signal.The motivation was to get new useful information from the EMG during sleep, specifically during REM. This information is independent of the signals' amplitude, which may be influenced by its quality.
Methods: Thirty-four subjects (12 normal, 11 with OSAS and 11 with miscellaneous sleep disorders=misc) underwent standard polysomnography including surface EMG (Chin, Tibialis). Sleep stage, respiratory events, and arousals were scored manually, according to R&K and ASDA criteria. Afterwards, nine variables were calculated throughout the night: (i) time domain variables: mrEMG=mean amplitude of the rectified EMG; ZC=number of zero crosses; Turns=number of first derivative's sign change; (ii) frequency domain variables: nPWR=total power calculated from the power-spectrum; MF=median frequency of the spectrum; MPF=Mean Power Frequency; EZC&Complexity= second and fourth moment of the spectrum; PVAR=variance of the spectrum.
Results: Three of the nine variables disclosed significant changes (one tailed, paired t-test; *p<0.05; **p<0.01; ***p<0.005) between different sleep/wake states: For Chin EMG: (i) wakefulness versus any given sleep stage (mrEMG, PVAR, nPWR were higher for normals*, apneics***, misc***); (ii) stage1 versus stage2 (no significant difference); (iii) stage1 versus SWS (nPWR and PVAR higher* in normals and misc groups only); (iv) stage2 versus SWS (mrEMG higher* in all groups, nPWR and PVAR higher* only in apneic and misc groups); (v) REM versus any other sleep/wake state (mrEMG, PVAR, nPWR minimal in all groups** or***). All the above results were more significant for Chin than for Tibialis EMG.As to the differences between the subject groups: normalized values of mrEMG were similar in each stage for all groups. PVAR and nPWR differed* in misc versus other groups in SWS; differed* in normals versus others in REM. The comparison between each variable, mrEMG, nPWR, PVAR, during the first, mid and last third of the night, performed separately for each sleep stage did not reveal any significant trend across the night.
Conclusions: The analysis of specific properties of EMG can deepen the understanding of sleep physiology. The frequency domain variables (nPWR, PVAR) add information, which allows differentiating between sleep stages better than the amplitude. A quantitative description of muscle activity in sleep can be obtained by means of these variables in normal as well as in abnormal subjects. New criteria for automatic sleep scoring and diagnosis of sleep disorders can be based on these variables and increase the reliability of the scoring.

0990.R

Continuous Electrocardiogram Recordings Reveal Valuable Concealed Information on Sleep and Respiration

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Introduction: The growing interest in sleep and its disorders caused a continuously increasing need to perform sleep investigations for academic and clinical purposes. To achieve reliable information, the sleep study is attended, usually in a special facility, while the patient is hooked to a polysomnograph that records multiple physiologic inputs required in order to characterize sleep and decide whether it is normal or abnormal. Sleep is characterized according to standard criteria (R&K) and well-defined disorders are evaluated. The described procedure is uncomfortable for the patient, artifacts are frequent and cause difficulties in data interpretation. Automatic data scoring, although available, is not very reliable. Manual data interpretation is time consuming and tinted with subjectivity. Standard sleep studies are thus expensive and cumbersome; their reliability is often limited. New, simpler techniques based on physiologic variables, which are easier to acquire and more comfortable to the patient, are needed in order to obtain reliable, easily reproducible and cheaper diagnosis/screening of sleep disorders.
Methods: We developed a method a sleep scoring and diagnosis based on continuous ECG recording during sleep. The algorithm is based on the analysis of the ECG in the time domain (detection of arousals, REM, isolated apneas), frequency domain (SWS detection, recurring apneas detection), morphology of the ECG signal(R wave duration for the detection of body position). We developed separately each of the above parts of the algorithm and published preliminary and partial results. The algorithm was developed on several sets of data from different laboratories. The validation was then obtained on new data from 33 subjects. Standard sleep scoring based on R&K criteria and OSA diagnosis based on ASDA criteria was performed by a sleep expert and the subjects were divided in 3 groups: normals (12), apneics (11), miscellaneous (various sleep complaints-11). Automatic analysis based on the new algorithm was performed by a different-blinded staff member. At final stage the results of the two analyses were compared.
Results: For the sleep analysis the following variables were obtained from ECG: Sleep Onset (SO), body position (BP), SWS, light sleep (LS), REM, arousals and respiratory events. Body position was detected correctly in 90% of cases. SO as detected from the ECG was found within +2 epochs from the SO in 85% of cases; SWS was detected correctly 80%; arousals 80%; REM and LS were well differentiated in only 60%. Respiratory events were correctly detected automatically 85%.
Conclusions: Analysis of sleep architecture can be based on the ECG recording, at least for clinical purposes when a complete sleep study is too cumbersome and expensive. It can be employed as a screening procedure until the discrimination between REM-LS will be improved. The detection of sleep related breathing disorder is reliable and may be used in routine clinical work both as a diagnostic and as a follow-up tool, provided sleep analysis is also performed by means of the ECG.

0991.R

Homeostatic Regulation of Human Rapid Eye Movement Density: a Comparison with EEG Slow-Wave Activity

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Introduction: Among a variety of physiological measures, the duration of rapid eye movement sleep (REMS) shows a strong circadian control. In contrast, the density of rapid eye movements during REMS shows little circadian modulation and is considered to be predominantly regulated by the sleep homeostat (i.e. amount of time awake/asleep). Here we investigate the effects of differential sleep pressure conditions on rapid eye movement density during REMS (REMden) in the following recovery night to validate and compare REMden with the classical marker for NREM sleep pressure, EEG slow-wave activity (SWA, EEG power density between 0.75 and 4.5 Hz).
Methods: Following two scheduled days in the laboratory during which subjects slept at their habitual times, 8 male and 8 female subjects (age

range 21-31y), underwent a 40-h sleep deprivation (SD) or a 40-h nap protocol (NAP) in a balanced crossover design (intra-subject comparison) under constant posture conditions. In the NAP protocol, subjects were scheduled to an alternating cycle of 150 min of wakefulness and 75 min of sleep. Sleep EEGs were recorded from 12 brain sites during the baseline nights preceding the SD and NAP protocol and during following recovery nights. All EEGs were subjected to spectral analysis. Two bipolar EOGs were placed at the outher canthi of each eye. All 20-s epochs during REMS were visually inspected and scored for the occurrence of rapid eye movements. The intra-subject relationship between REMden and SWA was analyzed by multiple regression analysis, whereby the inter-subject differences were taken into account by dummy coding.

Results: Under high sleep pressure conditions (following 40-h of SD), REMden was significantly reduced, whereas after sleep satiation (following 40-h of NAP) a significant increase in REMden in the following recovery night was observed. The duration of REMS did not yield any significant change after these differential sleep pressure conditions. REMden was significantly and negatively correlated with SWA along the fronto-occipital axis (EEG derivations: Fz, Cz, Pz, Oz; intra-individual correlation: $r=0.76$; $p< 0.0001$, $N=16$ subjects, 64 data points). Interestingly, the increase in SWA after sleep deprivation was significantly more prominent than the decrease in REMden. In contrast, the increase in REMden in response to sleep satiation was more evident than the decrease in SWA. The latter was more pronounced in occipito-parietal than in fronto-central brain regions.

Conclusions: Our data indicate that REMden is a sensitive measure for NREMS sleep pressure. REMden and SWA in occipito-parietal regions are particularly susceptible to sleep satiation whereas frontal SWA responds particularly well to sleep loss conditions. These results support the hypothesis that the homeostatic Process S exerts an inhibitory influence on rapid eye movement density during REM sleep.

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0992.R

Nonlinearity and Nonstationarity in Human Sleep EEG Data

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Introduction: Traditionally the EEG is considered as a superposition of oscillations in certain frequency bands produced by some generators and embedded in stochastic background activity. Therefore, the EEG might be considered as resulting from a linear stochastic process and sufficiently characterized by linear features such as power spectra or correlation functions. Nevertheless, depending on the psychophysiological brain state the activity of the different generators may vary, therefore rendering the EEG nonstationary. Alternatively, it was proposed that the EEG might result from a chaotic deterministic process. This approach was reinvestigated in more recent studies. While it was not possible to find clear evidence for chaotic dynamics, a rejection of the null hypothesis of linear stochastic dynamics was reported in several cases. However, it remained an open question, whether this rejection was caused by nonlinear dynamics or might be explained by nonstationarity.

Methods: We selected 361 artefact-free segments from four all-night EEG recordings (C3A2 derivation). Only 1-min segments containing one single sleep stage were analyzed. The segments were divided into subsegments of various durations ranging from 1-30 seconds and for each subsegment an autoregressive(AR) model was fitted. The model order was determined by Akaikes information criterion. For every subsegment 100 surrogate data sets were generated by iterating the fitted model with randomly shuffled residuals. The correlation entropy H, a measure based on the correlation integral, was used as test statistic for linearity. It was examined whether the validity of the linear model depended on the length of the subsegments.

Results: No significant rejections of the linear model were observed for the 1-s subsegments. The fraction of subsegments for which the null hypothesis had to be rejected increased with the length of the subsegments. Further analyses revealed that this effect cannot be explained by stationary nonlinearity and is a clear sign of nonstationarity. The strongest sign of nonstationarity was found in segments from sleep stage 2, while REM sleep and slow wave sleep showed less nonstationarity. By interpolating the AR-coefficients estimated from 1-s subsegments it is demonstrated that the AR-model with smoothly varying coefficients in time is capable to generate realistic EEG-like time series.

Conclusions: Our analysis leads to the picture of a hierarchy of three time scales: A first time scale in the range of a few seconds contains the typical EEG patterns including spindles or K-complexes and can be modeled by linear models. A second time scale up to several minutes (microstructure of sleep) is characterized by the dynamics of the AR-coefficients. The dynamics of the AR-coefficients contains the slow oscillations (< 1 Hz) which govern the occurrence of sleep spindles and delta waves. A third time scale from minutes to hours (macrostructure) can be related to the sleep stages and is reflected by the slow dynamics of the mean AR-parameters.

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0993.R

Adverse Events During Polysomnography

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Introduction: Polysomnography (PSG) is widely performed for the diagnosis and as a treatment initiation monitor. Problems during a PSG fall into two categories: a) those resulting from the testing equipment and methods (electrode placement, latex allergy, colloid use, or electrical safety) and b) adverse cardiopulmonary or neurologic events noted by the technician or the patient. We report preliminary data from a prospective study to determine the prevalence of the adverse events during PSG.

Methods: Data were obtained from the technical scoring reports for PSGs performed between January 1 and October 31, 2002. Results were tabulated for three different scoring teams in a regional network of 77 beds; technicians with BLS or ACLS credentials staffed each facility.

Results: There was one fatality out of 9307 procedures. A 61 year-old male with known history of coronary artery disease and dilated cardiomyopathy (EF 20%) underwent an elective split-night PSG at a hospital-based facility for the indications of suspected sleep apnea on the basis of snoring, occasional pauses during sleep, irregular heart rate, sleeping on more than one pillow, and nasal congestion. He suffered a cardiac arrest during sleep in the early morning hours after successful application of CPAP for recurrent obstructive apneas. Retrospective analysis of the PSG showed premature ventricular beats before and after application of CPAP and brief (<3 seconds) non-sustained ventricular tachycardia, occurring 45 and 30 minutes before sustained ventricular tachycardia and then fibrillation, from which he could not be resuscitated. In the system, there were 19 instances during a PSG when the patient had symptoms and/or PSG problems (notably ventricular arrhythmia) that resulted in immediate physician evaluation and/or transfer to an emergent care facility. In 24 other instances complex ventricular arrhythmia were noted during the technical scoring of the PSG, and the referring physician was alerted to this finding. None of these 43 adverse events was associated with mortality within 2 weeks of the PSG. Adverse events were not related to the number of beds in the facility or

in the length of time that the facility had been performing sleep studies. **Conclusions**: The current rate of mortality is ~0.01% and of overall adverse events is ~0.5%, largely due to cardiovascular morbidity. Our observations support anecdotal observations that emergent medical problems during a PSG are uncommon. Despite the rarity of adverse events, written procedures, BLS certification, continuing education, and procedures for handling medical emergencies or adverse events noted in PSG scoring are necessary for any sleep facility.

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0994.R

Validation Of An Autoscoring Algorithm To Detect Obstructive Sleep Apnea

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Introduction: Historically, the scoring and analysis of sleep apnea records by hand represents a significant time investment and often contributes to the delay in the reporting of the results to the primary care physician. Additionally, significant inter-scorer variability is well documented in the literature, thus, providing evidence that manual scoring of sleep studies is not without inherent sources of error.
Methods: In attempt to improve the efficiency and accuracy of scoring sleep studies, the sleep studies of thirty patients suspected of having obstructive sleep apnea (OSA) were both handscored and autoscored using a novel algorithm. Patients were recruited from the Sleep Disorders Center at the Dallas VA Medical Center, as well as from a professional long-haul trucking company (age 43.0 + 12.4 yrs; weight, 102.6 ± 17.9 kg; neck circumference, 16.6 ± 1.3 in; BMI, 32.6 ± 6.2 kg/m2; Epworth Score, 10.7 ± 5.0) Patients underwent an in-home LifeShirt™ system (LS) (VivoMetrics, Ventura, CA, USA) cardiorespiratory sleep study. Ventilatory excursions were assessed via two respiratory inductance plethysmography (RIP) bands that were contained within the LS garment at approximately the level of the fourth intercostal space and the umbilicus. Pulse oximetry was also measured. Data were written and stored on a compact flash card within the recording unit of the LS and then uploaded the next morning via the Internet to a data center. Sleep recordings were manually reviewed and scored by two experienced sleep technicians to determine the apnea/hypopnea index (AHI). Sleep records were then auto scored using the LS system proprietary software. Hand scoring always preceded autoscoring to ensure that the sleep technicians would not be influenced by the algorithm.
Results: Results revealed a strong linear relationship between autoscoring and handscoring for AHI (r = 0.92). Agreement for AHI between manual score and algorithm was determined using the concordance correlation coefficient (rc = 0.90). Additionally, there was no significant difference between mean AHI as determined by handscoring (24.4 ± 19.9) and the autoscoring (27.0 ± 18.7).
Conclusions: In conclusion, we have developed an algorithm that yields a high degree of agreement for AHI when compared to a hand scored cardiorespiratory sleep study in patients with obstructive sleep apnea.

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0995.R

Diagnosing OSA with a Simple Device Based on Peripheral Arterial Tone: In-Lab Polysomnographic Validation and Ambulatory Studies in the Home

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Introduction: Studies continue to demonstrate the risks associated with undiagnosed OSA. Ambulatory monitoring for the detection of OSA in the home is an attractive alternative to attended PSGs in the sleep laboratory. Ambulatory monitoring technology should be easy to use for the patient and require minimal post-acquisition analysis. The Watch_PAT100 (WP100), a portable device based on Peripheral Arterial Tone (PAT), oximetry, and actigraphy, has the potential to simplify the evaluation of patients with sleep disordered breathing.
Methods: Subjects (n=58 to date: 53 patients referred for suspected OSA, 5 normal volunteers) underwent in-lab polysomnography (PSG) concurrently with WP100 recording. 28/58 subjects (all referred for suspected OSA) received instruction for self-administered WP100 recordings and then completed a WP100 sleep study in their home in addition to their in-lab PSG (random order for the home and lab studies). PSGs were scored for respiratory events according to recent AASM criteria (1999) with the scorer blinded to the WP100 results. WP100 recordings were analyzed on-site with an automated algorithm to calculate a PAT respiratory disturbance index (PRDI). The unedited PRDI (either from the lab; Lab-PRDI, or home; Home-PRDI) was then compared to the RDI from polysomnography using linear regression and receiver-operator characteristic (ROC) curves. Subjects were considered abnormal (having OSA) for the ROC curve if the RDI was > 20 events per hour of sleep on the PSG.
Results: For the larger group [n=58, 39M/19F, age 45±13, BMI 32.5±7.5, ESS 9.3±4.8], the prevalence of OSA was 53%. The Lab-PRDI (25.9±15.7) correlated with the RDI measured by PSG (27.6±15.7) in the lab (R=0.87, p<0.0001). The area under the ROC curve (AUC) for the Lab-PRDI was 0.89. For subjects completing both in-lab and home studies [n=28, 20M/8F, age 43±11, BMI 34.2±7.1, ESS 9.3±4.7], all 28 individuals successfully completed their home study on the first attempt. For this smaller group, the prevalence of OSA was 71%. The PRDI calculated from studies in the home and lab correlated with the RDI measured by PSG in the lab [Lab-PRDI (28.8±15.2): R=0.86, p<0.0001; Home-PRDI (26.2±15.9): R=0.74, p<0.0001]. The AUC for the Home-PRDI was 0.89 (abnormal cases defined by PSG-RDI). Optimum sensitivity (85%) and specificity (87.5%) were achieved on home WP100 studies using a PRDI > 16.1 to define OSA. The Home-PRDI also correlated with the Lab-PRDI (R=0.76, p<0.0001).
Conclusions: This study assesses the diagnostic accuracy of the WP100 with both in-lab PSG validation and patient-administered studies in the home. The results suggest the WP100 is both reliable (no data acquisition or automated analysis failures) and accurate (based on its ability to differentiate subjects with and without OSA using the ROC curve).

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0996.R

Assessment of a New Automated Sleep Scoring System

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Introduction: The classification of sleep stages is a vital component of any polysomnogram (PSG). Manual scoring by a trained technologist remains the standard method for generating these data. However, this

process is time-intensive and vulnerable to inter-scorer variability. Automated scoring (real-time or post-acquisition) offers the advantage of reduced cost, efficiency, and objectivity. The automated algorithms used in this study are based on adaptive segmentation, fuzzy clustering, and hidden Markov models.
Methods: We selected 51 consecutive nocturnal ALICE3 PSG recordings for the study (25 all-night PSGs and 20 split-night PSGs for sleep disordered breathing (SDB), and 6 all-night CPAP titrations). All recordings used a standard montage for SDB including 4 EEG channels (C4-A1, C3-A2, O2-A1, O1-A2 with A1-A2 linked). Sleep stages were scored automatically using the Morpheus I Sleep Scoring System (A) and manually by 2 registered PSG technologists (M1 and M2) according to the Rechtschaffen and Kales manual. Arousals were also scored according to ASDA criteria. Each scorer was blinded to the results of the other scorers. Standard PSG sleep stage measures were tabulated for each record by each scorer. Agreement and Cohen's Kappa were tabulated using a sleep stage epoch by epoch agreement matrix (5x5: W, S1, S2, SWS, REM) and an arousal scoring epoch by epoch agreement matrix (3x3: 0,1,2 arousals/epoch) for each pair.
Results: 49 recordings had sufficient signal fidelity for automated analysis. Measurements for scorers A, M1, and M2 included mean: total sleep time (min) 312.4, 300.9, 307.1, sleep efficiency (%) 73.9, 71.1, 72.5, duration of REM sleep (min) 39.7, 50.6, 46.7, and arousal index (arousals per hour of sleep) 25.2, 25.1, 51.3, respectively. The agreement and Cohen's Kappa were 76.9% & 0.66, 74.8% & 0.64, and 85.5% & 0.79 between pairs A-M1, A-M2, and M1-M2 for the 5x5 sleep stage agreement matrix. When stages 1 and 2 were combined to yield a 4x4 matrix, the agreement and Cohen's Kappa were 82.4% & 0.71, 82.0% & 0.70, and 91.7% & 0.86, respectively. The arousal agreement and Cohen's Kappa were 81.5% & 0.24, 74.0% & 0.25, and 82.4% & 0.49, respectively.
Conclusions: Agreement between manual scorers was very close to the average pairwise agreement of 87% reported in the Sleep Heart Health Study (SHS). The automated classification of sleep stages was relatively close to this standard and improved when stages 1 and 2 sleep were combined. These data suggest that if SDB can be adequately evaluated, then fully automated sleep stage scoring of PSGs can yield agreement approaching the optimum established in the SHS. Cohen's Kappa for the arousal scoring pairs suggests that interobserver agreement is poor regardless of the pair combination.

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0997.R

Validity of the Pittsburgh Sleep Quality Index: Subjective Sleep, Objective Sleep and Depression

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Introduction: The PSQI is a widely-used measure of sleep complaints; however, relatively few studies have examined the validity of the PSQI relative to both subjective and objective sleep, as well as depression. There has also been little investigation of the psychometric properties of this instrument in healthy adults, despite its wide use in this population.
Methods: A group of 59 younger (mean age=23) and 53 older (mean age=66) healthy adults wore a wrist actigraph for one week, and also completed a PSQI, CESD (a depression self-rating), and one week of sleep diaries. Correlations were computed between PSQI global and component scores with actigraphic sleep parameters, sleep diary reports, and CESD. Spearman's rho was used, due to the non-normal distribution of the data.
Results: Correlations with PSQI global score, were moderate for sleep diary variables (r=-.307 for total sleep time (TST), .262 for wake time after sleep onset (WASO), and .480 for sleep latency (SL); all values $p<.01$) and moderate for CESD (r=.305; $p<.01$) but very low for objective actigraphic sleep parameters (r=.046 for sleep efficiency, .130 for TST, .011 for WASO and .022 for SL; all values $p>.05$). With respect to component scores, some PSQI components (Subjective Sleep Quality, Sleep Latency, Sleep Duration, Habitual Sleep Efficiency and Daytime Dysfunction) were correlated with sleep diary scores, but sometimes the CESD correlated as well or better. Surprisingly, there were no significant correlations between PSQI components and actigraphic data, except a significant correlation of the actigraphic TST with the Sleep Duration component and a positive correlation of the actigraphic TST with the Sleep Latency component. Overall, the PSQI correlated appreciably with sleep diary variables and CESD, but not with any actigraphic sleep variables.
Conclusions: These results suggest that the PSQI may reflect a negative cognitive viewpoint or pessimistic thinking rather than actual sleep physiology. The sleep complaints measured may often be more indicative of individual dissatisfaction than of any specifically sleep-related disturbance. PSQI components had similar correlations to each of the sleep diary measures, suggesting a lack of specificity in PSQI component scales, sleep diary components, or both. Although the sleep diary and PSQI are both subjective self-report measures of sleep, the present investigation shows that these instruments may not be measuring the same constructs well. It is interesting that PSQI correlated better with a depression scale and subjective sleep complaints than with objective sleep disturbances.

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0998.R

Does The Peak-End Effect Apply To Subjective Sleep Reports?

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Introduction: Pain like sleep is often assessed using subjective measures. One question that has been raised in the pain literature is whether a one-time pain assessment is an accurate reflection of average pain or whether it reflects something else. Some researchers have concluded that when people are asked a one-time question about their assessment of a painful period of time, their response is not a reflection of their averaged perceived pain during the time but is instead an average of the worst pain that they felt (peak) and the final pain that they felt (end). This is the Peak-End Effect. The purpose of this study was to assess whether a similar effect applies to subjective sleep reports.
Methods: Sixty-nine college students kept a sleep log for a 7-day period. The sleep log included information on sleep quantity and quality. The participants were asked to complete the log each morning immediately after awakening. At the end of the 7-day period, the participants were asked to complete a one-time sleep questionnaire that contained the same questions as the sleep log except that it referred to their average sleep over the last week. Standard regression models were run in SPSS to determine the best predictors from the sleep logs of the one-time responses to the sleep questionnaire. As predictor variables we used the average of the 7-day sleep log responses as well as peak-end and minimum-end composites. We considered the minimum-end combination for many of the sleep-related measures because the minimum would indicate the "worst" sleep just as the peak indicated the worst pain in the pain literature.
Results: The results indicate that one-time reports on sleep are based more on average values instead of a composite of peak-end or minimum-end effects. For example, the average reported time in bed across the 7-day sleep log period resulted in an r-squared of .67 in contrast to an r-squared of .192 for minimum-end. The average of sleep quality resulted in an r-square of .631 in comparison to an r-squared of .402 for minimum-end. The average refreshed feeling upon awakening resulted in an r-square of .596 whereas the minimum-end composite resulted in an r-

square of .391.
Conclusions: Unlike the results reported in the pain literature, one-time sleep reports are based more on average sleep habits than on composites that involve a "worst" sleep effect with an "end" or recency sleep effect. This result indicates that one-time sleep reports, such as those used in large epidemiological studies, are a reflection of average sleep times and quality and not a composite of "worst" sleep and recent sleep.

0999.R

Circadian Variation in Psychomotor Performance in a Normative Sample as Assessed with a Driving Simulator

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Introduction: Driving performance and incidence of sleepiness-related motor vehicle accidents have also been demonstrated to be subject to time-of-day variation irrespective of sleep-deprivation and shift-work. Utilizing a driving simulator we hoped to measure circadian fluctuations in psychomotor performance measures, and hence a naturalistic variation in driving ability over the course of a day. The secondary objective was to establish a normative reference for future comparison to patients with sleep pathologies.
Methods: Subjects were given a series of baseline questionnaires and underwent clinical screening to ensure assessment of normal individuals. Healthy adults with a valid driver's license were included; subjects were screened for iregular sleep schedule, as well as a history of a significant medical, psychiatric or sleep disorder. Concomitant use of sedating or stimulating substances was a further exclusion criterion. Using the York Driving Simulator (York Computer Technologies), subjects performed four intentionally soporific 30-minute driving simulations at two-hour intervals (i.e. at 10:00, 12:00, 14:00, and 16:00). Subjects were instructed to stay in the right-hand lane, obey posted speed limits, and keep both hands on the steering wheel. Measured variables included: lane accuracy, average speed, speed deviation, reaction time to virtual wind gusts, off-road events.
Results: Sixteen individuals (mean age of 30.8 $\pm$ 7.5) were included in the study. Mean values of each variable at every time of simulation were attained and analyzed using a general linear model and paired sample t testing. Reaction time to virtual wind gusts was found to show significant within-group variation (F=3.7, p=.02, df=3), with paired samples tests at df=15 showing reaction times at 10:00 significantly faster than at other times of the day: [RT10:00 - RT12:00 (p = 0.04) / RT10:00 – RT14:00 (p = 0.01) / RT10:00 – RT16:00 (p = 0.01)], but no significant within-group variation between other times of the day. All other variables (lane accuracy, average speed, speed deviation, and off-road events) failed to exhibit any statistically significant variation across the day.
Conclusions: With reaction time being optimal before the noon it appears that psychomotor performance and therefore driving ability is subject to circadian variation. Coincident with the known circadian pattern of diminshed alertness, this may help to explain the high incidence of motor vehicle accidents during the mid- to late-afternoon. It is hoped that data from this normative sample of healthy adults may be used in future comparisons to patients being screened for potentially impaired driving performance due to sleep-related and other neuropsychiatric disorders.

1000.R

The Effects of Patterned Neurofeedback on Sleep Continuity

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Introduction: Recently, our group has developed a form of neurofeedback as a treatment for insomnia. The signal itself is based on the spectral profile of EEG data obtained from subjects while relaxed with their eyes shut. The EEG spectral data is manipulated so that changes in the ratios of fast/slow activity are patterned to sound like music. Presented below are the PSG treatment efficacy data from our pilot study on this form of neurofeedback.
Methods: Twenty three medically and psychiatrically healthy patients with primary insomnia were treated with patterned neurofeedback over the course of a 4 week interval. Subjects received, in a double blind fashion, tailored feedback (neurofeedback derived from their own EEG signals [n=15]or "faux" feedback (neurofeedback derived from another subject's EEG signals [n=8]. Pre-Post changes in sleep latency, wake after sleep onset and total sleep time were analyzed using 3 Two-Way mixed model ANOVAs (Group * pre-post Tx) and paired t-tests. PSGs were acquired prior to Tx and following the 4th week of treatment.
Results: Subjects receiving true neurofeedback (TF) tended to improve on all threePSG measures of sleep continuity as compared to the subjects whoreceived "faux" feedback (FF) (SL, p. < 0.05; WASO, p < 0,01, TST, p <0.10). In general, positive improvements were only evident for the subjects receiving true neurofeedback and the treatment effects were of a large magnitude. The percent changes were SL TF: 45% vs FF: 6.4%; WASO was TF: 62% vs FF: 1.8% and TST was TF: 11% vs FF: 0.5%).
Conclusions: These preliminary results suggest that patterned neurofeedback thatis tailored to the individual produces robust changes in sleep continuity. Whether this represents a novel form of relaxation training or a formof neural conditioning or entrainment remains to be determined. The failure of the faux condition to produce significant pre-post change, however, suggests this form of neurofeedback may indeed directly influence brain activity so as to produce improved PSG measured sleep.

1001.R

Driving Simulation Test For Evaluation Of Sleepiness: Reliability Of A Monotonous Driving Scenario

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Introduction: Driving Simulators reproduce situations which require both tracking and visual searching, the main features of real driving. This study measured the reliability of a monotonous driving scenario to detect the circadian variations of alertness in healthy subjects.
Methods: Five men and five women (mean age=25.20 yrs, sd=1.55) with valid drivers' licenses were tested. Exclusion criteria were 1) symptoms of a sleep or medical disorder including excessive daytime sleepiness tested with Epworth Sleepiness Scale (score>10) and 2) alcohol, coffee or nicotine abuse. Subjects underwent a 30-minute driving simulation task with a few curves and without obstacles (STISIM 300 Systems Technology Incorporated, Hawthorne, USA) every two hours, from 10 a.m. to 12 a.m. of the following day without sleeping and without taking stimulants (coffee, tea, chocolate) during the study. Before each driving task subjects completed the Stanford Sleepiness Scale (SSS) and the Visual Analogue Scale (VAS). During a trial test they were instructed to drive in the right-hand lane, to maintain a speed between 80 and 120 Km/h respecting the variable limits and to attend a secondary task,

Divided Attention (DA). Driving performance data, grouped in three 10-minute blocks, included mean and standard deviation of lane position, speed and reaction times (RT) to DA, exceeding the speed limit and crash frequency data. Non parametric tests (Wilcoxon test and Kruskal-Wallis test) and Pearson's correlations ($p<0.01$) were used for data analysis.

Results: Driving performances deteriorated or improved according to the circadian variation of alertness. This variability was significant for crashes and standard deviation of lane position (Kruskal-Wallis test: alpha=0.00). Moreover, the comparison between the values of standard deviation of lane position in the first 10 minutes and in the last block of data of each task, showed significant differences when the vigilance is lowest, at 4 p.m. of the first day and from 6 a.m. to 12 a.m. of the second day (Wilcoxon test: alpha<0.05). Pearson's analysis showed the following correlations of driving parameters with SSS and VAS: standard deviation of lane position (respectively r=0.49 and r=-0.48), mean RT to DA (r=0.27 and r=-0.35), crash frequency (r=0.40 and r=-0.36) and exceeding the speed limit frequency (r=0.38 and r=-0.29).

Conclusions: The Driving Simulation Test we designed is characterized by a long and monotonous scenario. We demonstrated that it is suitable to detect the consequences of sleepiness related to the circadian variations of alertness. The parameter most significant for evaluation of sleepiness is the standard deviation of lane position, mainly comparing the differences among the 10-minute blocks in each task.

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1002.R

A Monotonous Driving Simulation Task: Correlations With Multiple Sleep Latency Test

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Introduction: Driving simulators have been used to study the performance decrements associated with drowsiness. Variability of results may depend on the characteristics of simulator and driving scenario. In order to validate a monotonous driving scenario, we correlated the results of a driving simulation task in different alertness conditions with objective (Multiple Sleep Latency Test, MSLT) and subjective (Stanford Sleepiness Scale, SSS, and Visual Analogue Scale, VAS) sleepiness measurements.

Methods: Five healthy men and five healthy women (mean age= 24.90 yrs, sd=0.57), with valid drivers' licenses, were tested. Exclusion criteria were 1) symptoms of a sleep or medical disorder, including excessive daytime sleepiness tested with the Epworth Sleepiness Scale (score >10) and 2) alcohol, coffee or nicotine abuse. The subjects were tested on two different days, after a normal night of sleep and after a night of complete sleep deprivation. Use of sedative or stimulant substances was forbidden during the study. The study consists of four sessions of MSLT, each one followed by subjective measurements of sleepiness (SSS, VAS) and by a 30 minute driving simulation task with a monotonous driving scenario (STISIM 300 Driving Simulator, Systems Technology Incorporated, Hawthorne, USA). During a trial test the subjects were instructed to drive in the right-hand lane, to maintain a speed between 80 and 120 Kmrespecting the variable limits and to attend to a secondary task (Divided Attention) which measured reaction times (RT) while driving. Driving performance data, grouped in three 10-minute time blocks, included mean and standard deviation (SD) of the lane position, of speed and of RT, exceeding the speed limit and crash frequency data. Performance data were analyzed with non-parametric tests with alpha<0.05 set and then related to sleepiness measurements with Pearson's correlations ($p<0.01$).

Results: The number of crashes and times exceeding the speed limit, the mean RT and the lane position variability showed significant differences in the different simulation sessions (Kruskal-Wallis test). In basal conditions, the SD of lane position of the three time blocks did not differ significantly. After sleep deprivation, lane position variability showed significant differences from the first block to the second and third blocks (Wilcoxon test) in all simulation sessions.The parameters that correlate most highly with MSLT are the SD of lane position (r=-0.532), the mean RT (r=-0.540), the crash frequency (r=-0.375) and exceeding the speed limit frequency (r=-0.333). Lower correlations were found between the same parameters and the subjective sleepiness scales.

Conclusions: The monotonous driving simulation we adopted showed significant correlations with MSLT and subjective sleepiness scales in healthy subjects. It seems suitable to evaluate excessive daytime sleepiness in patients.

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1003.R

Detection of Sleep Bruxism (SB) in Home Studies Using the BiteStrip®

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Introduction: The Bitestrip is a miniature single-use electronic screener for sleep bruxism (SB). It is comprised of EMG electrodes and an amplifier to acquire masticatory muscle signals, a CPU with real time software, which detects and analyses EMG patterns, a permanent chemical display which presents the outcome in the morning, a light emitting diode (LED) and a lithium battery. All elements are integrated on a single flexible substrate. At bedtime, it is attached to the cheek over the masseter. Patients are instructed to perform 4-5 maximum voluntary clenches (MVCs) in order to establish an individual threshold for bruxing events. In the morning, after removal of the device, the total number of bruxing events throughout the night is displayed. A good correlation between BiteStrip results and traditional EMG scoring of polysomnographic recordings has been reported previously. In the present study, performance of the BiteStrip is evaluated in unattended home studies.

Methods: Eleven adult subjects with a history of SB based on clinical evaluation participated in the study (BRUX). Six adult subjects with no history of SB based on subjective reports alone participated as controls (NBRUX). All subjects used the BiteStrip for one to three nights. BiteStrips were collected and final scores were averaged across nights per subject. As the BiteStrip final score represents not a single number but rather a range (e.g., 100-124), each subject had 2 scores: an averaged minimum (MINAVG) and an averaged maximum (MAXAVG). Non-parametric Mann-Whitney tests for 2 independent samples were performed between groups for MINAVG and MAXAVG scores.

Results: Altogether, 46 nights were completed. Eight nights were excluded due to battery failure (3), premature removal of the device (3) or unclear display (2). Mean ($\pm$SD) minimum scores were 130.53($\pm$130.41) and 7.67($\pm$13.46) and mean maximum scores were 178.30($\pm$177.22) and 31.67($\pm$13.46) for the BRUX and NBRUX groups respectively. Mann-Whitney U statistics were 2.5 for MINAVG ($p=0.001$, one tailed) and 3.5 for MAXAVG ($p=0.002$, one tailed).

Conclusions: These preliminary findings suggest that the BiteStrip is a useful tool for distinguishing between bruxers and non-bruxers. It is reliable enough to use in unattended home studies with a low failure rate.

1004.R

Effects of Increasing Differential Impedence on High Frequency EEG Activity

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Introduction: High-frequency EEG activity (HFA) tends to increase across the night. This may occur as a result of the discharge of the sleep homeostat (Process "S"), increasing sleep satiety, or may represent an increase in the pressure for wakefulness ("Process W"). It may, however, also occur as a method artifact. That is, over the course of the night electrode impedances tend to increase. These increases, particularly differential impedance, may result in an augmentation of HFA. The goal of the present study is to explore and quantify the effects of increased differential impedance on HFA.
Methods: 5 healthy subjects (3 male, 2 female) participated in this study. A mono-polar montage was used with C3 and C4 referenced to linked mastoids. A decade resistance box was placed in line between the C3 site and the head box. Subjects were instructed to close their eyes, relax, and to silently repeat the number "one" continuously for the duration of each sampling period. The EEG signal from C3 was sampled over nine conditions where the impedance was systematically increased across the following intervals: 0 kilo-ohms (K), 5K, 10K, 15K, 20K, 25K, 30K, 40K, 50K. The EEG signals were acquired using a Grass Model 8 electroencephalograph (Gain of 5 ìV/mm Low Pass Filter @10K with the notch filter in-line), then passed in series to a Krohn-Hite Low Pass Filter (LPF@300Hz-48dB/octave). Digital acquisition was governed by Stellate Harmonie-Luna software and accomplished by a BSMI 519 A-to-D board. The A-to-D board has a notch filter at 60Hz and a 1 pole (6dB/octave) low pass filter at 300Hz. The signal was sampled at 800Hz and then the power spectrally analyzed using the aforementioned acquisition software. Eight repeated-measures one-way ANOVAs were run, where the repeated measures factor was kilo-ohms resistance and dependent variable was spectral power. Each of the 8 ANOVAs corresponded to average power for each spectral band (delta, theta, alpha, sigma, beta-1, beta-2, gamma and omega).
Results: The lower frequency bands (delta, theta, alpha, sigma) were not effected by increasing impedance. The upper spectrum (beta-1, beta-2, gamma) showed a trend towards increased power ($p < 0.10$) to increasing impedance. This trend was significant for the omega band ($p < 0.001$). It also appeared that there was a non-linear increase in power that occurred at about 25 kilo-ohms resistance and that a similar trend was evident for the other HFA bands. The precise cut off for the non-linear increases in power remains to be determined.
Conclusions: Researchers studying high frequency EEG activity may do well to take into account the effects of differential impedance. It may be necessary to artifact reject, or statistically manipulate, any data that comes from sites with differential impedance of > 25K. This finding does not, however, rule out the possibility that increases in HFA across the night may also occur due to biological factors.

1005.R

Pressure Transducer vs. Thermistor: Inclusion of the Four Percent Os2s Desaturation Criterion Narrows the Discrepancy Between the Two Methods

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Introduction: In many sleep laboratories, thermistors (T) are being replaced by oral-nasal cannula pressure transducers (PT) which tend to be more sensitive to flow reductions.Hypothesis: The respiratory disturbance index (RDI), composed of apneas, hypopneas, and respiratory effort-related arousals (RERAs) will be higher using PT compared to T, but this discrepancy will be reduced by using the American Academy of Sleep Medicine (AASM) 2001 definition of the apnea-hypopnea index (AHI) which allows scoring of hypopneas *only if* there is accompanying oxygen desaturation of ³ 4%.
Methods: Eleven sequential patients referred for possible OSA were studied using simultaneous oral-nasal PT and T devices during an overnight diagnostic polysomnogram. There were 10 males and 1 female. The average age was 44.7 years ± 16 (mean ± S.D.), BMI was 31.7 ± 8.0, minimum SaOs2s was 86.3% ± 9.1, and the Epworth Sleepiness Scale Score (ESS) was 9.55 ± 7.2. Recordings were scored at different times by two registered polysomnographic technologists. Scorers were randomized with respect to the order of scoring (i.e., whether they first scored a patient using the PT or T device). The RDI, AHI and RERA indices were then calculated and compared.
Results: The PT-RDI was 37.6% greater than the T-RDI when not using the desaturation criterion for hypopneas (35.2/hr v. 25.6/hr, p=0.02). The difference between the two devices decreased to 31% when the desaturation criterion was introduced (39.3/hr v. 30/hr, p=0.012). However, among the four subjects with a T-derived AHI> 10/hr, the RDI using the desaturation criterion was only 19% higher with PT compared to T (43 v. 36).
Conclusions: PT results in a significantly higher RDI than T. The magnitude of the discrepancy is reduced in those with a higher AHI if the oxygen desaturation criterion is used. An RDI composed primarily of RERAs is more sensitive to the two different technologies than an RDI composed primarily of hypopneas with desaturations. The addition of the desaturation criterion appeared to promote the RERA events into the AHI category.

1006.R

The Initial Development and Validation Study of the Sleep Disorders Inventory for Students (SDIS)

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Introduction: It is estimated that 15% of all students have a sleep disorder (NIH Research & Grant Website, 2001), but are not being referred to sleep clinics because they appear perfectly healthy when awake (Wise, 1998). No valid sleep instrument exists in the schools to facilitate the screening of these students. One solution is the development of the Sleep Disorders Inventory for Students (SDIS) to be used to screen students for five sleep disorders (OSAS, Narcolepsy, PLMD, RLS, and DSPS) that negatively impact their school performance.
Methods: Content validation was completed with a committee of six nationally respected sleep specialists, one measurement professor, and two school psychologists. A pilot study was conducted using exploratory factor analysis (EFA) on the SDIS with 226 students from the Pasco, Florida Schools and two sleep clinics in Tampa Bay, Fl. MANOVA's were conducted on the SDIS total sleep scores and (1) Sleep Diagnoses vs. No Sleep Diagnosis, (2) Mental Health Diagnoses vs. No Mental Health Diagnosis, and (3) Special Educational Classifications vs. General Educational. Correlation studies were conducted to determine the relationship between the SDIS total scores and academic performance, as well as ADHD characteristics. Finally, a main research study was conducted on 450 students in Pasco, Florida Schools, Fl. and four AASM accredited sleep clinics. Confirmatory factor analysis, criterion-related validity, discriminate function analysis, internal consistency and test-retest reliability measures will be conducted on the main sample.
Results: The expert committee obtained 94% content validy on determining which sleep items should be retained in the SDIS and 86% consensus on which sleep disorders were described by each SDIS item. Using EFA, a six factor analysis was obtained with clear delineation of four factors (OSAS, PLMD, DSPS, and EDS). Two factors (Narcolepsy

and RLS) were unclear due to a small sample size of these disorders. To correct for this, larger samples of Narcolepsy and RLS-diagnosed children were gathered in the main study. When considering Total SDIS scores in the pilot study, there were significant variances between "Sleep Diagnoses" and "No Sleep Disorder"($p < .05$), between Mental Health Diagnoses vs. No Mental Health Diagnosis ($p < .0058$), and between Special Education Classifications vs. General Education. The ADHD group had a significantly higher Total SDIS Score than the "No Mental Health Diagnosis" group ($p < .05$). There were strong negative correlations between all academic subjects and Total Sleep Problems (n=191): The higher the reading, math, or written language performance, the lower the Total SDIS Score, and the lower the reading, math, and written language performance, the higher the Total SDIS Score (-.58, -.71, -.66).

Conclusions: EFA indicated four sleep factors for students: OSAS, EDS, PLMD, and DSPS. The pilot data indicated that students with sleep diagnoses, mental health diagnoses, and/or special education classifications are scoring significantly higher on the SDIS Total Score and exhibiting more sleep problems than students with no sleep disorder, no mental health diagnosis, and no special education programs. The pilot study results strongly suggest that students with academic or behavioral difficulties have more sleep problems and need to be screened by school or clinical psychologists. The main study results will be available for presentation by April, 2003.

1007.R

Assessment of a Re-engineered Inductance Plethysmography and Pressure Transducer in a Digital Polysomnographic System

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Introduction: With the advent of digital acquisition of polysomnographic (PSG) variables, inductance plethysmography, the gold standard for monitoring thoracic and abdominal activity, has been replaced with technologies such as piezoelectric sensors and impedance pneumography. Intrinsic limitations exist within these technologies; if piezoelectecric respiratory sensors become loose, signal polarities may invert and produce false paradoxical respiratory signals. Impedance pneumography cannot reliable distinguish obstructive apneic events. In this study, we evaluated respiratory monitoring technology engineered to overcome these measurement errors. The Embla N7000 PSG system (Medcare Flaga) employs a re-engineered type of inductance plethysmography, and a newly developed nasal airflow transducer. The inductance plethysmography system digitally assesses changes in electrical inductance within copper wires, sewn into elastic belts, placed around the chest and abdomen. During chest and abdominal expansion and contraction, corresponding changes in electrical impedance occur within the copper wire, producing a signal representing respiratory excursion.The nasal pressure sensor provides a direct semi-quantitative measure of airflow. Pressure changes occurring at the nares are communicated through a nasal cannula to a pressure transducer. A linearization process generates a signal with linear relationship to flow. Selective filtering of the signal yields additional information such as the presence or absence of snoring.

Methods: Eight subjects participated in overnight evaluations of polysomnographic variables recorded with this system. Present analyses focus upon respiratory variables. We calculated the percent of time that both respiratory and airflow signals provided technically acceptable (scorable) data. Criteria for scorable signals included stable baselines, consistency of respiratory pattern, and signal amplitudes consistent with observed respiratory activity. Other variables of interest included ease of sensor application, and subject tolerance of sensors.

Results: Seven of the eight subjects participated in two consecutive overnight PSG's, one subject completed one overnight PSG, totaling 15 studies. Recordings were 8.0 hours $\pm$ 15 minutes (mean $\pm$ 1 standard deviation of the mean) duration. Two subjects exhibited sleep disordered breathing, four subjects exhibited moderate to heavy snoring with upper airway resistance. Digital inductance plethysmography belts provided 94 $\pm$ 3% scorable data. Following successful biocalibration, neither respiratory belts nor nasal cannula required repositioning. Signal quality was neither affected by body position nor folding of the belts upon themselves during subject movements. The nasal pressure transducer provided 95 $\pm$ 2% scorable data. Both inductance plethysmography belts and nasal cannula were well tolerated by the subjects.

Conclusions: Our preliminary findings suggest that the re-engineered inductance plethysmography belts provided crisp measurements of thoracic and abdominal movement, regardless of subject position. Pressure-derived airflow signals provided stable and consistent measures of airflow activity occurring at the nares. These results warrant in-depth side-by-side evaluation of these technologies against current respiratory monitoring techniques.

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1008.R

The Maintenance of Wakefulness Test in Normal Healthy Subjects

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Introduction: The Maintenance of Wakefulness Test (MWT) examines an individual's ability to stay awake in an environment of decreased sensory stimulation. While this test is becoming more widely used, only one published study has systematically examined the test results in normal healthy subjects.

Methods: Data from forty-one normal subjects was collected as part of a Randomised Control Trial of treatment for mild Obstructive Sleep Apnoea. The normal subjects were randomly selected from the telephone directory within a 30-km radius of both the hospitals and were invited to participate via a telephone call. They answered a general screen for health complaints (respiratory, cardiovascular, and psychiatric disorders) and sleep difficulties (snoring, and periodic limb disorders) to create a group of healthy, good sleepers. Overnight polysomnography, and a MWT the following day, were performed on all subjects. Eleven had an AHI >10 and/or a BMI >40 and were excluded from the study. Therefore, analysis was conducted on 30 control subjects (age 48.7 + 9.6 (SD); 8 females) with an AHI of 4.6 + 3.1/hr (SD) and a BMI of 27 + 3.7(SD).

Results: The subjects' mean sleep latency to the first epoch of unequivocal sleep during the 40 minute trial MWT was 36.7 + 5.7 (SD) minutes. The lower normal limit, defined in previous studies as 2 standard deviations below the mean, was 25.3 minutes. The mean sleep latency was then calculated for a 20-minute trial duration with sleep latency defined as time to the first appearance of a brief sleep (10-second micro sleep or one epoch of any stage of sleep). This analysis produced a mean sleep latency of 18.6 + 1.9 (SD) minutes with a lower normal limit of 14.8 minutes.

Conclusions: These results are consistent with previously published normative data. However, the mean sleep latencies here are somewhat higher (3-6 minutes) than those previously reported. The subjects in this study were randomly selected from the general population. This sample may therefore be a truer representation of the normal population than in the previous study in which subjects were recruited via hospital advertisements and word of mouth.

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1009.R

Duration Of Sleep And Wake Stages Follow Principally Different Distribution Laws

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Introduction: Sleep fragmentation is evaluated by the number of transitions between sleep and wake stages. This does not really reflect the changes in sleep architecture. Therefore we evaluated the duration of sleep and wake stages statistically.
Methods: The duration of sleep stages grouped in wakefulness, light sleep, deep sleep and REM sleep originating from 39 recordings of normal subjects were taken to calculate distribution plots (number of occurance over duration of stage). These distribution plots were plotted using a single and a double logarithmic scale. When a linear decline was found in these distribution plots, a linear regression was used to calculate the slope.
Results: The distribution of all sleep durations revealed a linear slope in the single logarithmic plot. Therefore we combinded all sleep stages to one distribution with the same characteristics. The linear slope characterises an exponential law distribution. The slope for the distribution was tau=22 minutes for the characteristic time of sleep durations. The distribution of wake durations revealed a linear slope in the double logarithmic plot. This characterizes a power law distribution with an exponent alpha=1.3. Based on these distribution laws a model of sleep and wake state transitions could be formulated and proved to be successful.
Conclusions: The statistical analysis of sleep and wake stage durations did reveal completely different undelying mechanisms in the timing regulation. We assume that only different neurons can produce this different type of regulation. In our model we simulate the sleep wake transitions as a "random walk" between smaller sleep and wake states. In addition there is a bias towards sleep: if wake is found during sleep, then there is a high chance to fall asleep quickly. The longer the wake lasts the weaker the chance gets. The new model gives indications for further neuroanatomic research even if the results may be limited by the rules inherent to Rechtschaffen and Kales.

1010.R

Diagnostic Accuracy Of A Single Channel Nasal Pressure Recording In Patients Referred for Investigation of Sleep Apnea

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Introduction: Given the cost and resource limitations of polysomnography (PSG), the increasing clinical load of patients with OSA will necessitate simpler methods of diagnosis for clinical or population screening programmes. In order to determine the feasibility of such simpler methods, we investigated the applicability and reliability of a single channel recording (SCR) of nasal pressure analysed by an automated algorithm in patients with suspected OSA referred for a full PSG in the sleep laboratory.
Methods: Thirty-six consecutive patients (26 male, age 52±15 years, BMI 28.3 ± 6.7 kg/m2) undergoing a PSG investigation were analysed in two separate data sets by separate and blinded scorers. Eligible recording sessions were obtained from 33 subjects. The PSG recording included a standard montage ,including nasal pressure via nasal prongs (Compumedics, Australia). Signals were scored according to conventional criteria. The SCR consisted of the nasal pressure signal derived from the nasal prongs and fed in parallel into a separate device with a pressure transducer, A-D converter and data storage. Apneas ("A") and hypopneas ("H") were determined according to a specific in-house analysis algorithm. This algorithm evaluates aspects of the flow/pressure curve including amplitude and stability of the recording. The total number of scored "A", "H" and duration of events (individual and accumulated number). Index calculations were based on the total time in bed (lights-out to lights-on) minus self-estimated wake time after sleep onset. Two separate total count cut-offs, "low" (60 events) and "high"(80 events) were applied.
Results: Two out of the 33 (6.5%) SCRs could not be reliably assessed due to dislodgement of the pressure cannula. The SCR algorithm tended to slightly over score "A" and underscore "H" resulting in 24% overestimation of the total "A" + "H" events. There was also a 24% overestimation of the total duration of events. The correlation coefficients for the total "A" + "H" count and total event duration between the two methods were 0.93 and 0.92, respectively. Deviation was approximately similar over the range of severity (Bland-Altmann plot analysis). Assuming a PSG-AHI >=10 for OSA diagnosis 16 of the 31 evaluated patients fulfilled the diagnostic criteria. Using the low cut-off, the SCR algorithm identified all these cases and falsely predicted 10 additional cases. With the high cut-off positive prediction was 15/16 (missed case borderline) and falsely predicted 5 patients with PSG-AHIs of 3.2, 10.8, 5.4, 9.7 and 8.3 respectively. Thus, based on the higher cut-off value, sensitivity was 94% and specificity was 67 %.
Conclusions: OSA may be identified with reasonable accuracy using a single nasal flow/pressure recording. Such recordings subjected to automated analysis may prove useful as a well-tolerated and simple method for application in larger scale screening programs.

1011.R

Correlation of Actigraphic Measures Of Sleep Quality With Nightcap And Polysomnography In Diurnal Sleep Of Night Shift Workers

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Introduction: The objective measurement of diurnal sleep quality using polysomnographic recordings is not at all times practical in the study of the night shift worker. In this exploratory investigation, we consider the relationship of measured sleep characteristics to sleep parameters derived from wrist actigraphy data.
Methods: The day sleep of 12 night shift workers (7 women, 5 men; mean age ± SD: 41.1 ± 9.0 years) was recorded with the use of either the Nightcap method or an ambulatory method of polysomnography (HandySleep, Glonner, Germany). As a part of the experimental condition, the workers were given the instruction to remain in the dark and attempt to sleep for a single eight-hour period beginning two hours after the end of each night shift. Times in bed were recorded in appropriate logs, and workers rated the quality of diurnal sleep episodes in post-sleep questionnaires. Each worker wore an activity monitor (Actiwatch, Mini-Mitter, Bend OR) on the non-dominant wrist throughout the study duration, including during sleep periods. Our analyses included a total of 125 recorded sleep episodes, where 79 of these were derived from the Nightcap and 46 were from ambulatory polysomnography. All sleep episodes recorded by ambulatory polysomnography were scored in 20s epochs by a professional sleep technician. Actigraphic data were sampled at 1-min intervals with the exception of one subject whose activity was sampled at 2-min intervals. Sleep characteristics were based on an algorithm provided in the Sleepwatch software. From sleep episodes recorded simultaneously with the Nightcap and polysomnography, we previously determined that total sleep time (TST) and sleep efficiency correlated well between the sleep measurement devices ($r=0.623$, $p<0.001$ and $r=0.681$, $p<0.0001$). We therefore combined these measures for the comparison with those derived from the Sleepwatch software and sleep-wake logs. Non-parametric correlations were used to qualify the relationships.
Results: Mean TST (± SEM) as determined by the Sleepwatch software was 394.0 ± 14.8 minutes. This method of measurement correlated significantly with that of polysomnography and the Nightcap ($r=0.72$,

p<0.0001) where mean TST by these methods was 416.9 ± 12.8 minutes. Actigraphic measures of TST also correlated significantly with sleep quality (r=0.36, p<0.001). Mean sleep efficiency measured by actigraphy ranged from 68.3 to 90.9%, while these values ranged from 70.2 to 99.1% when measured by polysomnography and Nightcap. Sleep efficiency measured by actigraphy did not correlate significantly with polysomnography and Nightcap (r=0.03, p=0.7) or with sleep quality (r=0.16, p=0.1).

Conclusions: The usefulness of actigraphy as an ambulatory measure of sleep duration (but not sleep efficiency) has been previously described in laboratory and field studies, and is supported by our results. Our data is limited by the use of the Nightcap device instead of polysomnography recording in a significant subset of our study. Nevertheless, they represent data collected in the field from shift workers sleeping at a variety of circadian phases.

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1012.R

A Statistical Procedure to Classify Pattern Configurations from Electrophysiological Sleep Recordings

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Introduction: Sleep staging is the most widely applied procedure to analyze polygraphic sleep recordings. The procedure requires the comparison of a given segment (epoch) of the record with a limited set of sleep stages. A main unsolved problem with sleep staging is the intra-state variability. There have been different approaches in the literature to break down sleep stages into more homogeneous sub-states, e. g. to allow a more fine-graded description of the transition from wakefulness into sleep, or to differentiate between tonic and phasic segments of REM sleep. In the present study a statistical classification procedure (Configural Frequency Analysis, CFA) was applied to sleep data. The method allows to extract typical pattern configurations from multidimensional contingency tables of categorial variables.

Methods: The CFA was applied to all night sleep recordings from eight normal subjects and three patient groups (insomnia, sleep apnea syndrome, narcolepsy; n = 8 per group). Digital sleep data were stored for later analysis and sleep stages were visually analyzed. Three additional parameters were computed from the recordings, (1.) the Alpha Slow Wave Index (A), i. e. the ratio of EEG alpha and slow wave activity, (2.) a continuous EEG parameter (E), and (3.) the Rest Index (R), a continuous measure, based on phasic EMG activity. Each of these variables was transformed into a binary variable by separating the distribution of all epoch values at the median. The combination of the three binary variables (AER) results in 8 different patterns (+++, ..., —-), whereby '+' means above and '–' below the median. The frequency of occurrence of the eight patterns was tabulated for each sleep stage. From these multidimensional contingency tables, the probability of occurrence of the AER patterns was computed by means of the CFA.

Results: Significant AER patterns appeared for each sleep stage. The +++ pattern was typical for wake and sleep stage 1, which had a second significant pattern (-++). Stage 2 had four typical patterns (+-+, +—, —+ and —-), none of them overlapping with stage 1e 1, but two of them with the stage 3 patterns +— and —-. Only one pattern was significant for stage 4 (—-). REM sleep had three significant patterns (++-, -++ and -+-), one of them (-++) overlapping with stage 1, but none with stage 2. 2.

Conclusions: The results suggest that mainly stages 2 and REM are inhomogeneous states which can be subdivided into meaningful sub-states. The diagnostic groups showed only minor differences in regard to significant patterns. The CFA analysis may be used as a filter procedure to define homogenous sub-states for computerized sleep analysis. Finally, the method can also be applied to other physiological signals than those used in the present study.

1013.R

The Use of the Sleep Assessment Questionnaire\copyright symbol\/ As A Measure Of Responsiveness To Nasal CPAP Treatment For Obstructive Sleep Apnea

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Introduction: The purpose of this study was to determine the value of The Sleep Assessment Questionnaire\copyright symbol\/ (SAQ\copyright symbol\/) in assessing changes in the sleep-related symptoms of sleep apnea patients, following treatment with nasal CPAP.

Methods: The SAQ\copyright symbol\/ is a 17 item self-rated validated questionnaire, with favorable sensitivities and specificities for the following six factors: insomnia, nonrestorative sleep, sleep schedule disorder, daytime sleepiness, sleep apnea, and restlessness1. In order to determine the value of the SAQ\copyright symbol\/ in assessing response to a standard treatment procedure, the SAQ\copyright symbol\/ was applied to a population of people who were diagnosed, by clinical assessment and polysomnography, with obstructive sleep apnea. These patients were selected from a database of 3370 patients who completed the SAQ\copyright symbol\/ on the nights of their sleep studies. Patients were entered into the study providing they fulfilled criteria for sleep apnea before treatment and reported in a CPAP Evaluation Form that they used nasal CPAP for a minimum of 1 month and at least 5 nights a week. Of the patients who completed the 392 CPAP Evaluation Forms only 52 patients (13 females, 39 males, mean age = 49.9, s.d. = 11.1) fulfilled criteria. The mean respiratory index at baseline was 46.3 (s.d. = 26.64) and 14.9 (s.d. = 13.3) post treatment. Paired t-tests were used to compare pre and post treatment SAQ\copyright symbol\/ total and factor scores.

Results: SAQ Factors Mean Pre SAQ Scores Mean Post SAQ Scores T df PTotal SAQ 25.8 19.8 4.330 32 <0.0005Insomnia 7.2 6.0 2.723 45 0.009Non-restorative Sleep 6.2 5.1 3.585 45 0.001Sleep Schedule Disorder 1.7 2.2 1.062 42 0.294Daytime Sleepiness 2.8 2.1 2.410 47 0.02Sleep Apnea 4.2 2.5 3.975 49 <0.0005Restlessness 1.9 1.5 1.662 48 0.013Statistically significant changes were found for improvement in the Total SAQ\copyright symbol\/ score and Insomnia, Non-restorative, Daytime Sleepiness, and Sleep Apnea factors of the SAQ\copyright symbol\/.

Conclusions: The SAQ\copyright symbol\/ is a favorable, brief assessment tool for assessing treatment response to nasal CPAP in patients with sleep apnea who use the treatment faithfully for at least one month. Such patients report overall improvement, specifically in self-ratings of insomnia, nonrestorative sleep, daytime sleepiness, and sleep apnea factors.

1014.R

Laboratory and Home Validation of a Portable Unattended Sleep Recorder, Using Automatic Analysis

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Introduction: Ambulatory / Home recorders are being used to facilitate the diagnosis of Obstructive Sleep Apnea Syndrome (OSAS). The Watch_PAT 100 Device is a patient-applied, unattended home recorder intended to diagnose OSAS. The 4-channel device is based on the recording of Peripheral Arterial Tone (PAT) from the fingertip. By using automatic algorithms it detects respiratory events and allows an analysis

of sleep/wake state. The respiratory disturbance index (RDI) and the Sleep Time of the device were evaluated against standard in-lab polysomnography (PSG). In addition, the diagnostic reliability for an unattended home use was assessed.

Methods: Fifty-six subjects with suspected OSAS were evaluated at two sleep centers, 20 in Winnipeg, and 36 in St Louis (61% male, age 44.4 ± 9.9 years, BMI 34.9 ± 9.6 kg/m2). The subjects underwent in-lab simultaneous Device and PSG recording, and Device data was additionally collected at home on 51 of the subjects during an unattended ambulatory study. PSG data were manually scored using standard criteria for sleep stages, and respiratory events. Device RDI (PRDI) and Device Sleep Time were scored and calculated automatically using a proprietary software algorithm. Data analysis includes: in-lab PSG versus Device RDI and Sleep Time, in-lab PSG RDI versus Home Device RDI. Various PSG RDI values were tested as 'cut-off' values in the ROC analysis. Correlations are reported with Pearson r, standard error of estimate (SEE), and the p value. Area under the receiver operator characteristic (ROC) curve is expressed as a fraction, along with 95% Confidence Intervals (95%CI).

Results: RDI data was evenly distributed over a broad range (0 - 138 events/hr). The PRDI was highly correlated to PSG RDI (r=0.87, SEE=9, p<0.0001). The area under the ROC curve was 0.92 [95%CI 0.85-0.99], 0.95 [95%CI 0.89-1.00], and 0.91 [95%CI 0.84-0.98] for PSG RDI cutoff values of 10, 15 and 20 events/hr, respectively. PSG sleep time and the Device sleep time were highly correlated (R=0.77, SEE=66, p<0.0001). For a PSG RDI value of 15 event / hour of sleep defining 'positive', the maximum sensitivity and specificity for the Device was achieved with a device cutoff value of 22 events / hour (Sensitivity 85.7%, Specificity 95.2%, Positive Predictive Value = 0.97, Negative Predictive Value = 0.80). Home Device PRDI data were reasonably correlated with in-LAB RDI (R=0.70, p<0.0001). Home device studies were successfully collected in 91.4% of recordings. Unsuccessful studies were due to either technical issues, or an insufficient period of valid sleep time recorded on the Device.

Conclusions: The Device offers a simple, accurate and reliable tool for in-home, unattended detection of sleep disordered breathing events, and reporting of RDI.

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1015.R

Information Cost Function Analysis of Neonatal Sleep States

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Introduction: Various time-series techniques are used to categorize and model observed systems. The prediction of the short-term evolution of a dynamic system can be achieved in such a way that captures features of its longterm behavior. One specific method, information cost function (ICF) is a specific time-series analysis strategy which can be used to analyze sleep behaviors. In past research, ICF was used to analyze physiologic time-series of sleep behaviors to help differentiate individuals who have sleep apnea from a normal group despite no discernible differences on the visual analysis of their sleep recordings.

Methods: ICF is a signal processing method that is based on Shannon's theory of information, applied to the wavelet decomposition of a signal. This particular method of time-series analysis uses wavelet transforms to analyze complex data sets of signals. This method was applied to neonatal EEG/polysomnographic information to evaluate its usefulness as a sleep state detector and to differentiate two clinical groups who were clinically at risk for neurodevelopmental sequelae.ICF was estimated at one-minute intervals for 7 neonates with respect to specific state assignments by an experienced neonatal polysomnographer. ICF was also applied to two large datasets comparing a healthy neonatal cohort with a medically at risk cohort.

Results: Significant correlation coefficients were noted between various trend estimates for 7 neonatal patients regarding three pairs of datasets: ICF/breathing rhythm .44, ICF/tracé alternant quiet sleep .38 and tracé alternant quiet sleep/breathing rhythm .63. In the second set of analyses, the healthy cohort was found to have significantly different means from the clinically at risk cohort based on ICF analyses. Using a Satterwaite modified T-test for unequal variances, the ICF correlated with age for the medically at risk group (p < .0001, N=270), while there was borderline significance for the healthy group (p=.08, N=106).

Conclusions: We have previously published on a time-series analysis strategy that relies on feature extraction to recognize tracé alternant quiet sleep in healthy newborns. Results from the present study utilizes a different time-series analysis strategy that predicts both neonatal sleep state transitions and cohorts who are medically at risk. Future studies will compare various methods of time-series analyses with respect to feature extraction and state prediction to better anticipate brain organization and maturation for cohorts with medical illnesses.

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1016.R

Snapshot Actigraphy for Sleep Quality

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Introduction: Actigraphy, the measure and epoch-by-epoch analysis of wrist activity, is commonly used as a measure of sleep efficiency. Because of the complexity of download and PC algorithm analysis, actigraphy has been primarily utilized as a research, rather than clinical, tool. This study compared sleep efficiency, as determined by epoch-by-epoch analysis of activity, with simpler measures of total and hourly averaged activity.

Methods: Data from a previous NIH-funded study were re-examined. The sample was comprised of 9 normal controls, 8 persons with Insomnia, and 10 persons with RLS. A board-certified sleep specialist evaluated all participants. For the study, each person wore an actigraph on the wrist in addition to undergoing a standard PSG evaluation for one night. The actigraphy data were downloaded and analyzed using the device's standard software package. Comparisons were made for sleep efficiency, total activity for the sleep period, and average activity per hour. Duration of sleep was also included in the analysis. A series of one-way ANOVAs were conducted to examine differences between groups of participants, and correlations were completed with the variables of interest.

Results: PSG data indicated that duration of the sleep period was statistically equivalent for all groups. Groups were significantly different in expected areas: for sleep efficiency, controls (mean= 0.89, s.d.=6.14E-02) were significantly higher than both insomnia (mean= 0.63, s.d.=8.25E-02) and RLS (mean=0.67, s.d.=0.15) participants. For Total Activity, controls (mean=1606.78, s.d.=779.49) were significantly lower than RLS (mean=3466.25, s.d.=1245.85) but not Insomnia (mean=2648.33, s.d.=653.64) participants. For Average Activity per Hour, controls (mean=229.38, s.d.=107.79) were significantly less than RLS (mean=499.39, s.d.=260.53) but not Insomnia (mean=378.74, s.d.=103.45) participants. Insomnia and RLS participants were not significantly different on any measure.Diagnosis was observed to be correlated with sleep efficiency (r=0.592, p<0.01), total activity (r=0.62, p<0.01), and average activity per hour (r=0.56, p<0.01). More importantly, activity was also significantly correlated with sleep efficiency: average activity and sleep efficiency were associated (r=-0.68, p<0.01), but the stronger association was found between average activity per hour

and sleep efficiency (r=-0.74, p<0.01).
Conclusions: The goal of this study was to determine whether simple measures of activity, without undergoing PC download and analysis, could accurately approximate sleep efficiency. The results indicate that total activity, and especially hourly averaged activity, accurately approximates sleep efficiency. A sleep profile constructed from hourly averages of activity could be considered a measure of sleep quality, since activity occurring in each hour of sleep is not affected by duration of the sleep period. Future goals are to develop an actigraph designed for one-night testing that would display a "snapshot" score of sleep quality. This may be useful for clinicians, who require a less complicated and cost-effective tool to measure sleep quality.

1017.R

Nonlinear Dynamical System Analyses of Neonatal Sleep State

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Introduction: Progress in mathematical modeling of nonlinear dynamical systems can provide novel methodologies for the study of biologic time-series such as sleep-wake cycling. While specific algorithms function as feature extractors to identify when state changes occur, other signal processing tools can more eloquently describe the process by which a complicated system operates which will lead to sleep state transitions. Correlation dimension (CD) is an estimation strategy that has been used to analyze the dynamical properties of the time-series of EEG activities during adult sleep and epileptic seizures. Changes in correlation dimensions are estimated from the time-series EEG data which can predict these novel events.
Methods: Our neonatal sleep research consortium applied the CD to the time-series of a single channel of neonatal EEG for one healthy preterm compared with one fullterm neonate. Two 3-hour EEG-sleep studies were annotated by an experienced neonatal polysomnographer who identified neonatal EEG-sleep states. Forty epochs of 4 minutes each were identified from which the CD was calculated to estimate the process by which state changes would occur.
Results: Preliminary findings indicate that the CD dimensions correlate positively with sleep state alterations for both neonates. Based on a T-test analysis the estimated dimension changes vs. sleep state was calculated, for preterm infant with $p < .0001$, and for the fullterm neonate was at $p < .07$.
Conclusions: While certain algorithms function simply as feature extractors, other algorithms such as CD provide an understanding of the process by which neuronal aggregates function to predict a state change. Our preliminary analysis suggests that state changes can be predicted in two neonates with greater reliability at the more immature gestational age for this small pilot group. Future studies will investigate changes in CD for a larger neonatal cohort at successively older gestational ages, and in the context of medical illness; CD may serve as an important functional measure of brain maturation or encephalopathy.

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1018.R

Are Current MSLT Termination Criteria Ending Naps Prematurely?

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Introduction: The multiple sleep latency test (MSLT) has two vital functions. First, it provides an objective measurement of physiological sleepiness; and second, the presence of two or more naps with rapid eye movement (REM) sleep supports a clinical suspicion of narcolepsy. The American Academy of Sleep Medicine (AASM) MSLT criteria dictate that naps end at precisely 15 minutes of recording time after sleep onset. Although this "15-minute rule" will provide a good measurement of sleepiness, we hypothesize that naps often are terminated prematurely (prior to REM onset) and may decrease sensitivity in identifying potential narcoleptics. Indeed, 15-25 percent of narcoleptics with cataplexy do not show two or more naps with REM sleep using similar termination criteria. Since narcoleptics typically have fragmented sleep, our Institute terminates the MSLT after 15 minutes of total sleep time (TST), often extending the nap several minutes beyond the AASM "15 minute rule" because of intervening wakefulness.
Methods: A total of 194 consecutive MSLT's were analyzed from 1999 through 2001 at our Institute. Naps were terminated after 20 minutes if no sleep occurred or after 15 minutes of TST; however, to prevent extended nap lengths, a nap was terminated prior to 15 minutes of TST if an awakening of at least one minute and 20 minutes of total wake time had transpired. Data were analyzed to compare sensitivities of REM sleep detection using the two different nap termination criteria.
Results: Nap durations were an average of 3.3 minutes longer using our revised nap termination criteria with respect to AASM criteria (25.4 min. vs 22.1 min., p<0.001). A total of 106 patients (54.6%) demonstrated at least one REM period on the MSLT; and of this group, at least one REM period would have been missed in 24.5% (26 patients) using the AASM criteria. Moreover, of all patients demonstrating at least two REM periods using our termination criteria, 16.4% would not have met the two nap minimum for a presumptive diagnosis of narcolepsy using AASM guidelines. Finally, at least one REM period would have been missed in 16.7% of all narcoleptics with definite cataplexy, and in 8.3% not making the two nap minimum, had the AASM criteria been used to define nap termination.
Conclusions: Classic cataplexy is often difficult to elicit by history, even in patients with a high clinical index of suspicion for narcolepsy. The MSLT is, therefore, an important diagnostic tool for identifying potential narcoleptics, a population typically demonstrating fragmented sleep. By minimally increasing the average nap duration, these data suggest that our nap termination criteria significantly increase the sensitivity for REM sleep detection by allowing 15 minutes of TST, compared to the AASM criteria which strictly terminate the nap 15 minutes after the first epoch of sleep. We suggest that nap termination criteria be revised to increase sensitivity of REM detection.

Research supported by Ohio Sleep Medicine and Neuroscience Inst.

1019.R

Activity-Guided Timing for Bright Light Therapy

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Introduction: When timed properly, bright light therapy shifts the circadian pattern. Exposure to light before Circadian Time (CT) Zero (0) induces a phase delay, while exposure to light after CT 0 induces a phase advance. This study utilized activity, as measured by a wrist-worn actigraph and analyzed with Fast-Fourier Transforms (FFT), to estimate CT. Activity minimums guided the timing of bright light exposure to produce a phase advance. The times of activity minimums and Dim Light Melatonin Onset (DLMO) were compared.
Methods: Four normal controls participated in a four-week study. Throughout the study, participants wore an actigraph and completed sleep diaries. At the end of a 2-week baseline period, a Dim Light Mela-

tonin Collection (DLMC) protocol was completed: participants remained awake and in dim light (<50 lux) from 15:00 to 2:00; saliva melatonin samples were collected hourly from 19-22:00, then every half hour until 2:00. Samples were immediately placed in tubes and refrigerated. The actigraphs were downloaded and data were analyzed using FFT to estimate CT 0. Participants were given a light box, instructed in its use, and told to sit for one hour each day in front of the box, beginning as close as possible to CT0 + 4 hours (translated by the researchers into standard time for the participants). At the end week 3, participants returned to the lab, and the actigraphs were downloaded. Once again, the activity data were analyzed using FFT, and a new therapy start time (CT 0+ 4 hours) was assigned to the participant. At the end of week 4, participants underwent a final DLMC protocol. The timing of melatonin onset, determined by analysis of the salivary samples, was compared to the activity minimums to determine the relationship between activity and DLMO phase.

Results: Both DLMO and activity minimums indicated a phase advance of about one hour, with correlations between the two variables ranging from 0.64 to 0.95. Correlations between the DLMO and activity minimums at baseline and after light treatment ranged from to 0.88 to 0.95. The standard deviations of the activity minimums were about 0.7/hr, which is comparable to those reported for core body temperature (s.d.=0.78/hr) and cortisol (s.d.=0.65/hr)*.

Conclusions: In this study, activity adequately estimated CT and successfully guided the timing of bright light exposure. Future research will examine the utility of activity-guided light therapy on individuals with circadian disorders.*Klerman, E.B., et al.(2002). Comparisons of the variability of three markers of the human circadian pacemaker. J Biol Rhythms;17(2):181-193.

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1020.R

Comparison of Sleep Assessment Devices in a Mixed Sample of Sleep Disordered Patients

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Introduction: Although polysomnography (PSG) is the "gold standard" measure of objective sleep, it is a costly and burdensome procedure that is not feasible for many clinical and research applications. Methodologies such as actigraphy (ACT) and sleep logs (SL) are alternatives commonly used to provide estimates of sleep-wake parameters, and newer devices such as the REMView (RV; Respironics, Inc., Pittsburgh, PA) have become commercially available. However, data directly comparing various sleep assessment devices are lacking. The present study compared the performance of RV, ACT, and SL against PSG for estimating common sleep parameters in a sample of sleep-disordered patients.

Methods: Participants were 19 (17 male) VA primary care outpatients (Mage = 60.8 yrs., SD = 12.7 yrs.) undergoing screening procedures for an insomnia treatment study. Each participant underwent a clinical interview with the first author that included structured psychiatric (SCID) and sleep (SISD) interviews. Eligible participants were scheduled for one night of ambulatory PSG using the Compumedics P-Series Plus Sleep System. Participants slept unattended on the hospital lodging unit. On this night of PSG recording, participants also wore an Actiwatch-L (Mini-Mitter Co., Inc., Bend, OR) actigraph and the RV device. They completed an electronic Palm-Pilot sleep log the following morning. RV, ACT, and SL yielded estimates of time in bed (TIB), total sleep time (TST), total wake time (TWT), sleep onset latency (SOL), sleep efficiency (SE) and wake after sleep onset (WASO) that were subsequently compared to corresponding PSG-derived values.

Results: Nine patients were diagnosed with inadequate sleep hygiene, 6 with sleep apnea, 2 with periodic limb movement disorder, and 2 with insomnia associated with an anxiety disorder. Using DSM-IV criteria, 11 patients had at least one current or past Axis 1 psychiatric diagnosis; and 8 had no current or past psychiatric diagnoses. Spearman correlations between sleep devices were calculated and compared to PSG, and repeated-measures ANOVA with Dunnett's adjustment for multiple comparisons was used to investigate mean differences between PSG and the other devices. Correlations for TIB ranged from .82 – 1.0; means were not significantly different between recording devices. For the remaining sleep measures, ACT correlations with PSG ranged from .51 - .72; ACT significantly overestimated SE and TST and underestimated TWT and WASO. RV correlations ranged from .49 - .80; RV overestimated SOL and underestimated WASO. SL correlations ranged from .38 - .75; SL underestimated SE and TST and overestimated SOL and TWT.

Conclusions: Alternative sleep assessment methodologies show moderate to high correlations with sleep measures from PSG, yet the accuracy of different devices varies depending on the sleep parameter of interest (except for TIB, which is consistently measured by all devices). The new RV device performed as well as or better than ACT and SL in this mixed sleep disorders sample.

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1021.R

The use of Polyvinylidene Fluoride (PVDF) Film Airflow Sensors: An Alternative to the Air Pressure Transducer for Measuring Respiratory Events

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Introduction: The esophageal balloon is considered the ideal method for detecting respiratory effort in identifying sleep related breathing disorders (SRBD). The esophageal balloon is an invasive technique, so most sleep labs therefore use thermistors, thermocouples, or an air pressure transducer (APT) with a nasal cannula. APTs coupled with cannulas perform better than thermistors and correspond very well with esophageal balloons. However, a new device called a PVDF sensor is now available. It has a faster response time and greater sensitivity than conventional thermistors and thermocouples, and may present an attractive alternative to the cannula in sleep studies.

Methods: The esophageal balloon and APT with nasal cannula were utilized in order to evaluate the effectiveness of PVDF sensors. Eight individuals who had either symptoms of sleep apnea, or a previous diagnosis of sleep apnea, were included in the study (5 men and 3 women, ages 31-62). These individuals visited our laboratory on two occasions on the same day. In the late afternoon, the participants arrived and an esophageal balloon catheter was inserted into the mid esophagus. Later that evening, the participants returned for complete polysomnography with the addition of the PVDF sensor and the APT with cannula. A sampling of respiratory events across three different patients has been analyzed. First, two raters judged respiratory events, including both apneas and hypopneas. There were two criteria for an event to be considered a "true event": there had to be at least a 3% oxygen desaturation, and at least one of the three measures (PVDF sensor, cannula, or balloon) had to reflect that an event had occurred. Based on these criteria, 90 events were selected for analysis. Second, for each event, it was noted as to whether each of the three measures did or did not reflect the event. Both raters had to agree on all ratings or the event was thrown out.

Results: The PVDF sensor and the esophageal balloon had only a moderate agreement of 53%. Similarly, the APT with cannula vs. balloon showed 51% agreement. On the other hand, when the PVDF sensor was compared to the cannula, there was 84% agreement. Although it has been argued that the esophageal balloon is the gold standard, in our initial analysis it failed to detect many events that both raters agreed were

true events (see criteria above). Therefore, rather low agreement rates were shown for both the PVDF sensor and cannula vs. balloon. But there was good agreement between the PVDF sensor and cannula.
Conclusions: The PVDF film sensor appears to be an accurate device for detecting respiratory events, as compared to the APT with cannula. Only modest agreement of either the PVDF sensor or cannula with the balloon was obtained.

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1022.R

Making The Total Transition From Laboratory Based to Home Based Diagnosis and Treatment of Obstructive Sleep Apnea

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Introduction: Although laboratory-based polysomnography is still considered the gold standard, the benefits of making the transition to home-based diagnosis and treatment from current laboratory practice may far outweigh the possible reduction in diagnostic accuracy. Among the benefits of this transition include the ability to routinely screen for apnea in patients with congestive heart failure or medication resistant hypertension and the increased ease in treating the frail elderly for whom travel is problematic. The James A Haley (JAH) Veterans Hospital in Tampa FL. has detailed a five year plan to make the final transition to home-based diagnosis and treatment of obstructive sleep apnea, making the sleep laboratory nearly obsolete for OSA. This plan begins with an (ongoing) in-lab simultaneous study of portable versus standard polysomnography equipment, and ends with moderately–sized studies of auto-CPAP in the patients' homes. The completed transition also incorporates patient follow-up of all patients prescribed CPAP for CPAP compliance and efficacy. The authors will provide the details and status of the five-year plan.
Methods: At this initial study phase, the simultaneous study has been completed in five of the 24 patients to be enrolled. Patients underwent complete polysomnography including monitoring of central and occipital electroencephalogram (EEG), chin and surface anterior tibialis electromyogram (EMG) and electrocardiogram (ECG). Respiratory monitoring included nasal and oral airflow (thermisters), chest and abdominal respiratory movements and oxygen saturation by standard pulse oxymetry (SaO2). Data was simultaneously recorded by both portable and standard equipment(Medcare,Inc.). The interpretation and scoring of the portable data and standard data was carried out by two separate individuals. The scoring assignment (standard or portable) was based on a previously generated random schedule.
Results: The five patients (four male, one female) ranged in age from 48-80 years (mean=63). Average score on Epworth Sleepiness Scale ranged from 8-18 (mean score =12.2). Technicians reported good clear signals with no lapses in recording for five initial patients on the portable equipment, comparable to the standard equipment. Respiratory disturbance index (RDI) pairs (standard, portable) for the five completed patients were (1.7,3.9),(65, 56),(18,15), (10,18), (14,13). The interclass correlation coefficient (ICC) for the RDI was 96%. The ICC for minimum oxygen saturation was 85%.
Conclusions: The portable equipment appears valid for major parameters when used in a laboratory setting.

1023.R

Sleep Diary and Actigraphy Assessment in Adolescents Recovering from Substance Abuse

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Introduction: In many treatment outcome studies, it is not feasible or cost effective to use polysomnography. Often, actigraphy is used as an objective supplement to sleep diaries. Although there have been some reports comparing actigraphy to polysomnography, there are relatively fewer research studies comparing actigraphy and sleep diaries. Even less data are available for adolescents with sleep and daytime sleepiness problems. The data that has been reported indicates that there are some systematic differences between most if not all sleep variables between these two methods. This report is an examination of the relationship between baseline sleep diary data and wrist actigraphy on a range of sleep variables for adolescents who have been in treatment for substance abuse.
Methods: The 25 participants (15 males and 10 females) ranged in age from 14-18 years old, described themselves as having persistent trouble falling asleep, staying asleep or experiencing daytime sleepiness. Participants were asked to complete a daily 11-item sleep diary every morning and wear a wrist actiwatch every night for a minimum of seven consecutive days. Participants were asked to wear a wrist actiwatch from the time of getting into bed until time of getting out of bed. Corresponding actigraphy sleep measures were obtained and scored using the default scoring algorithm sensitivity settings of the Minimitter software package. Analyses only included data from days when both sleep diary and actiwatch were available. Compliance with data collection was a problem with this sample and approximately 50% of the data for any specific day was incomplete.
Results: To evaluate the relationship between diaries and actigraphy on sleep variables, two-tailed Pearson Product correlation coefficients were calculated across-subjects for each of the seven baseline days. This produced seven correlations for each measure. The mean correlations were: sleep latency ($r = .213$, $p < .10$), wake after sleep onset ($r = .268$, $p < .05$), number of awakenings ($r = .191$, $p < .10$), time in bed ($r = .826$, $p < .001$), total sleep time ($r = .644$, $p < .001$), and sleep efficiency (.159, ns).
Conclusions: The results of this study are consistent with previously reported data comparing sleep diaries and actigraphy with insomniacs. There were small positive correlations for sleep latency, WASO, and number of awakenings and strong positive correlations for time in bed and total sleep time. These findings extend the utility of including actigraphy as a supplementary objective measure to adolescents with sleep problems. Compliance with assessment procedures remains a major issue with this population and caution in interpreting the generality of the results is warranted.

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1024.R

Active Cushion Technology Improves Mask Sealing Characteristics

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Introduction: Difficulties with mask comfort and leak are among the most common problems reported by CPAP users. One of the most important qualities of a mask is the ability to achieve a seal. Masks which maintain a seal with the least headgear tension are more comfortable. The ability to maintain a seal under displacing forces will deter-

mine the number of adjustments that will be required, and therefore the number of disturbances occurring during use. A recently developed mask utilises an active cushion technology to automatically minimize leak and improve comfort. The aim of these experiments was to compare the ability of the new mask with currently available masks, to achieve and maintain a seal under a variety of conditions.

Methods: A sample of 20 patients was selected, including a diversity of facial shapes and ethnic backgrounds, from the Vancouver Sleep Disorders Center database. Four masks were compared in the experiment: Fisher & Paykel Acclaim (Acc); Respironics Profile Lite (PL); ResMed Ultra Mirage (UM); and ResMed ACTiva (ACT), with each subject being fitted with the optimal sized mask from each of the four ranges. Two different tests were conducted with subjects lying down wearing the masks inside a specially designed head box. A flow generator supplied mask pressure of 10cm, and leak measured using a pneumotach in the circuit. The minimum strap tension required to achieve a seal at 10cm pressure was determined by gradually reducing tension (300g of weight hanging from the bottom straps of the mask) until a leak was detected. A further 50 grams was added to this minimum and was used as the baseline tension for remaining tests. The second test involved loosening the lower strap of the headgear in 3mm increments to measure the amount of deviation that could be tolerated from the original strap setting.

Results: Leak flows of greater than 0.1L/sec were designated positive and data are presented as the probability of the mask leaking. ACT and UM required less tension than Acc or PL to achieve a seal (Fig 1). Figure 1. ACT showed significantly better seal maintenance with lengthening of the headgear straps (Fig 2).

Conclusions: The ACT mask demonstrated a superior ability to achieve a seal than the other masks tested. The ability to maintain a seal was also superior despite the headgear tension being on average considerably less than the other masks that were used as a comparison. These differences in mask sealing characteristics may have a positive impact on patient comfort and sleep quality when using CPAP.

Research supported by ResMed

1025.R

Comparison Of A New Combination Airflow/Snoring Sensor To Nasal Prong Pressure

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Introduction: A device has been recently introduced that may combine desirable attributes of both thermal and nasal prong pressure (NPP) means of flow sensing. The device (Dymedix Corporation, Minneapolis, MN) utilizes polyvinylidene fluoride film (PVDF) to create a sensor that has very low thermal mass. The sensor purports to have the fast response time of the NPP, while retaining linearity. It also purports to detect snoring events from the nasal / oral airflow placement site. The purpose of this study was to compare the differences in respiratory event identification between the PVDF sensor and nasal prong pressure, as well as to compare the snoring information derived from this combination nasal airflow/snore sensor and a 'conventional' neck placed piezo vibration sensor.

Methods: 40 patients scheduled for routine polysomnographic testing for sleep-disordered breathing were evaluated with both a PVDF airflow/snoring sensor and nasal cannula (Pro-Flow, Pro-Tech Services). Sampling was during baseline acquisition, not during NCPAP therapy. Filter settings: Airflow: 0.01 Hz– 15Hz. Snore: £ 10 Hz to ≥ 120 Hz, sampling rate ≥ 200 samples/sec. Each patient had the PVDF sensor applied first, with the nasal cannula placed over it. The signal coming from the PVDF sensor for snoring data was recorded simultaneously with a second "conventional" piezo movement sensor placed on the patient's neck, resulting in two separate snore channels. Physiological Events used for Comparison:- Apnea: 80 – 100% reduction in waveform amplitude with 10 second or more duration.- Hypopnea: 20 – 80% reduction in waveform amplitude, 4% SAO2 desaturation with 10 second or more duration- Snore event

Results: The data indicates that the PVDF airflow sensor revealed many respiratory events consistent with hypopneas, which were presented by NPP to be apnea. PVDF and NPP provided nearly identical results for the sum of apnea and hypopnea events. Ratios of scored events (PVDF/NPP): Apnea - 0.43*, Hypopnea - 3.51*, Total Respiratory Events – 0.97, Apnea Hypopnea Index (AHI) - 0.67*, Snore – 1.13. * statistically significant by paired t-test at $p<0.01$)

Conclusions: While total respiratory events were virtually the same, NPP "over scored" apneas in most cases as compared to the PVDF sensor, most likely due to its non-linearity. The PVDF sensor appears to be more sensitive to the patient's oral/nasal airflow than NPP and will likely more accurately differentiate between true apnea and hypopnea. A comparison of the wave shapes suggests that the sensitivity of the PVDF sensor may be advantageous to the clinician as a non-invasive method of detecting and displaying very subtle, mild changes in respiratory patterns (i.e. flow limitation), as well as respiratory patterns associated with more frank obstructive events as compared to NPP. The snoring information obtained from the PVDF sensor compares well with the piezo ceramic neck sensor.

1026.R

Reproducibility of Short Verses Long-Duration Heart Rate Variability: Implications for Obstructive Sleep Apnea Research

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Introduction: Heart rate variability (HRV) has been used to evaluate cardiac autonomic function in obstructive sleep apnea patients by measuring variations in electrocardiographic R-R intervals between cardiac cycles. Traditionally, HRV has been measured using long duration sampling intervals, however recent methods have been devised to acquire the data with brief periods of data collection. Controversy exists concerning the potential for brief sampling intervals to yield reproducible measures of HRV. The purpose of this study was to compare the reproducibility of HRV data obtained by an 8-hour data daytime collection interval versus a brief (512 cardiac cycles) sampling duration.

Methods: Thirteen apparently healthy volunteers (age = 41 $\pm$ 7.8 years, BMI = 29.5 $\pm$ 4.6) participated in this study. Each subject performed two HRV trials on separate days with a Cardiovit AT-10TM (Schiller AG, Baar, Switzerland) using a data collection interval of 512 cardiac cycles. Subjects rested quietly in the supine position, while wearing headphones from which an auditory cue was provided to pace respiration at 10-12 breaths/min. On each day, subjects subsequently performed an 8-hour HRV trial (recorded during waking hours) in which subjects wore a small battery powered single-lead ECG recorder. After correcting the data for ECG artifact and extrasystoles, HRV was analyzed as the standard deviation of all normal R-R intervals (SDRR). Pearson correlations were performed for SDRR for each device between days and between devices for each day. Paired t-tests were performed to test mean heart rate between days and devices.

Results: Within-instrument correlations were high between days for SDRR for both the Schiller ($r = 0.71$, $p=0.007$) and 8-hour ($r = 0.68$, $p=0.011$) devices. In contrast, correlations were low for Schiller versus 8-hour SDRR measurements in day 1 comparisons ($r = -0.003$, $p=0.99$), as well as day 2 ($r = -0.33$, $p=0.27$). Group mean RR intervals between days were not significantly different for either Schiller (mean RR interval = 910 ms versus 894 ms; $p = 0.61$) or 8-hour devices (mean RR interval = 708 ms versus 680 ms; $p = 0.24$); however, mean RR interval was

different between devices for day 1(p = 0.001) and day 2 (p = 0.001).
Conclusions: Time domain HRV analysis, using long or brief sampling intervals, were found to be reproducible from day to day, however these different methods were found to give disparate results when compared to each other. This suggests that HRV measured during a brief office visit differs from HRV measured during an extended monitoring period of wakefulness. More research needs to be done to determine the combination of HRV measures and methods that have the most utility in evaluating autonomic function in obstructive sleep apnea patients.

1027.R

The Relationship Between Pupillography And The Subjective Assessment Of Sleepiness With The Stanford Sleepiness Scale

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Introduction: The use of pupillography as an objective and time-saving method to measure daytime sleepiness is increasing continuously. Reports referring to the correlation between objective assessments of sleepiness by pupillography and subjective ratings such as the Stanford Sleepiness Scale (SSS) vary across studies. The aim of the present study was to investigate the correlation between the objective assessment of sleepiness by pupillography and the self-assessment of sleepiness by means of the Stanford Sleepiness Scale in sleep-deprived subjects, healthy non-sleep-deprived individuals and hypersomnic patients.
Methods: Data from 23 sleep-deprived healthy subjects, 28 healthy subjects after a normal night's sleep and 21 hypersomnic patients entered the analysis. Sleep deprived individuals underwent pupillography and subjectively assessed sleepiness every two hours during sustained wakefulness in an experiment lasting from 9 p.m. to 11 p.m. the following day. Healthy subjects had no history of sleep disturbance and were examined once between 9 a.m. and 12 a.m. after a normal night's sleep. Hypersomnic patients were examined every two hours from 9 a.m. to 5 p.m. after a night in the sleep laboratory. Spontaneous pupillary oscillations were recorded by means of infrared video pupillography for a duration of 11 min. and Pupillary Unrest Index (PUI;mm/min) was used. Comparisons of the groups are based upon measurements at 11 a.m. while intraindividual variations refer to the respective measurement times in each group.
Results: Correlation between PUI values and SSS proved not to be significant in any of the three groups. However, the correlation was positive with r=.30 for sleep-deprived subjects and r=.27 for normal controls, whereas for hypersomnic patients correlation turned out to be negative (r=-.42). By contrast, mean intraindividual correlation between PUI and SSS over the time course of the experiment was positive in hypersomnic patients (mean r=.21) with 7 out of 21 patients showing a negative relationship between SSS scores and PUI values. Spearman correlation coefficients ranged from -.95 to .95. For sleep-deprived subjects intraindividual correlation over the time course was positive (mean r=.51). PUI and SSS correlated significantly in 10 out of 23 individuals ($p<0.05$), Spearman correlation coefficients ranged from .15 to .85.
Conclusions: Like in other studies spearman correlation coefficients were between .2 and .4 in normal subjects as well as in sleep-deprived subjects. In contrast to previous findings correlation was not significant. Furthermore, correlation was found to be negative in patients suffering from hypersomnia. Intraindividual correlation between PUI and SSS was lower than suggested by other studies. The reason why patients suffering from excessive daytime sleepiness show a negative relationship between subjective and objective sleepiness remains unclear. Lack of adequate self-perception or the misinterpretation of symptoms of fatigue and tiredness as sleepiness might be one explanation. Another explanation may be that, the higher the level of sleepiness and/or the higher the subjective distress resulting from suffering from a sleep disorder, the less accurate subjects are in estimating their sleepiness level.

1028.R

An Automatic Sleep-Scoring Program Using Multiple Dimensions of Input Criteria for a Variety of Data Acquisition Platforms

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Introduction: The growth of bioinformatics in sleep research can be enhanced with a universal platform for scoring sleep?waking states accommodating a variety of binary file formats for electroencephalogram (EEG), electromyogram (EMG) and/or other biopotential signals. In an initial effort at developing such a universal platform, we took power spectral density parameters of frontal-parietal EEG and time-integral squared amplitude of the nuchal EMG and incorporated them into the Matlab program, which reads binary files at recording?defined digitization rates. Data collected with different digitizing boards were run through the autoscore program to establish its versatility across most recording platforms.
Methods: 7 male F344 rats age 4-5 months (Simonsen Labs, Gilroy, CA) were implanted under sodium pentobarbital anesthesia with 2 nuchal EMG and 3 screw electrodes leads over the frontal and parietal cortices. After 1 week of recovery from surgery, they were housed on a 12/12 light dark cycle and recorded 23 h/day for 10 days. EEGs were analyzed in 10-second epochs using a Fast Fourier Transform in Matlab. The power spectral density of each epoch was estimated using Welch's averaged periodogram method. It was post-averaged in three different frequency bands: delta (0.4-4.0 Hz), theta (5-10 Hz) and sigma (11-14 Hz). The Hanning window used in the method helped to reduce large fluctuations in bias and variance of the periodogram, while post-averaging helped to improve the spectral resolution. Epochs of EMG, Delta/Theta and Sigma*Theta power (as used by Benington, Kodali & Heller, 1994) were displayed on a three?dimensional graphical user interface (GUI). The 3-D scatter plot could be rotated to visualize the distribution of power across epochs for the determination of thresholds for the respective axes. The state of sleep was distinguished from waking when EMG was below threshold. When the Delta/Theta ratio was below threshold, REM sleep was differentiated from Quiet sleep. When Sigma*Theta was low higher than threshold, the waking state was scored. When Sigma *Theta and EMG were zero, the unhooked state was assigned. Behavioral states of active and quiet waking, quiet sleep, and REM sleep were also hand?scored, using sleepscorer, also created in Matlab, and each epoch was compared to the autoscored record for validation. Autoscored and manual scoring summary results for total time in each state as well as number of episodes and episode length were compared during baseline and REM deprived day/night conditions.
Results: An 88-90% agreement rate was confirmed between the autoscored and manual scored records. The number of REM episodes were 97% in agreement.
Conclusions: This program provides a reliable method for automatically scoring sleep states from data digitized by a variety of preexisting platforms. Inclusion of logical limiters for state determination should increase the accuracy of state determination.

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1029.S

Sleep Model to Predict Active and Passive Performance

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Introduction: Sleep is one of the essential requirements for human life. Like air, water, and food, sleep renews and sustains body functions, strengthens the immune system, and improves mental alertness and performance. Unfortunately, many people under appreciate the value of sleep and mismanage their life. Both high school and college students

seem to have difficulty in understanding the importance of sleep. Academic performance suffers and sometimes death occurs from traffic accidents. A need, thus, exists to provide tools to educate people about the importance of sleep management.

Methods: In 1993, a computer program GREG (Grade Requirements Evaluation Game) was developed to predict grade point average in college as a function of study and time management, teaching styles, prior learning, and other inputs to the teaching-learning system.A sleep component was added in 1998. Data were obtained from reviewing various sleep papers, and mathematical equations were developed to describe various sleep components. A total of 12 equations were developed to describe the various processes.From these equations, active and passive performances were predicted. Active and passive performances were used as efficiencies to adjust the various components in the learning model. An independent sleep model was later developed with expanded functionality. Each equation in the model was tested with non-linear regression techniques to determine R-square values and significance level. Significance levels were also adjusted to deal with any data sets with clustering.

Results: A mathematical model has been developed to predict the growth or decline in sleep debt and to predict performance such as active and passive learning. The model includes the effects of circadian cycle and shifts the cycle in response to jetlag (either west or east) or shift work. The model predicts the length of sleep needed as a function of age and adjusts REM sleep in response to sleep length, and alcohol and caffeine levels at the beginning of the sleep period. Passive performance is enhanced by caffeine. Both active and passive performance functions are reduced as alcohol levels increase. The model works for total or partial sleep loss events. The model also predicts the time to fall asleep as a function of time of day and sleep debt. Severe sleep debt reduces the time to fall asleep to about the duration of a red traffic light. The combination of sleep debt and alcohol severely reduces all types of performance. A website is under construction and is currently functional to allow people to see the effect of sleep management on performance. Severe changes in sleep debt, sleep cycle, or both take three to five weeks to reach new steady-state patterns.

Conclusions: The sleep model has become one of many useful tools that the College of Engineering uses to help students. Doctors at the Student Health Clinic now sometimes send students to Engineering to learn how to better manage their sleep.

1030.S

Self-HelpActivities by the Patients of Hypersomnia via Internet

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Introduction: In Japan, some of the patients with various types of diseases have been developing self-help activities by independently organizing groups or leagues of patients (Watt1984,Hosaka2001). In recent years with the remarkable development and progress of Internet (IT), many of these groups have their own home pages (HP) on IT. The patients with sleep-wake disorders are able to obtain a lot of information from IT now. In the present article, we report a web site operated and managed by a patient of narcolepsy.

Methods:

Results: DETAILS OF HP HP name is Quatre Saisons (QS).The person in charge of the HP is a 28-year-old woman, who was diagnosed as narcoleptic. Time of opening HP: April 20, 1999. Major contents of HP:- Diaries of the person who opened HP; - Explanations on narcolepsy with illustrations to facilitate understanding; - Medical history of the HP opener; - Bulletin board: a bulletin board on sleep and arousal disorders and a bulletin board to which the details of other diseases are to be added. Number of accesses from the time of opening the HP up to March 15, 2002: 105,804. Some patients were motivated by this HP to receive medical examination. In the bulletin board where the details on sleep and arousal disorders are discussed under the principle of "Let's solve the problems together", the patients are willingly writing their opinions, while there are also comments from specialist, doctors and other care providers. Through IT, diverse opinions and comments are presented and more information is exchanged.

Conclusions: The number of accesses to the HP we have introduced here has already exceeded 100,000, and this shows the fact that many of the patients with sleep and arousal disorders have expressed their opinions and interests on this web site. Many of the patients of sleep and arousal disorders started to visit hospital for medical check-up after seeing the HP, and HP contributed much to the decision of the patients to receive the medical treatment in an early stage of their disease. In particular, the patients with hypersomnia have been in agony for a long time and have been often charged as being lazy. Particularly, in case of narcolepsy, the patients who were ultimately diagnosed as such had also needed a long period of nearly 10 years until they received medical check-up and the definite diagnosis. In Japan, there are still not many doctors specialized in sleep and wakedisorders, and it seems that there may be many potential patients of sleep and wake disorders who are actually not under medical treatment. In the future it would be necessary to have more frequent chances of information exchange on IT, to promote more intense activities among the patients themselves to exchange their opinions and to receive useful advice from specialists so that more patients of sleep-wake disorders will have better opportunities to receive medical examination and treatment at earlier time.

1031.S

Epidemiological Survey Of Obstructive Sleep Apnea Knowledge Assessment In Children (OSAKA-KIDS) Among Primary Care Physicians In Kentucky: A Preliminary Report

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Introduction: Obstructive sleep apnea (OSA) is a common condition in children with an estimated prevalence of 2-3%. Consequences of OSA in children may include neurobehavioral and cardiovascular impairments. Due to the high prevalence and clinical significance of OSA in children, the ability of pediatricians to recognize, diagnose, and treat this disorder is of utmost importance.

Methods: A confidential survey of pediatric primary care physicians in Kentucky was undertaken to determine their knowledge of (OSA), and was mailed to 973 practitioners. Questionnaire items primarily addressed physician demographics, and relevant issues related to OSA including clinical presentation, associated medical conditions, diagnostic techniques, and treatment. In addition, the physicians' self-perceived ability to identify and manage children with OSA was also examined. Data were tabulated and assessed using descriptive statistics.

Results: Thus far, 150 (15.4%) questionnaires have been received. 59% of participating physicians were male; ages ranged from 30-74 years, and the year they graduated from medical school ranged from 1953 to 1999. In general, less than 80% of the physicians reported correct answers regarding basic knowledge of OSA, including etiology, clinical manifestations (snoring, hyperactivity, and learning deficits), and evaluation, and treatment. While >70% of participating physicians felt that identification of OSA was important, <40% felt confident in identifying children at-risk for OSA, and in their ability to manage children with OSA.

Conclusions: Primary care physicians demonstrate reasonable awareness to the existence of OSA, yet few are confident in their ability to identify or manage children at-risk for OSA. Thus, targeted instructional interventions aiming to correct these knowledge-based deficiencies among practitioners should improve OSA detection in children and outcomes.

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1032.S

An Investigation Of Knowledge Of Sleep Disorders In Primary Care Physicians

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Introduction: Primary care physicians routinely under-diagnose sleep disorders. The purpose of this study was to further investigate primary care physicians' knowledge of sleep and sleep disorders associated with medical conditions.
Methods: A 2-page questionnaire was distributed by mail to 130 primary care physicians who had previously referred patients to the sleep clinic. The questionnaire also served as part of a quality of care assessment for our sleep clinic. The questions asked physicians how often they asked patients about sleep and sleep-related problems and how often they inquire about medical conditions associated with sleep disorders.
Results: A total of 92 physicians responded to the questionnaire giving a response rate of 71%. Their response indicated that 51% of physicians recognized sleep disorders in less than 25% of their patients, and less than 25% of patients were being prescribed hypnotics. The majority of physicians almost always asked their patients about tiredness or fatigue (84%) and about sleep problems they might experience (74%). However, a little over half (58%) asked about daytime sleepiness on a regular basis. Other findings include that the majority (73%) of primary care physicians almost always asked obese patients about sleep apnea symptoms, yet less than half (45%) routinely asked hypertensive patients about sleep apnea symptoms. In total, 78% of the primary care physicians surveyed requested more information about sleep disorders. With regards to the assessment of the quality of care, the majority of the physicians rated the sleep clinic good to excellent in terms of wait time for appointment (78%) and booking of patients (81%), and in the time it took the sleep study results to reach them (88%). The overwhelming number stated that the sleep report they received was helpful (87%), clear (94%) and with good attention to detail (98%). Overall, 85% of primary care physicians felt that the clinic was providing very good to excellent patient care.
Conclusions: Previous findings state that 80-90% of patients with sleep disorders have not been diagnosed. The detailed sleep reports received by physicians who routinely refer patients to our clinic has in part served to help provide education about sleep. The majority of the primary care physicians in our study appear to have a fair to good knowledge of sleep disorders but nevertheless affirm that further information is necessary. We believe that quality of care assessments with questions assessing knowledge about sleep are an important method of ensuring proper standard of care and assessing the Continuing Medical Education needs in referring physicians.

1033.S

Medical Interviewing in the Sleep Laboratory: An Effective Strategy for Teaching Sleep Medicine to Year 1 Students

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Introduction: The medical school curriculum is crowded and sleep medicine faculty have limited time and resources. The result is that many US medical schools have an inadequate sleep medicine curriculum, though most of these schools are affiliated with hospitals that offer clinical sleep services. This abstract describes the results of an innovative method for teaching sleep medicine, namely having students interview sleep medicine patients, in the context of their Year 1 medical interviewing course.
Methods: At the University of Minnesota, medical interviewing is taught to first semester, Year 1 medical students. Groups of eight students meet ½ day weekly for six weeks with faculty mentors. During the rotation, the students interview and then present patients to their mentor. Forty students and five mentors were asked to participate in this study. None of the mentors had a particular interest in sleep medicine. All students completed two surveys, prior to and following their medical interviewing experience: a survey of confidence levels in history taking, patient communication, and gathering a sleep history; and an assessment of sleep knowledge. Confidence was assessed using an adaptation of a 10-point scale, widely used in the self-efficacy literature. Knowledge was assessed using a validated instrument. Twenty-four students were in the intervention group. These students received: a laminated card describing a sleep history, a four page overview of sleep, and a fifty page monograph on sleep, and were assigned to interview a patient in the sleep laboratory at some time during the six week course. The sixteen control students were given neither supplemental materials or specifically assigned to sleep patients. At the end of the study, both groups completed the same surveys. The students in the intervention group also rated their use and the usefulness of the various interventions.
Results: Twenty-two students in the intervention group and sixteen students in the control group completed both pre and post study questionnaires. Students in both groups significantly increased their confidence in communicating with patients, and in gathering a medical history. Only the intervention group increased their confidence in taking a sleep history and their knowledge of sleep medicine. All of the students in the intervention group rated the patient contact as valuable and 75% rated the supplemental materials as valuable.
Conclusions: The opportunity to take a history from a patient with a sleep disorder, along with the provision of appropriate materials to facilitate the history taking and the understanding of the sleep problem is an effective strategy for teaching sleep medicine to year 1 medical students. This can be accomplished during a course on medical interviewing. This intervention leads to an increase in students' knowledge, as well as their confidence levels.

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1034.S

Effects of Education on Ratings of Culpability of Sleepy and Drunk Drivers

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Introduction: Although sleepiness is a major contributing factor to the occurrence of motor vehicle accidents, the public holds sleepy drivers less responsible for motor vehicle accidents than drivers who have been drinking. The purpose of the present study is to assess the effectiveness of educational intervention on ratings of culpability of sleepy and drunk drivers.
Methods: Three hundred undergraduate students (mean age = 20.2 years), who gave their informed consent, were randomly assigned in equal numbers to read one of five vignettes describing a motor vehicle accident. All vignettes described a driver who, after attending a retire-

ment luncheon for a colleague, strikes a child on the drive home (Control). The other four vignettes included low and high levels of both alcohol consumption and being continuously awake since the previous night due to shift work. Subjects then rated the culpability of the driver on a 0-9 scale. An educational information sheet describing the dangers of driving while sleepy and after drinking alcohol was then presented to all subjects who then received the same vignette as before and rated the driver's culpability. Subjects were also asked how much alcohol or sleep loss someone could endure and still be able to drive safely, as well as how willing they would be to drive with someone that had been drinking or sleep deprived.

Results: This study used a split-plot design with driving scenario as the between-subjects factor and the before to after effect of educational information as the within-subjects factor. Analyses of variance yielded a significant interaction effect ($F(4,295) = 2.44$, $p < .05$). Paired t-tests ($p < .01$) examining the differences in culpability ratings before and after education revealed significant increases of culpability ratings for drivers in both of the sleep loss conditions and the low alcohol condition with no changes in ratings for the control or high alcohol condition. Subjects' willingness to drive with someone who had been drinking or who was sleep deprived also decreased following education along with their estimates of the amount of time one could remain awake and drive safely.

Conclusions: Presentation of educational information regarding the hazards of drowsy driving can alter people's perceptions of the culpability of, and their willingness to drive with, sleepy drivers. Future research needs to investigate the duration of this educational effect and if this change of opinion translates to change in behavior.

1035.S

Watching and Educating those that Watch Sleep

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Introduction: The sleep behavior of young adults has been examined in the laboratory and in the field. Largely, comparison studies have been conducted to examine the sleep quality and to provide a differentiation point to the clinical group of study. Based on data summarized from laboratory and field (i.e., survey and self-report measures), young adult sleep is compromised. Sleep deprivation, delayed sleep phase disorder, insomnia and insufficient sleep disorder symptomology have been reported with this population. More broadly defined measures and ongoing sleep logs for this population in their natural surrondings are necessary to more clearly understand sleep quality in young adults. This investigation was designed to measure young adult sleep quality in a college setting. Both resident advisors and residents of a college residence were trained in the basics of sleep logging and ratings for this purpose.

Methods: Twenty-five resident advisors and twenty-five residents of a residence hall at a midwestern college were recruited to attend a sleep class and participate in monitoring for one month following that class. The sleep class was composed of presentation of basic sleep science and explanations/rationale for sleep logging and self-report measures. Basic descriptive information and some sleep perception and knowledge self-report measures were collected prior to the class. All participants in the class received an explantion of the investigation. 18 resident advisors and 15 residents completed these materials, attended the class and self-monitored their sleep for four weeks after the class. All participants signed an informed consent after receiving an explanation of the study.

Results: All results were tabulated into a data set and analyzed using SPSS PC. All results were tablulated in terms of sleep latency onset, number and amount of time of awakenings, wakeup time and sleep quality rating. These sleep ratings and the self-report measures were compared in terms of the resident advisor group (those that must be "on-call" and often having their sleep interrupted when on duty) and the resident group (seemingly typical young adult college student sleep). Despite the accountability and opportunity for interrupted sleep due to work constraints, the residents' sleep quality was poorer, overall. Both groups had poor sleep, in general. A sleep class aimed at the education of sleep enhancement strategies has been planned for the groups.

Conclusions: 1.Young adult sleep is poor.2.Despite work constraints, resident advisors' sleep, compared to residents' sleep was less compromised.3.Young adult college students residing in residence halls may choose variable sleep schedules of an extreme degree in order to fullfill their interest and curiosity of events they generate or are invited to in the residence hall.4.This group of sleepers may benefit from an educative intervention focused in the enhancment of their sleep. Such a class is underway.

1036.S

Sleepy Pre-Teens: Second Pilot of Sleep-Smart Program in 7th Graders

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Introduction: Previous evaluation of the Sleep Smart Program – a preventive-intervention curriculum based on the social learning model designed to teach middle school students healthy sleep hygiene – indicates that this is an effective countermeasure. Encouraging trends seen in the original pilot (Rossi et al., 2002) motivated a second evaluation with added actigraphy assessment

Methods: 26 participants (7 males, 19 females) were recruited from 2 randomly selected 7th grade health classes at an urban public middle school. 12 students from one class comprised the prevention group with the others a comparison. Ages ranged from 12-14 (M=12.5, SD=.6), 47% were ethnic minorities, and 79% were from households with annual incomes < $30,000. Prevention group met with research assistants for 8 sessions over 5 weeks. Participants completed a sleep habits questionnaire and sleep efficacy measure pre- and post-Program. Sleep patterns were also estimated using one-week actigraphy and diaries twice for 5 participants in each group. Sleep variables BT, RT, and TST (school- and weekend nights), delay (weekend BT – school BT), and oversleep (weekend TST – school TST) were compared.

Results: Prevention group showed improved sleep pattern regularity and self-management confidence over time, based on self-report and actigraphy, whereas the Comparison group developed poorer habits on some variables. *Sleep Habits Questionnaire:* Pre- to Post-Program, prevention group went to bed an average of 25 minutes earlier on school nights and 73 minutes earlier on weekends (p=.08), whereas the Comparison group went to bed 11 minutes earlier on school nights and 43 minutes later on weekend nights. Prevention group also reported more consistent school-weekend bedtimes (delay decreased by 48 minutes) while the comparison group's schedule became more inconsistent, (delay increased by 27 minutes, p=.10). Also, the prevention group slept an average of 30 minutes more on school nights, 65 minutes more on weekends, and had a shorter oversleep than the Comparison group post-Program. *Actigraphy:* Although there were differences between groups pre-Program, the prevention group shifted to a more consistent sleep pattern. They slept only 6 minutes more on weekends than on school nights, in contrast with the Comparison group's oversleep of 113 minutes (p=.08). Sleep period means for post-Program are as follows: school nights: M(prev)=516 (18); M(comp)=464 (58), p=.09; weekend nights: M(prev)=520 (76), M(comp)=590 (88), ns. *Sleep Efficacy*: Post-Program, the prevention group maintained their baseline confidence in self-management of sleep, whereas the comparison group decreased considerably (p=.02).

Conclusions: The aim of the Program was to increase the quantity and regularity of sleep in middle school students. Results from self-report and actigraphy – especially sleep regularity – are encouraging. However, some limitations remain, such as the small number of participants, compliance issues, and lack of follow-up. Nonetheless, this pilot supports introducing a sleep curriculum into health education.

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1037.S

A Profile of American Adults' Sleep Habits

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Introduction: An annual Sleep in America poll has been conducted every year from 1998-2002 to describe and quantify America's knowledge and attitudes about sleep as well as their sleep habits and experiences, quality of their sleep, daytime sleepiness and the prevalence of sleep problems/disorders. Results are presented to the public and shared with the sleep community. The poll provides insight into the need for sleep education, research and public policy initiatives.
Methods: A task force of scientists was assembled to review the research, design questions and analyze the results. Professionally trained interviewers polled a nationally representative random sample of at least 1000 adults each year via telephone interviews, lasting approximately 20 minutes. To date, 5,209 adults have been polled. The maximum sampling error of the data per poll is 3.1 percentage points at the 95% confidence level.
Results: Data was abstracted from all five polls to develop an overall profile of America's sleep over a 24-hour period. In general, 34% of American adults do not keep a regular sleep schedule. Nearly ½ (46%) of younger persons, ages 18-29, report irregular sleep schedules. Before bed, most adults (87%) are watching TV followed by spending time with family or friends; 21% drink caffeinated beverages, as do 26% of younger adults. During sleep, 59% sleep with another adult while 34% sleep alone. Overall, 40% report their sleep as excellent-very good. Mean hours of sleep reported from 1998-2002 is 6.9-7 hours per night with 31-39% stating they sleep less than 7 hours per night. Over the years, 51-58% have reported symptoms of insomnia at least a few nights a week; 34-41% say they or someone told them they snore, 9-12% report symptoms of sleep apnea and 13-16% experience RLS symptoms. Common causes of disruptions are stress (22%) and pain (20%). When awakened, 78% report that they toss and turn and 61% worry. To awaken, almost ½ (46%) of American adults need an alarm clock and 24% experience difficulty waking-up two or more workdays per week. During the day, 37-42% of adults report daytime sleepiness that interferes with daily activities a few days a month or more. Many (87%) accept it and keep going while 61% say they use caffeinated beverages. Many adults (38%) nap during the day. Younger adults and those who have sleep problems/disorders are more likely to experience daytime sleepiness.
Conclusions: Many Americans are not getting into a natural, regular sleep-wake schedule that includes receiving sufficient quality sleep and feeling alert the next day. Sleep habits, disruptions and problems are more closely associated with our American lifestyle than with our internal sleep-wake cycle. Self-reports demonstrate a high prevalence of sleep problems/disorders as well as disruptions such as stress that may not be resolved adequately. Sleep problems are more prominent among younger people indicating a need for education and establishing better sleep habits.

1038.S

Sleep Investigation In Australia 1990-2002 – Data From National Health Insurance Statistics

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Introduction: Since 1989, the procedure fee for polysomnography (PSG) has been reimbursed by the Australian national health insurance system, Medicare. Medicare covers all Australians with either citizenship or residency. Services on inpatients of public hospitals are not billed via Medicare. In 1998-9, Medicare limited PSG services to physicians who had specific sleep accreditation through the Royal Australasian College of Physicians (RACP). We examined insurance data to determine PSG utilisation, utilisation characteristics, the rate of increase in services over time and the influence of accreditation on service provision.
Methods: Records of the Health Insurance Commission electronic database for PSG were examined for financial years 1990-1 through to 2001-2. Age data was broken down into 0-yrs then by decade to 85 yrs. Gender and region specific data for PSG as well as information on uvulopalatopharyngoplasty (UPPP) were obtained. Data from 1994 was adjusted for services per capita (pc, per 100,000 population). Expenditure was calculated by multiplying fee per service by number of services.
Results: Expenditure on PSG's increased over the decade from $US0.6 million(m) to $US10.2 m. Services increased from 94/95 to 01/02 , 104 to 247 PSG's pc (237%). In contrast, over the decade, lung function tests (LFT) increased by 61% and exercise ECG by 31%. The current rate of increase in PSG's is 13% per annum (vs 7% for LFT's and 3% for ECG) and has been stable since 1996. This rate of increase for PSG's has been similar since 1996. PSG's are more common in men than women (359 vs 135 pc) and are most common in the 55-64 yr age group (864 pc in men, 355 pc in women). Children less than 14 accounted for < 4% of PSG's. Scalpel UPPP has decreased from 11 to 8 operations pc over the decade. The decrease has been greater with laser UPPP, 4 to 1 procedures pc.
Conclusions: As expected there has been a marked increased in Medicare paid PSG services in Australia in the past decade. Some of this increase may reflect a shift from inpatient sleep studies in public hospitals to Medicare billable procedures. The rate of increase has been stable since 1996 and has not been altered by physician accreditation. Service utilisation mirrors the age and gender aspects of the epidemiology of OSA epidemiology. There has been a decrease in UPPP over the past decade, particularly laser UPPP.

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1039.S

Alertness Management Program Increases Sleep Duration in Sleep Technicians

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Introduction: Introduction: Approximately 20% of American workers perform shift work, which causes a reduction in sleep quantity and quality. Medical problems such as peptic ulcer disease (Segawa et al., 1987) and coronary heart disease (Knutsson et al., 1999) appear common in shift workers. Because sleep disorders center (SDC) technicians often perform shift work, sleep programs have the onus to educate their staff about proper sleep and sleep optimization. Therefore, we initiated an educational program to improve sleep duration, quality, sleep knowledge and mood.
Methods: Methods: Sleep technicians initiated the study by completing a comprehensive patient intake questionnaire inquiring about sleep disorders, sleep patterns, sleep hygiene, past medical history, social history, family history and full review of systems. They were blinded concerning the purpose of the study. Technicians also completed the Sleep Attitudes and Knowledge Questionnaire, a two-week sleep log, the Epworth Sleepiness Scale (ESS) and the Profile of Mood States (POMS). At week three, in a seminar format, the principal investigator (RDV) reviewed normal sleep and changes with aging, circadian rhythms, alterations with shift work, costs of insufficient sleep, optimal sleep hygiene, driving home after work, sleep disorders and scheduling. Technicians received

AASM handouts on Shift Work, Sleep Hygiene, Circadian Rhythms and the NSF Drowsy Driving Fact sheet. From weeks 4-7 the intake questionnaire was reviewed privately with each technician. On weeks 8-9 technicians again completed the questionnaires. At approximately week 10, technicians not receiving the initial sleep education attended the seminar by the same discussant. From weeks 11-14 the comprehensive patient intake questionnaire was once again reviewed. Finally, in weeks 15-16 the technicians again completed the full complement of forms.
Results: Results: Six women and four men completed the study. One technician had obstructive sleep apnea syndrome and utilized nasal continuous airway pressure(CPAP). Total sleep time (TST) by sleep log increased from 7.1 + 0.9 to 7.5 + 0.9 hours ($t = 2.9$, $df = 8$, $p = 0.019$). No change occurred in number of sleep periods (1.1 + .14 vs. 1.2 + .21). Technicians did not evidence sleepiness on the ESS with pre and post education means of 4.3 + 3.9 and 4.0 + 3.2 (p = ns). The POMS evidenced a non-significant decrease in anger. Finally, no improvement occurred in the Sleep Attitudes and Knowledge (mean scores 14 + 1.5, 12 + 1.8 and 13 + 2.2).
Conclusions: Conclusions: A brief educational intervention lengthened reported sleep duration in SDC technicians without improving mood or sleepiness. Distressingly, no improvement in sleep knowledge occurred over time. This test indicated that despite working in a SDC, technicians were not particularly knowledgeable about sleep. Nor are sleep technicians immune from sleep disorders that might interact negatively with insufficient sleep. Follow-up studies will require objective measurement of TST and continuing educational efforts on sleep knowledge.

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1040.S

Objective Standardized Clinical Examinations (OSCE) in Sleep
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Introduction: Objective standardized clinical examinations (OSCE) are performance based examinations during which trainees "show how" they do things; as opposed to paper and pencil tests which evaluate if trainees "know how" to do things. This format for testing clinical competence utilizes standardized patients (SP) who portray specific clinical problems. SP's are given a specific script, and are coached regarding the clinical problem they are to portray.
Methods: At the University of Minnesota an OSCE has been given to second year medical students since 1988. The examination is composed of twenty stations, each of five minutes duration, four minutes of which is devoted to the student demonstrating a specific skill, and one minute for feedback. Prior to taking the OSCE, students have had six hours of dedicated lectures on sleep medicine during the first two pre-clinical years. The sleep OSCE, which has been used since 1999, is a 45 year-old man and his wife who come in for an evaluation of the husbands snoring. In addition to snoring the patient has excessive daytime sleepiness (EDS), and hypertension. The student is instructed to gather a history, communicate a probable diagnosis to the patient and make a recommendation for further evaluation. An examiner observes and evaluates the students performance using a standardized checklist of 25 items that assess the history from the patient and spouse, the identification of the likely cause of the problem, supporting evidence, and recommendations for further evaluations. The OSCE has been well received by medical students since it was first introduced. It has been perceived as an excellent tool for both assessment of clinical skills, and for teaching those same skills. Students evaluate each of the OSCE stations. 99% of the students felt the sleep station was fair, and that they had an adequate amount of time.
Results: Student performance on the sleep OSCE was variable. Out of 25 items in the sleep OSCE performance checklist, the student performance ranged from 6 to 24 items correct, with a mean of 16. 90% of the students correctly identified the problem as possible OSA and 65% recommended polysomnography as the appropriate diagnostic evaluation. However, 70% of students did not correctly address the following items: EDS, hypertension, + FH of OSA, spousal history of observed EDS, or caution regarding alcohol.
Conclusions: An entirely lecture based medical school curriculum in sleep medicine during Year 1 and 2 may not be adequate in teaching the appropriate evaluation for patients with OSA.

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1041.S

A Qualitative Analysis of Sleep and Caffeine Alertness Management Strategies Used by Medical Trainees
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Introduction: Operational changes such as work hour regulations to limit duty hours have been proposed to address problems related to sleep loss and fatigue in medical training. Little is known, however, about the use of and attitudes towards personal countermeasure strategies such as napping and caffeine by trainees themselves.
Methods: Twenty-two resident focus groups (N=156) were conducted at 5 US Medical Schools (Brown University, Case Western Reserve University, University of Kentucky, University of Michigan, and the University of Medicine and Dentistry of New Jersey-RWJ Medical School) with 6 specialties (Family Medicine, Internal Medicine, Emergency Medicine, Surgery, Obstetrics and Gynecology, and Pediatrics). Discussions were audio taped, transcribed, coded, and analyzed using NVivo Software. All references made by residents to use of sleep-related strategies and caffeine were coded for specific characteristics mentioned (eg, timing and duration of naps, form of caffeine used), perceived effectiveness of the strategy, perceived barriers to use of the strategy, source of information about the strategy, and whether that behavior represented a change for the individual since residency. Caffeine references were also coded for negative vs neutral terminology cited by the resident to describe use.
Results: There were a total of 48 resident responses coded as napping strategies and 13 as other sleep strategies (eg, delay/advance bedtime, sleep extension post-call); timing of naps varied from lunch to early evening and nap duration ranged from 5 minutes to 3 hours. Residents were equally likely to nap at home and at work, but perceived more (14 responses) work-related barriers (lack of time, interruptions, negative feedback from supervisors) than interference from family (2 responses). Residents were more likely to perceive naps to be ineffective or have an adverse effect (15 responses) than a positive impact (12). Caffeine was mentioned by residents 50 times, largely in the form of coffee. Despite its' prevalence, caffeine was considered to have a negative or no impact in 16 responses compared to 3 responses with a positive effect. While 35 responses used neutral ("drink" or "have") terms to describe caffeine, 23 references were to negative or substance abuse-related terms such as "addicted" and "dose up".
Conclusions: The results of this qualitative analysis suggest that residents do utilize countermeasure strategies such as napping and caffeine, but specific applications are highly variable across individuals, which may contribute to a perception of ineffectiveness. There is a clear need for resident education regarding use of countermeasures to address sleep loss and fatigue.

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1042.T

Strain Differences In Shock-Induced Fos Activation In The Amygdala: Implications For Amygdalar Modulation of Sleep

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Introduction: Compared to C57BL/6J (B6) mice, BALB/cJ (C) mice show more behavioral indices of anxiety and exhibit greater suppression of REM sleep in response to shock training and fear-conditioned cues in the conditioned fear model of anticipatory anxiety (Sanford et al., Behav Genet 33: 43-58, 2003). The amygdala plays a central role in fear conditioning and is implicated in the formation of fearful memories. The amygdala also modulate sleep and wakefulness, in particular REM sleep. We examined Fos activation in the amygdala in B6 and C mice in response to shock training in order to assess the possibility that differential responsiveness in this area could be correlated with strain differences in the effects of conditioned fear on REM sleep.
Methods: Male B6 and C mice were obtained from Jackson Laboratories. Shock-trained mice of both strains were given 15 identical tone-shock pairings at 0900 h and perfused one hour later. Naïve B6 and C were perfused at the same time as a control. Coronal sections through the amygdala (interaural: 1.98-2.10 mm) were cut at 50-mm, and every fifth section was collected and processed for Fos immunohistochemistry. Fos-positive nuclei in medial, cortical, lateral, basolateral, basomedial and central nuclei of the amygdala were counted (Metamorph Imaging System) and expressed as the number of Fos-positive nuclei per mm2.
Results: There was no significant strain difference in the number of Fos-positive nuclei in the naïve condition. Following tone-shock pairings, the number of Fos-positive nuclei was increased in all areas of the amygdala in both B6 and C mice compared to their respective naïve controls. There was a greater degree of Fos activation in shock-trained C mice compared to shock-trained B6 mice in all areas that we examined (medial nucleus [C: 1033.6 ± 76.9, B6: 482.1±95.0]; cortical nucleus [C: 637.3 ± 98.8, B6: 409.0 ± 21.9]; lateral nucleus [C: 474.2 ± 58.6, B6: 95.4 ± 16]; basolateral nucleus [C: 498.5 ± 70.2, B6: 135.1 ± 25.6]; basomedial nucleus [C: 284.9 ± 104.7, B6: 51.1 ± 7.3] and central nucleus [C: 112.5 ± 21.3, B6: 14.1 ± 4.7]).
Conclusions: The C strain showed greater Fos activation in the amygdala in response to shock training than did the B6 strain. These results are consistent with data indicating that the C strain is more reactive, and exhibits greater alterations in sleep in response to shock training. The greater level of Fos activation in various areas of the amygdala in C mice may reflect their involvement in the greater impact of shock training on sleep in this strain. Alternately, in some regions, it may be associated with the formation of shock-related memories that lead to the greater effectiveness fear-conditioned cues have in suppressing REM sleep in C mice.

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1043.T

Gene Expression Profiling of the Response to Sleep Deprivation in Rat Brain Using Affymetrix DNA Chips

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Introduction: We have reported changes in gene expression in mouse cortex during sleep deprivation (SD) and during recovery sleep (RS) using the Clontech Atlas Mouse 1.2 array (Terao et al., Neuroscience, in press). In those studies, only a subset of genes from two categories were affected by SD: immediate early genes and heat shock proteins. In the present study, we have used Affymetrix GeneChips to survey gene expression in rat brain during SD and during a 2-h period of RS subsequent to SD.
Methods: Male Wistar rats (Charles River Laboratories, Wilmington, MA) aged 2-3 months were surgically prepared, recorded, and subjected to SD as described (Terao et al., 2000, Sleep 23:867-874). Rats were randomly assigned to one of four groups: (1) SD from light onset (ZT0) to ZT6; (2) control rats for the SD group; (3) SD from ZT0 to ZT6 followed by RS from ZT6 to ZT8; (4) control rats for the RS group. SD and control animals were sacrificed at ZT6, just after a 6-h SD period, and brains were dissected into multiple regions; groups 3 and 4 were sacrificed at ZT8. Total RNA was extracted from each cortex (Cx), basal forebrain (BF), and hypothalamus (Hy) and combined into 12 RNA pools (3 brain regions x 4 groups). cRNA probes were prepared for hybridization to duplicate Affymetrix rat U34 Neurobiology arrays (a total of 24 GeneChips). Candidate genes from the arrays were further verified by quantitative real-time PCR.
Results: After 6-h SD, significant increases in sleep bout length and EEG delta power were observed during the subsequent RS period, indicative of a sleep debt. Of the 1322 genetic elements represented on the U34 Neurobiology array, 556 were found to be expressed in the BF, 523 in the Cx, and 560 in the Hy in the ZT6 control group. Relatively few genes and ESTs were affected by SD: using the Cx as an example, 17 genes were upregulated 2-fold during SD and 30 genes were downregulated 50%. When all three regions were compared at ZT6, only one gene was found to be commonly upregulated by SD: the kinase JAK2 (Genbank #AJ000557) increased 2.9-fold in BF, 1.97-fold in Cx, and 4.05-fold in Hy. Although each brain area exhibited its own set of genes that increased during RS, only one gene was upregulated in all three regions: phosphoinositide 3-kinase p85 (Genbank accession #U50412) increased 3.5-fold in BF, 1.9-fold in C and 3.25-fold in Hy.
Conclusions: These results indicate that the expression of a subset of genes respond to SD in the rat. Comparison of information obtained in multiple species should help identify those genes that are truly responsive to SD and RS.

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1044.T

Apolipoprotein E e4 Allele Is Associated With Sleep-Disordered Breathing: The Sleep Heart Health Study

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Introduction: There is considerable evidence that obstructive sleep apnea (OSA) has a strong heritable component, even after adjustment for body habitus, although the genetic basis of this heritability remains largely unknown. In the Wisconsin Sleep Cohort Study, there was a significant association between the Apolipoprotein E (ApoE) e4 allele and the presence of OSA (Katotani et al., JAMA 2001), although no such association was found in the Honolulu-Asia Aging Study (Foley et al., JAMA 2001). To further explore the possible association of ApoE genotype with OSA, we examined their association in 1775 participants in the Sleep Heart Health Study.
Methods: All subjects were participants in either the Framingham Heart Study or the Cardiovascular Health Study and had ApoE genotype determined by these studies. Overnight polysomnography was performed in the home and scored at a central reading center. Apneas and hypopneas were identified from oronasal thermocouple and respiratory inductance plethysmograph signals, and required a fall in oxyhemoglobin saturation of ≥4%. Apnea-hypopnea index (AHI) was considered both as a continuous variable and as a dichotomous variable which defined OSA as AHI >15 events/hour. The relation of ApoE genotype to AHI and OSA was

examined adjusting for age, sex, and BMI, using generalized estimating equations to account for non-independent observations of individuals from the same sibship.
Results: The mean age of the 1775 subjects was 71 years, 55% were female, and 88% were white, with 12% black and <1% other race. At least one e4 allele was present in 25% of subjects, with only 1% e4/e4 homozygotes. After adjustment for age, sex, and BMI, the presence of any ApoE e4 allele was associated with a 1.7 event/hour higher AHI (10.6 ± 0.7 [SE] vs. 8.9 ± 0.3, p=0.02) and a 42% increased odds of OSA (OR 1.42, 95%CI 1.07 - 1.88, p=0.01). The effect was approximately twice as great in subjects <75 than in those ≥75 years old. In the younger subjects, the presence of an ApoE e4 allele was associated with a 32% increase in mean AHI and a 67% increased odds of OSA. The association of the ApoE e4 allele with higher AHI was seen in both black and white subjects. Compared to ApoE e4 heterozygotes, homozygosity for the e4 allele was not associated with higher AHI or greater odds of OSA in the overall sample, although in subjects <75 yo the OR for OSA increased from 1.58 in e4 heterozygotes to 3.08 in e4 homozygotes.
Conclusions: These findings support the previous report of an association between the ApoE e4 allele and OSA, and suggest that the discrepancy between prior studies may be due in part to age-dependency of the association.

Research supported by National Heart, Lung and Blood Institute

1045.T

Sexual Dimporphism and Critical Periods Influence Sleep in D. Melanogaster
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Introduction: Male and female individuals of a species frequently exhibit distinct physical and behavioral characteristics. These differences arise during critical periods when genetically determined cellular processes such as neurogenesis, synapse formation and cell death bring about structural modification of the CNS. Given long standing theories implicating sleep in developmental processes and synaptic plasticity, it is interesting to note that many animals, ranging from *D. melanogaster* to humans, exhibit sexual dimorphisms in sleep parameters. Sexually dimorphic sleep behavior can be observed in wild-type flies; males spend 30% more time asleep than females. As in mammals, sleep timing is influenced by the circadian clock and the increased sleep time observed in males occurs during the noon-time siesta (NTS). Discussions between our group and that of Joan Hendricks led to the observation that female flies mutant for the circadian clock gene *cycle*(*cyc01*) display a larger homeostatic response than males. These results suggest that elucidating mechanisms regulating homeostatic drive may be possible by manipulating molecular processes underlying sexual differentiation.
Methods: Using an enhancer trap protocol that allows for the expression of genes of interest within a specific subset of cells, we feminized male brains by activating the female-determining gene *transformer* (*tra*). Previous studies have shown that the misexpression of *tra* in specific regions of the male fly brain produces bisexual or suppressed courtship behavior. We tested flies where UAS-*tra* was expressed in subsets of neurons using specific GAL4 drivers. Three day old transgenic male and female flies (n=200) were evaluated for 4 days using the Trikinetics activity monitoring system (25 °C; 12:12hr LD cycle). Both the timing and amount of sleep were calculated for each transgenic line.
Results: We find that complete feminization of male sleep can be accomplished when the *tra* gene is expressed widely in the fly CNS (e.g., cholinergic neurons). Typically, male flies show a 2.0 fold increase in the NTS compared to female flies while expressing similar amounts of sleep during the night. However, both day-time and night-time sleep in transgenic *Cha*-GAL4/ UAS-*tra* males was indistinguishable from females. Restricting *tra* expression to smaller subsets of the male fly brain (e.g. mushroom bodies, central complex) did not alter total sleep time. These data indicate that over expression of *tra* does not alter the phenotype *per se*. Interestingly, over expressing *tra* widely in the larval brain (*elav*-GAL4) does not alter adult male behavior, suggesting that the critical period for plasticity extends into adulthood.
Conclusions: We show that by manipulating the timing and spatial expression of a gene involved in sexual differentiation we can alter the timing and duration of sleep. It is interesting to note that because the critical period for sexual dimorphism occurs in the adult, the underlying plastic mechanisms can be evaluated in behaving animals. These protocols provide a powerful tool to evaluate several current theories pertaining to sleep function.

Research supported by Neurosciences Research Foundation

1046.T

The Effects of Acute Sleep Deprivation, Starvation and Heat Exposure on Life-Span in Drosophila
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The Neurosciences Institute

Introduction: Flies mutant for the circadian clock gene *cycle*(*cyc01*) are extremely sensitive to sleep loss yet survive longer than other clock mutants when exposed to heat, starvation and oxidative stress. Thus, the latency to observe mortality following extended sleep deprivation (SD) is 10 hrs in *cyc01* flies vs. 65 hrs in both wild-type flies(*Cs*) and flies mutant for the circadian clock gene *period* (*per01*). In contrast to their response to SD, *per01* flies are extremely sensitive to stressful environmental challenges. Moreover, the extent to which these manipulations modulate the expression of stress response genes is dependent upon genotype. Current theories on aging suggest that manipulations that influence metabolism (i.e. caloric restriction) and increase resistance to stress promote longevity. The differential sensitivities of *cyc01* and *per01* flies to SD on the one hand and stress on the other provide a unique opportunity to evaluate how sub-lethal exposure to an environmental challenge can influence longevity
Methods: Flies were cultured at 25°C on a 12:12 L:D cycle. Three day old *cyc01*(n= 300) and *per01*(n = 150) females were placed into Trikinetics monitors and evaluated for two days. On day 3, flies were either sleep deprived for 7 hrs, or Starved for 24 hrs by replacing their food with 1% agar. Sleep was evaluated during each manipulation. Alternatively, age-matched flies were exposed to 36°C for 3 hours in culture vials. Following the manipulation, flies were divided into three groups, placed into fresh culture vials and maintained as above along with untreated controls. The number of deceased flies was calculated until all flies had perished.
Results: Exposure to near-lethal levels of sleep deprivation did not alter the median life span of *cyc01* mutants compared to untreated controls (38 ± 5 vs. 38 ± 3 days, respectively). Nor were there changes in the maximum life-span. As expected, median life-span was unchanged in *per01* flies which received the same amount of physical stimulation as *cyc01* flies yet only 10% of the lethal dose of SD (54 ± 3 vs. 54 ± 3 days in controls). Three hours of heat dramatically increases the expression of stress response genes yet this manipulation did not influence median life span in either *cyc01* or *per01* flies vs. controls (39 ± 5 vs. 40 ± 3 days and 57 ± 3 vs. 60 ± 6 days, respectively). Similarly, a normal life-span was observed in *cyc01* flies that had been exposed to near-lethal levels of starvation (37 ± 5 vs. 37 ± 3 days).
Conclusions: *cyc01* flies that survive 12 hrs of sleep deprivation (50%) show dramatic increases in daily sleep that appear to be permanent, suggesting that the effects of sleep deprivation can be long lasting. However, even though these acute treatments place the animals very near death, none of them affect life-span. These results are consistent with anecdotal reports in sleep deprived rats.

Research supported by Neurosciences Research Foundation

1047.T

Central Administration of Interleukin-1 Beta Increases Growth Hormone-Releasing Hormone Receptor mRNA in the Hypothalamus

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Introduction: Interleukin-1b(IL-1b) is a key element in the brain cytokine network involved in non-rapid eye movement sleep (NREMS) regulation. Injection of IL-1b into the cerebral ventricles increases NREMS in rats. Administration of anti-IL-1b antibodies, the IL-1b receptor antagonist or the soluble IL1b receptor inhibits spontaneous sleep. Brain IL-1b mRNA and IL1 protein vary with sleep propensity. IL1-induced GH release is mediated via hypothalamic growth hormone-releasing hormone (GHRH) and IL-1b and GHRH receptors co-localize on cultured hypothalamic neurons. The somnogenic actions of IL-1b and GHRH are linked in the sense that anti-GHRH antibodies attenuate IL1-induced sleep. The GHRH receptors responsible for sleep regulation reside in the hypothalamus. Incubation of cultured hypothalamic neurons with IL-1b increases GHRH-R mRNA in a dose-dependent fashion. The aim of the current experiments was to determine the in vivo hypothalamic GHRH-R mRNA response to IL-1b by means of real-time reverse transcription-polymerase chain reaction (PCR), and to visualize central GHRH-R mRNAs by means of in situ hybridization.
Methods: Male Sprague-Dawley rats (280–350 g) were implanted with a guide cannula in the lateral cerebral ventricle. Six groups of rats were used. Group I received physiological saline (PS); Group II received 2.5 ng human recombinant (hr) IL-1b and Group III received 25 ng hrIL-1b at 5 h after light onset and were sacrificed 2 h later. Group IV received PS, Group V received 2.5 ng hrIL-1b and Group VI received 25 ng hrIL-1b and were sacrificed 5 h later. The hypothalamus was quickly dissected, total RNA was extracted using TRIzol reagent and analyzed for GHRH-R mRNAs using real-time PCR. Another group of untreated rats were killed and their brains removed and frozen quickly. Coronal sections were thaw-mounted, post-fixed, acetylated and hybridized with [\sups35 S]-labeled antisense or sense cRNA probes to the GHRH receptor mRNA.
Results: Hypothalamic GHRH-R mRNA increased significantly 5 h after IL-1b injection (2.5 ng or 25 ng; F \subs(2,20) = 6.685, p = 0.006, one-way ANOVA) but was not significantly altered 2 h after icv IL-1ß treatment (F\subs(2,20) = 3.91). Posthoc analyses using the Student-Newman-Keuls test revealed no differences between the two doses of IL1. In situ hybridization of GHRH-R mRNA showed expressions in neurons along the midline adjacent to the 3rd ventricle as anticipated from the localization of the immunoreactive fibers for GHRH.
Conclusions: The results suggest that central administration of IL-1b up-regulates GHRH-R in the hypothalamus.
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1048.T

Molecular Correlates of Fatal Familial Insomnia

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Introduction: Fatal familial insomnia (FFI) is a prion disorder characterized by near-complete loss of sleep associated with various neurological symptoms and spongiform degeneration in selected brain regions. FFI is invariably fatal after a course of a few months to 2-3 years. In short-term FFI (<1 year), insomnia is almost complete from the onset and spongiform degeneration is mainly restricted to the thalamus and inferior olive. In long-term FFI, insomnia develops more gradually and spongiform degeneration is found in most cortical regions. Long-term sleep deprivation in rats and other animals produce a syndrome that resembles FFI in several aspects, including increased metabolic rate, weight loss, activation of the sympathetic system and, eventually, death. In this study we performed a genome-wide analysis of transcriptional changes in post-mortem cerebral cortical tissue from short-term FFI patients, long-term FFI patients and age-matched controls. The aim of the project was to assess the molecular consequences of prolonged sleep loss in humans and determine whether they are similar to those observed in animal models.
Methods: Cases selected for this study included subjects with confirmed FFI (PrPsc positive on immunoblot) and age-matched controls. Clinical data were available in all cases, and medical records always included at least one neurological examination. Total RNA was extracted from frontal cerebral cortex (controls n = 8; short-term FFI n = 5; long-term FFI n = 4). Total RNA was used to hybridize human cDNA microarrays (Clontech 7736-1) and high-density oligonucleotide arrays (Affymetrix HG-U133A, B).
Results: A recent genome-wide analysis performed in our laboratory using high-density oligonucleotide arrays has shown that only a small number of genes change their expression in the cerebral cortex of rats after long-term (6-14 days) sleep deprivation. In agreement with this finding, only 7 out of the ~600 brain-specific genes represented in the Clontech array were differentially expressed in short-term FFI cases relative to the other experimental groups. Among these genes was alpha-B crystallin, a small heat shock protein that we also found induced in rats after long-term sleep deprivation. Analysis of the Affymetrix arrays is in progress.
Conclusions: We have recently shown that several molecular correlates of sleep deprivation are shared across distant species. For instance, mitochondrial genes and chaperones/heat shock proteins are induced after sleep loss in flies, hamsters and rats (Cirelli and Tononi, Neuropsychopharmacology 25:S28-S52, 2001). The results of this study suggest that such similarities may extend to humans. Work in progress with high-density oligonucleotide arrays will determine whether such similarities hold true at a whole-genome level.

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1049.T

Sleep in Drosophila Melanogaster: A Mutagenesis Screening

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Introduction: Sleep in the fruit fly is: 1) consolidated into long period of quiescence, 2) characterized by increased arousal threshold, 3) homeostatically regulated; 4) modulated by stimulants and hypnotics, 5) associated with changes in brain electrical activity, 6) associated with changes in gene expression (Shaw et al., 2000; Hendricks et al., 2000; Nitz et al., 2002). Because of short generation times and low gene redundancy, the fruit fly is well suited to the rapid screening of sleep phenotypes. We have started a systematic screening of sleep mutants to identify Drosophila lines that i) are short sleepers or ii) do not show a sleep rebound after sleep deprivation (SD).
Methods: Motor activity of individual flies (7-11 day-old, n = 10-16 /line) was recorded at 1 min intervals using the infrared Drosophila Activity Monitoring System (DAMS) during 3 baseline days, 24hSD (ending at light onset) and 2 days of recovery. Sleep continuity was measured using the S-score (Biesiadecki et al., this meeting). Short sleepers and no-rebound lines were examined for their ability to respond to a complex stimulus to assess vigilance levels during waking (Biesiadecki et al., this meeting).
Results: We tested 4,000 mutant lines, including deficiency lines (~100

lines), the primary Berkeley Drosophila Genome Project (BDGP) collection of mutations obtained through insertional mutagenesis (1045 lines), the Rörth collection of EP-lines (2300 lines), ion channel and other CNS mutants (~ 30 lines) and newly generated lines carrying EMS-induced mutations in the X chromosome (~500 lines). The amount of sleep in mutant lines ranged from 250 to 1100 min/day and on average was similar to that in Canton-S flies and in > 100 other wild-type strains (female flies, mean ±SE, Canton-S: 664±81; other wild-type strains: 655±122; mutant lines: 616±112). Forteen mutant lines slept consistently < 300/min day (short sleeper lines). Sleep amount and sleep continuity increased after 24hSD in all but 3 lines, which lost >80% of their sleep during 24hSD but showed no sleep rebound during recovery day 1 or 2. One of the short sleeper lines, EP(2)2162, carries a transposon in the gene encoding the regulatory (inhibitory) subunit of protein kinase A (PKA). Mobilization of the transposon in 6 independent revertant lines abolished the short sleeper phenotype, demonstrating that the PKA gene is responsible for the reduced amount of sleep in the EP(2)2162 line.
Conclusions: The sleep phenotype in fruit flies is well preserved across >4000 mutant lines. Flies are diurnal; males sleep more than females; SD is followed not only by a sleep rebound but also by increased sleep continuity. Forteen short sleeper lines and 3 lines with no rebound after 24hSD have been identified so far. The analysis of the short sleeper line EP(2)2162 points to a major role for PKA in regulating sleep amount.

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1050.T

Genetic Dissection of Theta Oscillations Reveals A Major Role for Short-Chain Fatty Acid b-Oxidation in Sleep

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Introduction: In rodents paradoxical sleep and exploratory behavior are characterized by brain theta oscillations (4-8 Hz) in the electroencephalogram. Theta is involved in long term potentiation and memory.
Methods: 24-h sleep recordings with spectral analysis, microarray and real-time RT-PCR analysis in inbred mice.
Results: We show that theta during exploratory behavior and paradoxical sleep are under different genetic control and that a slow theta variant during paradoxical sleep is caused by a short-chain acyl-Coenzyme-A dehydrogenase (*Acads*) deficiency. We show also that *Acads* mRNA and protein are expressed in brain regions involved in theta generation, notably the hippocampus. Microarray analysis of brain gene expression indicates that *Acads* mutation is responsible for the up-regulation of glyoxalase I, a gene involved in the detoxification of metabolic byproducts. In contrast, long-chain acyl-coenzyme-A dehydrogenase deficiency does not affect theta and glyoxalase I gene expression. Feeding Acads deficient mice with acetyl-L-carnitine partially recovers the slow theta and glyoxalase I gene expression.
Conclusions: Short-chain fatty acid b-oxidation plays a major role in rhythmic neuronal activity in the sleeping brain through an under-appreciated metabolic pathway with potential role in sleep and brain maturation.

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1051.T

CLOCK Polymorphism in Extreme Evening-Type and Morning-Type Individuals and in DSPS Patients

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Introduction: A CLOCK polymorphism situated in the 3' untranslated region (3'-UTR) has been associated with human diurnal preference (Katzenberg et al., 1998). CLOCK 3111C has been reported as a marker for evening preference. In this study, we hypothesized that differences in CLOCK genotypes could be observed if extreme morning-type (M-type) subjects were compared with extreme-evening type (E-type) subjects. We also investigate a possible relationship between CLOCK 3111 and Delayed Sleep Phase Syndrome (DSPS).
Methods: Morningness-eveningness tendencies of 502 subjects were measured by the Horne-Ostberg questionnaire. On the basis of their score, 19 extreme morning-type (M-type) and 17 extreme evening-type (E-type) subjects were selected for genetic analysis. M-type score average was 28,5 (±3,3) and E-type score average was 67,5 (±3,7). Eleven subjects with Delayed Sleep Phase Syndrome diagnosed according to the International Classification of Sleep Disorders criteria were studied. CLOCK 3111 genotyping was performed by PCR-RFLP using the restriction enzime RSA I.
Results: We do not observed any difference in the frequencies of 3111C allele neither in the DSPS patients group nor in extreme-evening types. More surprisingly the two 3111C homozygous subjects in our sample were M-type.
Conclusions: Genetic analysis suggests that there was no association between the CLOCK 3111 polymorphism and diurnal preferences or DSPS. These results corroborate recent study that have not found association between gene CLOCK and diurnal preferences (Robilliard et al., 2002)

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1052.T

Hypocretin/Orexin Gene Expression in the Developing Zebrafish

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Introduction: The neuropeptide hypocretin (also known as orexin) is involved in sleep regulation, and has been implicated in the neurological disorder narcolepsy. To understand the functional regulation of hypocretin, we are examining the expression of hypocretin in zebrafish (Danio rerio), an animal model ideally suited for developmental and genetics research.
Methods: Digoxigenin-conjugated riboprobes complimentary to zebrafish hypocretin mRNA were hybridized to wholemount wild-type (AB or Scientific Hatcheries) larval zebrafish and immunohistochemically visualized. cRNA was 627 basepairs long and targeted sequences encoding signal peptide, complete hypocretin 1 and 2 peptides, and 3' untranslated region (398 bp; see Faraco, et al., APSS 2003). Sense probes served as a control. Larvae were 3 to 7 days old and fixed at about 10 a.m.; lights-on = 9 a.m.-11 p.m. Labeled cells were counted in 20 fish that were approximately 120 hours (5d) post-fertilization, and 20 fish at ca. 120 hours (7d) post-fertilization. In a pilot circadian experiment, larvae 5-7 days old were fixed at 10 a.m., 2 p.m., 6 p.m., and 8 p.m.

Results: Signal was detected in a bilateral group of cells in the ventral diencephalon of larvae of all ages. The cells were loosely clustered near the ventral midline and generally appeared round or oval in shape, measuring 5.7-8.0 um long. Occasionally cells appeared elongated, pyramidal, or even stellate - especially when labeling spread into proximal dendrites. An average of 5.2 $\pm$ 0.3 labeled cells per hemisphere were counted in 5d-old fish, and 5.3 $\pm$ 0.3 labeled cells/hemisphere were observed in 7d-old fish. Sense control probes yielded no signal. In the pilot circadian experiment, visually-assessed signal levels appeared similar among the timepoints measured.
Conclusions: These results indicate that hypocretin mRNA is expressed in developing zebrafish, beginning by at least 3 days post-fertilization, in a pattern and location similar to that observed in mammals. Our data suggest that zebrafish may be employed as a useful animal model to study hypocretin regulation in vertebrates, and they complement other experiments performed our laboratory using hypocretin peptide immunohistochemistry in larval and adult zebrafish (A. Ray, unpublished observations). Hypocretin studies could be combined with simple locomotor assays to examine the relation of hypocretin expression to rest and activity in the zebrafish.

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1053.T

The Temporal Pattern of Changes in Gene Expression with Progressive Increases in Wakefulness is Different in Cortex and Hypothalamus: A Microarray Study

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Introduction: Substantial progress has been made in describing the phenomena of sleep, and uncovering the fundamentals of the neuronal circuitry. However, little is known about the molecular processes that underlie sleep homeostasis. A number of candidate genes have been studied in order to elucidate their roles in sleep and wakefulness. It has been demonstrated, using high throughput strategies that transcripts of many genes change as a function of behavioral state. However, all of the previous experiments were performed in only one brain region (cerebral cortex) and with a limited duration of sleep deprivation; thus, the dynamic nature of changes in gene expression has not been identified. The aim of this study was to perform a comprehensive investigation of the temporal changes in gene expression with increasing durations of sleep deprivation in different brain regions.
Methods: Experiments were performed on C57B/6J mice. Animals (n=8 per group) were sacrificed after 3, 6, 9 and 12 hrs of sleep deprivation performed by gentle handling. Control animals were sacrificed at the same diurnal time points as the sleep deprived mice. Brains were dissected to obtain samples of cerebral cortex and hypothalamus. RNA was pooled to create three groups and labeled with Cy3 and Cy5 fluorescent dyes; a reference RNA was also included in the experiment. 27,010 genes were subjected to analyses. Data derived from 12 sources were analyzed using a "multi-step filtering protocol".
Results: With progressive sleep deprivation 532 array elements in the cerebral cortex and 129 in the hypothalamus changed their expression levels (271 and 41 genes increased and 187 and 74 decreased expression in the cerebral cortex and hypothalamus, respectively). There was a characteristic temporal pattern of changes in expression in both brain regions. In the cerebral cortex, the change of expression in the majority of genes occurred early during deprivation. The highest level of expression occurred after 3 hrs of deprivation with the transcript level declining to nearly baseline in spite of ongoing sleep deprivation. In comparison, the temporal pattern of gene expression in the hypothalamus exhibited a significantly different pattern, i.e., there were no changes in the transcript level following 3 hrs of sleep deprivation but a significant increase (or decline) after longer durations of wakefulness. In the hypothalamus the majority of transcripts peaked at both 9 and 12 hrs of sleep deprivation.
Conclusions: Our results demonstrate different temporal patterns of changes in gene expression in mouse brain during sleep deprivation in different brain regions. The early up-regulation of genes in cortex may help promote cortical activation while the slower, more delayed changes in hypothalamus may include signals for sleep promotion.

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1054.T

Can Direct Digital Video Analysis of Mice Be Used As a Non-Invasive High Throughput Phenotyping Strategy to Estimate Durations of Sleep and Wake?

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Introduction: Mutagenesis strategies to identify sleep mutant mice require high throughput methodology. Conventional methods using direct recording of EEG/EMG following surgical implantation of electrodes represent a barrier for mutagenesis studies. We hypothesize that direct digital analysis of video images will provide sufficiently accurate estimations of sleep and wakefulness that can be used for mutagenesis screens.
Methods: In our approach, mouse activity is measured by analyzing video images recorded on-line at an average frame rate of 20 frames per second using a mini-CCD infrared camera. Video images can be acquired continuously in both light and dark conditions. The captured video is digitized and images are input to a computer for real time analysis. We use a gray-scale detection algorithm that distinguishes and tracks the mouse in its home cage. The software identifies the perimeter of the mouse, locates the "center of gravity" and estimates the area (size) and shape by calculating the aspect ratio, i.e. length of longitudinal axis of "elliptical" mouse to length of cross-sectional axis of the mouse. For a perfect circle, the aspect ratio would be one. The software also calculates the speed of movement of the mouse by calculating the derivative, i.e. velocity of the change of position of the "center of gravity" of the mouse on adjacent frames.
Results: A 3D cluster analysis of speed, size and aspect ratio shows a distinct cluster when the mouse is not moving and the cross-sectional area is small and more circular. We postulate that these points will represent sleep.
Conclusions: One of the advantages of digital video analysis versus conventional activity monitoring by electronic beam splitting is that in addition to measuring movement, video images provides additional information about size and shape. We hypothesize that these additional data will be useful in improving estimates of sleep and wakefulness since mice tend to have unique postures during sleep. A validation study comparing rest/activity by infrared beam splitting, EEG/EMG recording and digital video analysis is currently in progress.

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1055.T

A Whole Genome Scan For Obstructive Sleep Apnea And Obesity In African-American Families

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Introduction: Obstructive sleep apnea (OSA) is a common, chronic, complex disease associated with substantial cardiovascular co-morbidity, including hypertension and diabetes. Obesity is the most characteristic feature of OSA in adults. OSA and obesity are both prevalent in African-Americans, who are also at increased risk for secondary complications. Genetic studies of OSA in this population are therefore an important priority.

Methods: To identify susceptibility loci for OSA, we undertook a 9cM genome scan in 59 African-American pedigrees (n=277 subjects) ascertained on the basis of either an affected individual with laboratory-confirmed OSA, or a proband who was a neighborhood control. Multipoint variance component linkage analysis was performed for the OSA-associated quantitative phenotypes apnea-hypopnea index (AHI) and body mass index (BMI).

Results: A candidate region on chromosome 8q (lod=1.29, empirical P=0.006) gave the only evidence for linkage to AHI. BMI was linked to multiple regions, most significantly to markers on chromosome 4q (lod=2.63, empirical P=0.0006), 8q (lod=2.56, empirical P=0.0007) and 10q (lod=2.08, empirical P=0.002). Extended modeling indicated that the evidence for linkage to AHI was only slightly reduced after adjustment for BMI (adjusted lod=1.09). After adjustment for AHI, some of the primary linkages to BMI were greatly reduced while others remained suggestive.

Conclusions: Our results suggest that there are both shared and unshared genetic factors underlying susceptibility to OSA and obesity, and that the genetic determinants of obesity in this population are modulated by OSA severity.

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1056.T

Clock-related Gene Expression in non-SCN Brain Regions Following Sleep Deprivation in Wildtype and Cryptochrome Knockout Mice: Relevance to Sleep Homeostasis

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Introduction: The patterns and timing of sleep are largely determined by homeostatic and circadian influences, however, the two processes appear to be independent. Nonetheless, accumulating evidence suggests that "clock"-related genes may underlie parts of both processes. In the SCN, considerable evidence suggests bmal1, clock, per1,2, cry1,2, etc. underlie the circadian pacemaker. In areas outside the SCN, these genes may influence both circadian and non-circadian functions. Several clock-related gene knockouts (KOs) have sleep alterations not entirely predicted by circadian disruptions. Cry1,2 double KOs have especially large alterations in sleep variables indicative of a high sleep pressure, such as high baseline EEG delta power, even though these KOs sleep more (see related abstract Wisor et al.). These results suggest a potential role for cryptochromes in sleep homeostasis and led us to investigate clock-related mRNAs in non-SCN brain regions in control and sleep deprived (SD) wildtype and Cry1,2 KO mice.

Methods: SD began at light onset for 1, 3 or 6 hrs followed by by brain removal, dissection and freezing. RNA was extracted from brain samples and mRNAs examined by quantitative real-Time PCR (including per1, per2, per3, dbp, clock, bmal1, npas2, cry1, cry2, csnkle). Real-Time RT-PCR experiments were validated with multiple controls, and were consistent with Northern blot experiments. Additional brains were examined by in situ hybridization. Lactate dehydrogenase A (ldha), activated by bmal1/npas2 and implicated in brain energy metabolism was also examined.

Results: Cry1,2 KOs have 3-5x higher mRNA levels for per1,2 and dbp under daytime baseline conditions. Normal mice have increased per1,2 following 6 hrs of SD, especially in the cortex and cerebellum. Per mRNA levels return to baseline following recovery sleep. In situ hybridization studies show widespread and non-uniform increases throughout the cortex. Conversely, in the SCN, per mRNA levels decrease with SD, due perhaps to phase shifting effects of SD or the antiphase relationship of per mRNA levels in the SCN vs. Cortex (SCN levels peak in mid-day, cortical levels peak in early or mid-night). Most other clock-related genes examined thus far do not change expression significantly. However, dbp mRNA levels decrease with SD specifically in the cortex and ldha mRNA levels increase in the hypothalamus. Experiments underway include timecourses and KOs vs. controls following SD.

Conclusions: Behavioral data from KOs and molecular data on clock-related genes following SD are consistent with a role in sleep homeostasis independent from the role they play in circadian rhythms. The changes in mRNA levels in cortex appear more similar to an hourglass (turning over with sleep and wake periods) than to the self-sustaining oscillation in the SCN.

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1057.T

HLA Typing in Patients with Kleine-Levin Syndrome

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Introduction: Kleine-Levin syndrome (KLS) is a rare disorder characterized by discrete episodes of hypersomnia lasting for 3 days or more, occurring at least twice a year, with a return to normalcy between episodes. There may be other associated symptoms such as hyperphagia, personality changes, disinhibition and hypersexuality.

Methods: A retrospective chart review was performed on 7 patients evaluated at the Cleveland Clinic Foundation between 1991-2001 for periodic hypersomnia who also had blood samples drawn for HLA typing, including HLA-DRB1* and HLA-DQB1* alleles.

Results: KLS was diagnosed in 7 patients based on the history of discrete episodes of hypersomnia lasting for at least 3 days, occurring 2 or more times per year with a return to normal alertness in between episodes. There were other associated symptoms to varying degrees. During the episodes of hypersomnolence, 5 patients had hyperphagia, 4 had personality changes, 1 had hypersexuality and 1 had disinhibition. There was a male predominance in this group, with 6 males and 1 female. The average age of symptom onset was 17 years. Five of the 7 patients had a polysomnogram and 3 patients had a MSLT. Neither HLA-DRB1*15 (DR2) nor DQB1*0602 (DQ6) were increased in the KLS patients, with no DRB1*15 cases and only one apparent DQB1*0602. A previous report of two KLS patients showed the presence of HLA-DR1 in both. In our patient cohort, DR1 was not statistically increased, DRB1*01 being present in 2 of 7 (28%) KLS patients compared to 20 of 135 (15%) controls. Similarly, no other DRB1* or DQB1* allele was statistically increased compared to controls in this group.

Conclusions: HLA typing confirmed that KLS is distinct from narcolepsy. Neither DRB1*15 nor DQB1*0602 are associated with KLS at the level observed in narcolepsy and DRB1*01 is not overwhelmingly associated with KLS. The small size of the patient group does not exclude an HLA association with KLS. Further study of patients is needed to address any possible genetic component of KLS.

1058.T

Cortistatin Gene Polymorphisms and Sleepwalking

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Introduction: A novel neuropeptide, cortistatin (CST), is unique as a sleep candidate gene because its expression is restricted to a subset of cortical and hippocampal GABAergic interneurons. CST accumulates during wakefulness and CST mRNA level depends on the homeostatic state of sleep pressure. In rats, intra-cerebro-ventricular administration of CST-14 promotes slow wave sleep (SWS) and cortical synchronization by antagonizing the effects of acetylcholine. Sleepwalking is a highly frequent specific SWS parasomnia with high genetic component even if non-genetic factors have also to be considered. Twin studies demonstrated a high degree of concordance (0.64 in monozygotic vs 0.13 in dizygotic twins) and 25% of parents of sleepwalkers have been sleepwalkers themselves during their childhood.Since the pathophysiology of sleepwalking seems to be the inability of the brain to fully awaken from deep SWS and because CST is a key substance for SWS/wakefulness/SWS transition, we sought to determine whether cortistatin polymorphisms might be associated with this sleep disorder.
Methods: To date, 15 families have been studied (trios, sib-pairs and pedigrees; probands: n=15; relatives: n=47). All probands underwent sleep and psychological evaluation including: sleep questionnaire habits, Epworth scoring, MMPI-2 and polysomnography. Relatives have been screened for the presence of parasomnia. After extraction of genomic DNA from blood samples, the promoter and the two exons of the cortistatin gene have been sequenced (after amplification of genomic DNA by PCR) in all 15 probands. Genotyping of the most informative polymorphism was performed by combination of PCR and restriction fragment length polymorphism in all relatives.
Results: Clinical characteristics of our population are similar to those described in the literature. On average the episodes occur 2 hours after sleep onset and are preferentially induced by anxiety or sleep wakefulness rhythm disturbances. Sleep architecture is normal on polysomnography except a high level of awakenings or arousals during the first part of the night. Four different polymorphisms that do not modify the protein structure have been observed from the sequencing data (exon1: serine13, C->T; exon2: alanine70, C->T; serine85, C->T; arginine86, A->C). Because this result do not exclude the hypothesis of a functional polymorphism located in non-amplified regions that might be associated to sleepwalking, the analysis of the inheritance of the most informative polymorphism (alanine70) was performed. Although non-significant, due to the small size of the sample, the result of the desequilibrium transmission test is very encouraging (p=0.07) and 40 more trios are already enrolled and under current investigation.
Conclusions: These preliminary data suggest that cortistatin gene polymorphism may confer susceptibility to sleepwalking and current investigation of more families should answer question in the next few months.

1059.T

Sleep Deprivation Affects Transcripts of Different Classes of Genes: A Functional Genomics Approach

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Introduction: A homeostatic regulation of sleep suggests that following sleep deprivation there are changes in the brain at the physiological, biochemical and/or molecular levels, and that uncovering these alterations will provide clues as to the functions and mechanisms of sleep. Functional genomics is the systematic effort to understand the function of genes and gene products. Array-based gene expression monitoring of tens of thousands of transcripts simultaneously is an useful tool in functional genomics. There have been efforts to functionally characterize genes that change their expression level following sleep deprivation. Although, a number of key observations have been made, these efforts have not been comprehensive. Therefore, the aim of this study was to identify genes whose transcripts varied in different brain regions as a result of increasing durations of sleep deprivation and to describe comprehensive functional characteristics of those genes.
Methods: Experiments were performed on C57B/6J mice. Animals (n=8 in each group) were sacrificed after 3, 6, 9 and 12 hrs of total sleep deprivation. Expression levels of 22,000 genes were assessed in the cerebral cortex and hypothalmus following hybridization of pooled RNA to target PCR amplicons on slide microarrays. Data was analyzed quantitatively through a “multi-step” filtering protocol. The functional characterization of genes that change their expression level in the brain after different durations of sleep deprivation was performed after the assignment of a gene ontology (GO) identification number and the compilation of a name and definition of a GO term(s). The assignment of a gene into a metabolic pathway was performed with an Enzyme Commission number using the metabolic pathways database of the Kyoto Encyclopedia of Genes and Genomes.
Results: Following sleep deprivation 532 array elements defining 391 genes in the cerebral cortex and 105 genes in the hypothalamus changed the expression level. The majority of genes (63.4% and 69.5% in the cerebral cortex and hypothalamus, respectively) were of unknown molecular function, biological process, and/or cellular component. In the GO category – a molecular function, ligand binding/carriers, enzymes and structural molecules were most commonly affected by sleep deprivation. In the category - biological process, in both the cerebral cortex and hypothalamus genes involved in metabolic processes were strongly impacted by sleep deprivation. In the category - cellular component (genes coding for elements of the mitochondrion and ribosome), in both the cerebral cortex and hypothalamus, the largest group of genes were assigned to pathways related to oxidative phosphorylation, purine metabolism and ATP synthesis.
Conclusions: Our results demonstrate that a diverse group of genes change in expression pattern following sleep deprivation. This diversity implies that a number of distinct cellular processes are affected by sleep deprivation.

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1060.T

A Role For Cryptochromes In Sleep Regulation

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Introduction: Sleep is regulated by circadian and homeostatic processes. At the molecular level, circadian rhythms are generated by a negative feedback loop. The transcription factor CLOCK:BMAL1 can drive the transcription of period and cryptochrome (cry1,2) genes. CRY1,2 proteins are strong inhibitors of CLOCK:BMAL1-induced transcription thereby down-regulating their own transcription and thus closing the negative feedback loop. Consistent with their central role in circadian rhythm generation, genetic inactivation of both cryptochromes (cry1,2-/-) results in circadian arrhythmicity. To determine whether the transcriptional regulation provided by CRY1,2 influences the homeostatic regulation of sleep, we studied sleep in cry1,2-/- mice under baseline conditions, under conditions of constant darkness (DD), and after sleep deprivation (SD). The expression of circadian genes that are regulated by cryptochromes were evaluated in cry1,2-/- mice and in sleep deprived wild-type mice. These molecular data will be presented in an accompanying abstract (O'Hara et al.).

Methods: cry1,2 -/- double knockout mice were derived from cry1-/- and cry2-/- single knockout mice. Eight wild-type and six cry1,2-/- male mice were surgically prepared for EEG and EMG recordings. The experiments were conducted under an LD12:12 cycle (lights-on = ZT0). Following two weeks of post-surgical recovery, 24-h baseline recordings, starting at ZT0, were followed by a 6-h SD by handling starting at ZT0. Three days later animals were subjected to one day in (DD). Amount and distribution of NREMS and REMS were determined. In addition, EEG delta power and NREMS episode length were analyzed as measures of sleep drive.

Results: Under LD and DD conditions cry1,2-/- mice exhibited the hallmarks of high NREMS drive; i.e., increases in NREMS time, NREMS episode length, and EEG delta power during NREMS. Baseline amount of REMS did not differ between genotypes. This difference in EEG delta power was specific for NREMS and did not extend to other EEG frequencies. After SD, wild-type mice displayed the typical increase in NREMS time, NREMS-bout duration, and EEG delta power above baseline levels. In contrast, cry1,2-/- mice did not exhibit significant increases in NREMS time or NREMS-bout duration after SD and only a brief increase in NREMS delta power was observed that was significantly smaller compared to wild-type mice. We quantified the relationship between EEG delta power and the sleep-wake distribution in baseline and after SD by estimating the time constants of the increase in delta power during wakefulness and its decrease during NREMS. In cry1,2-/- mice, a significantly shorter time constant for the increase was obtained.

Conclusions: Together with the molecular data (see abstract by O'Hara et al.) these results indicate that cry1,2-/- mice have higher sleep drive during baseline conditions and that a lack of cryptochromes is not simply a genetic model for lesioning the SCN. These findings add to the accumulating evidence that circadian 'clock' genes, including the cryptochromes, are implicated in the homeostatic regulation of sleep.

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1061.T

Gene Expression Profiling in Hypothalamic Brain Regions Involved in the Regulation of Behavioral State

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Introduction: Identifying the molecular underpinnings that differentiate circadian regulation from the homeostatic drive of behavioral state are critical in understanding how the sleep/wake and circadian systems are interrelated. This study uses cDNA microarray technology to identify and compare the diurnal variation of gene expression in the master circadian oscillator, the suprachiasmatic nucleus (SCN), to two brain regions known to affect sleep/wake behavior in mammals: the sleep-promoting ventrolateral preoptic area (VLPO) and wake-promoting perifornical region of the lateral hypothalamus (LH). Our goal is to identify genes that are altered during the diurnal cycle, and to determine molecular pathways important in the initiation and facilitation of behavioral state.

Methods: Forty-eight male C57BL/6 mice of 5 weeks of age were maintained for 5 weeks on a LD12:12 cycle. At ten weeks, two groups of 12 animals were each sacrificed at ZT6 and ZT18. Brains were dissected from VLPO, SCN, and LH. RNA was isolated, and cDNA was synthesized from 2.5-5 ug of total RNA as described (Affymetrix). The synthesis of biotin-labeled cRNA was done according to the BioArray High-Yield RNA Transcript Labeling Kit. Arrays (MG-U74Av2) were probed, hybridized, stained, and washed according to the manufacturer's protocol.

Results: To identify genes enriched in regions of the hypothalamus important in behavioral state regulation, RNA from the VLPO, SCN, and LH were used to screen Affymetrix microarrays. A comparative analysis of message abundance between regions revealed a list of candidate genes with an enriched level of expression. The largest number of enriched genes, 31, was found in VLPO. This list contained a cluster of hormones that included growth hormone and prolactin. Seven genes within the LH were found to be enriched compared to the VLPO and SCN. Of these, hypocretin was the most abundant. The SCN had the fewest number of enriched genes, and somatostatin was the most abundant. A comparative analysis at ZT6 revealed 3 transcripts that were elevated in all three regions. These included the transcription factor, Dbp, and the fatty acid-binding protein Fabp7. Analysis at ZT18 identified 2 genes elevated in all three regions, Chordc1 and Hsp70-1. As expected, the circadian clock gene Per2 was elevated at ZT6 in the SCN and its expression was in anti-phase to that found in VLPO and LH at ZT18. Fos, an often used molecular marker for neuronal activation, was elevated in VLPO during the sleep phase (ZT6) and elevated in LH during the wake phase (ZT18).

Conclusions: Using microarray analysis, we identified sets of genes expressed diurnally in the VLPO, SCN, and LH. These included transcription factors such as Dbp and Per2 that are involved in the regulation of circadian clock genes, and hormones, such as growth hormone, that may play a role in homeostatic regulation. Our results suggest both common and regionally specific molecular pathways that may be involved in the regulation of behavioral state.

1062.T

Novel Mutagenesis Model to Screen and Discover Genes that Affect the Sleep-Wake Cycle

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Introduction: Considerable evidence supports a role for genetic factors in the regulation of mammalian sleep and wakefulness as well as in the pathogenesis of sleep disorders, although at present, no major regulatory genes have been identified. Previously, a forward genetics approach

using chemical (ENU) mutagenesis with phenotypic screening was used to isolate, clone and characterize the first murine circadian clock gene, Clock, and provided a "proof of principle" that this approach is effective in discovering the genetic basis of complex behaviors. Currently, we are extending this mutagenesis approach to discover genes involved in the control of sleep and wakefulness.

Methods: Our mutagenesis and phenotypic screening program involves testing first generation (G1) offspring (from ENU mutagenized C57Bl/6J male mice) at 9-10 days of age in order to identify outliers, called putative mutants (putants), on any of a variety of sleep-wake parameters. In pups, the behavioral states of wake (W), quiet sleep (QS) and active sleep (AS) were differentiated by recording EMG activity with temporary fixed electrodes for a 2-3 hour period. G1 putants are bred and the G2 offspring are tested as pups to establish heritability of the mutant phenotype. All G2 pups demonstrating the phenotype will be bred and subsequently undergo full EEG/EMG sleep-wake recordings as an adult (3 months) to determine if an interesting sleep-wake phenotype is maintained into adulthood.

Results: To date, about 2,000 G1 pups have been screened and 67 have been selected as putative mutants compared to our database of normal behavioral sleep-wake states of C57Bl/6J mice. Among these interesting putants, 19 were short sleepers (low total sleep / high W%), 3 showed virtually no wake, 18 exhibited high QS% and low AS% and 27 had high AS% and low QS%. These putants are currently being bred to obtain second generation progeny (G2). At present, G2 offspring of two different selected G1 pups showed the same sleep-wake abnormalities as pups that were seen in their parents (short sleeper phenotype), with about a 50-50 ratio per litter.

Conclusions: Ultimately we plan to screen 5,000 G1 pups for sleep-wake alterations and to test for genetic inheritance and adult sleep-wake phenotype in all putant animals. At the completion of this mutagenesis and phenotypic screening program, we anticipate having generated a number of lines of animals in which a single gene mutation will have induced pronounced changes in neonatal and/or adult sleep-wake phenotypes; animals which can be used to uncover novel genes/alleles that are involved in the physiology and pathophysiology of sleep-wake regulatory mechanisms.

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1063.T

Characterization Of The Hypocretin/Orexin Ligand And Receptor Loci In The Zebrafish

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Introduction: Hypocretins (also known as orexins) are neuropeptides involved in sleep regulation and energy balance, and are implicated in the sleep disorder narcolepsy. To understand the development of this highly evolutionarily conserved system we have characterized the hypocretin ligand (zHcrt) and receptor (zHcrtR) loci in the zebrafish Danio rerio.

Methods: Zebrafish Bacterial artifical chromosome (BAC) clones containing zHcrt were isolated from the Genome Systems and CHORI BAC libraries through a two tier strategy using low stringency hybridization using pufferfish probes encoding STAT3, STAT5 and BEC2 (which are in close proximity to hypocretin in mammals and pufferfish), followed by hybridization with pufferfish hypocretin probes. zHcrtR BAC clones were identified using low stringency hybridization with pufferfish HcrtR probes. Exon structures were determined through direct DNA sequence of BAC DNA and subclones, and confirmed through sequence analysis of cDNA clones obtained through 3' and 5' RACE or rtPCR.

Results: Eight zHcrt BAC clones, and 8 zHcrtR clones were identified. The ligand and receptor loci in zebrafish have exon intron structures similar to those known in mammals xenopus and pufferfish, and zHcrt is in a region of locally conserved synteny (within 5 kb of BEC2 as in other animals). The zHcrt locus displays polymorphic variation between strains. The fish preprohypocretin protein is highly diverged compared to xenopus or mammals, displaying an insertion of 16 amino acids within the encoded Hcrt-1 peptide. Overall, conservation is primarily restricted to those residues of known functional importance at the C termini of each of the two hcrt peptides. The single zebrafish receptor locus is highly conserved with the hypocretin receptor genes in mammals and with the single receptor in pufferfish, but shows relative divergence at the N-terminal 35 amino acids and, as in pufferfish, is truncated for the last C terminal 20 amino acids compared with the human HcrtR2 sequence. Localization of zHcrt mRNA expression is consistent with that described in other animals (see Gaus et al.,APSS 2003).

Conclusions: The hypocretin/orexin system is evolutionarily conserved down through fish. These results provide the basis for conducting forward genetic experiments to identify genes required for the development and function of the hypocretin/orexin system.

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1064.T

Transitions from Short Rem Sleep Episodes, Revealed in Kv3.1/3.3 Mutant Mice, Correlates with High Wake-Sleep Turnover in a Subpopulation of Wild Type Individuals

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Introduction: Kv3.1 and Kv3.3 are potassium channels commonly co-expressed in fast-spiking gabaergic neurons throughout the brain including sleep-wake related structures. We recently reported (Espinosa et al., APSS abstract ,2002) a dramatic sleep loss in the Kv3.1/Kv3.3 double-knockout (DKO) mouse due to slow wave sleep (SWS) bouts 45% shorter than those in wild type mice. Episode-duration histograms revealed that Kv3.1/Kv3.3 DKO mice also has a bimodal distribution of REM period lengths with a selective (80%) reduction of short REM sleep episodes (< 60 seconds). To start exploring this issue, in the present work we asked the question weather a subset of wild type littermates also show bimodal REM sleep distribution.

Methods: Male DKO (n=10) and wild-type (n=15) mice were instrumented for chronic sleep recording (cortical and hippocampal EEG, and nuchal EMG). The records were visually scored in 15-sec epochs. Due to the fact that DKO mice and a subgroup of WT littermates show a high frequency of short SW sleep episodes that alternate with wake episodes (sleep-wake bursts, (swb)), we divided the wild type population in three subgroups: a high swb group with an SWS to wake (S-W) shift higher than 1.5 s.d. from the average, a low swb group with a S-W shift-rate lower than 1.5 s.d. from the average, and a remaining middle swb group (not used for the analysis).

Results: Compared to the low swb group, the high swb group shows a 44% reduction of short REM sleep episodes during the light period. Moreover, the proportion of episode-shifts from REM to SWS is also similar between DKO mice and the high swb group. In both cases 20% of short REM sleep episodes shift to SWS whereas in the low swb group it is 80%. In relation to the state shift of long REM episodes, a high proportion of them (almost 100% in WT and > 80% in DKO mice) is followed by wake, whereas in the low swb group no 'preference' seems to be present (50:50).

Conclusions: A subgroup of wild type mice selected for their high turnover of wake to sleep bursts shows similar behavior to DKO mice in REM sleep distribution and in state shifts of their short and long REM sleep episodes. These results suggest that the mechanisms responsible for the generation of short and long REM episodes are similar in both

genotypes and that the bimodal distribution of REM sleep durations is favored in the DKO mouse by the lack of Kv3.1/Kv3.3 channels.

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1065.T

Is it Time to Pay Attention to Octapeptide Repeat Deletions in Prion Diseases?

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Introduction: Meanwhile insertion mutations in the octapeptide repeat region cause prion disease, deletion mutation in the same region does not (Sy MS et al. Med. Clin. of North America 2002;86(2):1-17). However recent evidence in rats showed that although the octarepeat sequence is not essencial for sustaining prion replication and disease, it modulates the extent of these events and of disease presentation (Flechsig E. et al. Neuron 2000, 27:399-408). A novel disease mechanism, two-octapeptide repeat deletions, supports and extend this assumptiom showing progressive dementia consistent with Creutzfeldt-Jakob disease in an elderly woman (Beck JA et al. Neurology 2001; 57:354-356). This finding suggest that octapeptide repeat deletions could be causally related with the expression of prion diseases. In this presentation a peculiar sleep pattern previously reported in a patient with FFI will be reanalyzed in the light on this new molecular genetic evidence (Garay A. et al. Neurology 1994; Supl.2:218-219; Reder AT et al. Neurology 1995; 45:1068-1075). Since the understanding of the pathophysiology of the sleep disorder, the pathogenic mechanisms involved in neuronal loss, and the penetrance of the disease are still unresolved issues of FFI (Cortelli P. et al. J Sleep Res 1999; 8(S1):23-29; Delisle MB et al. Clin. Exp. Pathol. 1999; 47(3-4): 176-180), the findings reported here could help to re-evaluate the impact of the pathogenic PrP on sleep and over the course of the disease.
Methods: We analyzed extensively both, day and night polysomnograms (PSGs) totaling over 100 hours performed in a patient with proven FFI between 4 to 1 months prior to death. Interestingly, in addition to typical prion mutations, D178N-129M, this patient had a 24bp deletion in the R3 to R4 region of the octapeptide coding repeats between codons 51 and 91.
Results: Total Sleep Time (TST) was reduced to 8.3± 3.8% of Total Recording Time (TRT); aREMs onset (6/6 PSGs) and aREMs preceeding aSWS (3/6 PSGs) were observed during these studies. The aSWS consisted mostly of low amplitude theta and delta patterns without sleep spindles. After IRB approval, the patient received gamma-hydroxybutirate (GHB) which produced a very significant increase of TST but did not affect the aREM-aSWS sequence. This new "sleep" had an ultradian periodicity. A significant improvement of mental status and alertness was also observed .
Conclusions: 1) These atypical findings, not reported in other studies of FFI, suggest that one-octapeptide deletion may have a role in the expression of the altered sleep patterns; 2) The unanswered question of whether one-octapeptide repeat deletion or two-octapeptide repeat deletion may be causally related on a different expression of the pathogenic PrP linked to this polymorphism should be considered.

1066.U

Hospital Staff Nurse Work Hours and Patient Safety

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Introduction: Recent studies have found that hospital staff nurses report stressful working conditions associated with increased numbers of acutely ill patients, inadequate staffing, and prolong work hours. Although a few states restrict mandatory overtime for nurses, but there are no limits on the number of hours a nurse may voluntarily work in a 24-hour period, or over a seven-day period. Since there is very little information about the work patterns of hospital staff nurses and their effect on patient safety, a large national study was undertaken to assess among other things what the relationship was between the occurrence of errors and the hours worked by hospital staff nurses.
Methods: Three hundred ninety-one randomly selected nurses participated in this study. The majority of participants were female (93.2%), middle-aged (44.5 ± 9.2 years), and all worked at least 36 hrs/week. Data collected for 28 consecutive days included information about the participants' sleep, mood, scheduled work hours, actual work hours, errors and near-errors, episodes of drowsiness and actual sleep on duty, and difficulties driving home due to drowsiness. Nurses also recorded when they worked overtime, whether the overtime was mandated or voluntary, and why the overtime was necessary.
Results: Approximately 48% of the participants reported working overtime more than 10 days overtime during the 28-day data-gathering period, and about 40% of the subjects reported being mandated to work overtime at least once. There were 201 actual errors and 198 near-errors reported. Approximately 1/4 of the nurses reported making at least one error, and just under half the nurses reported catching themselves before they made an error. Almost 60% of the errors and near-errors involved medication administration.The risk of making an error was 1.67 times greater when the nurse worked ³ 12 hours (95% confidence intervals [CI]= 1.25-2.23), and more than double if the nurse worked overtime (odds ratio 2.11; 95% CI=1.32-3.37). Risks of near-errors were also significantly increased when nurses worked ³ 12 hours or overtime.
Conclusions: Errors and near-errors are more common than previously reported, with over 200 errors reported in a 28-day data-gathering period. If this error rate is reflective of the nurses' usual practice, then this sample of 391 staff nurses could make up to 2400 errors in a year. Since the risks of error are higher when nurses work shifts of >= 12 hours or overtime, fatigue is likely to be a major contributor to the errors made by hospital staff nurses.

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1067.U

The Effects of Tai Chi Training on Self-Rated Sleep Quality in Older Adults: A Randomized Controlled Trial

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Introduction: Elderly individuals often suffer from disturbed sleep such as frequent nocturnal awakenings or early morning arousal (Foley et al., 1995). The consequences of chronic sleep problems can be considerable with significant medical, psychological, and social disturbances (Vgontzas & Kales, 1999). Sleep disorders thus contribute significantly to declines in health and well-being and should be considered an important aspect of overall quality of life. Many researchers have recommended daily exercise as a sleep-promoting treatment (Neubauer, 1999; Vgontzas & Kales, 1999). One exercise modality suitable for older adults, is Tai Chi. Tai Chi is often performed in a slow, rhythmical manner, involving a sequence of movements (postures), linked to calm, controlled diaphragmatic breathing which facilitates feelings of relaxation and quiet concentration. These characteristics have the potential to enhance well-being and improve sleep. Tai Chi may also modify circadian rhythms (Ancoli-Israel et al., 1997; Neubauer, 1999) in a manner beneficial to improved sleep quality. This randomized controlled trial was designed to examine the effects of a simple Tai Chi program, in

comparison to a conventional, low-stress physical activity, on improving the quality of sleep among elderly individuals. It was hypothesized that, in comparison to the exercise control condition, Tai Chi would significantly improve self-reported sleep quality measures over a 3-month intervention.
Methods: A total of 80 community-dwelling participants aged 60 or over, with self-reported moderate sleep complaints and without involvement in any structured exercise programs 3 months prior to the study, were recruited and randomly assigned to a Tai Chi group (n = 40) or a low-stress physical activity control group (n = 40), which exercised 3 times per week, 60 minutes per session for 3 consecutive months. The Tai Chi training involved a set of static and moving Tai Chi movements drawn from the traditional Yang Style. The low-stress group involved exercise activity of mild stretching and light movements coupled with breathing and relaxation. Intervention outcomes were quality of sleep measures including the Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989) and the Epworth Sleepiness Scale (ESS; Johns, 1991) taken at baseline and post-intervention.
Results: No significant differences were found in participants on major baseline characteristics between the two experimental groups. With regard to outcomes, compared with exercise controls, participants in the Tai Chi training condition showed significant improvement in the PSQI subscales of sleep quality, sleep-onset latency, sleep duration, habitual sleep efficiency, and sleep disturbances, as well as ESS scores ($P < .05$).
Conclusions: The findings from this study indicated that older adults with moderate sleep complaints can improve their self-rated sleep quality through a Tai Chi program.

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1068.U

Effects of Three Watchstanding Schedules on Submariner Sleep Physiology

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Introduction: This U.S. Navy study focused on the watchstanding-schedule aspects of quality of life, personnel retention and submarine system performance.
Methods: Nine male Navy submariners experienced 144 h each of three watchstanding schedules: the 18-h, submarine (S) watch schedule (6-on, 12-off), the traditional, maritime (M) watch schedule (4-on, 8-off) and an alternative, compressed (A) watch schedule (6-on, 6-off, 6-on, 12-off, 6-on, 6-off, 6-on, 24-off) in the order, A, M and S. They spent 24 h stabilizing in the lab, 144 h on one watch Schedule, then 24 of recovery time in the lab. They spent 6 d off between these 8-d sessions. Sleep patterns were monitored with wrist activity monitors for 72-h periods before and after each session.
Results: During the second 72-h period of watchstanding, there was a significant effect of the Schedule factor on Total Sleep Time (TST): TST was significantly greater during A than during M and S. The participants acquired 2.7 and 4.0 hours more sleep across the 72 hours of A than M and S, respectively. The A was also the only schedule in which 7.0 h per 24 h of TST was achieved. There were no significant effects of schedule on sleep latency or the relative amounts of S1, S2, S3, S4, wake or REM. Salivary cortisol and melatonin results were consistent with the polysomnography observations. One night of ad lib recovery-sleep data were available from six participants. Percent S3 was significantly greater during M than S and A, and significantly greater during S than A. Conversely, %S2 was significantly greater during A than M and S.
Conclusions: Sleep quality was approximately equal across the three schedules and more sleep was acquired in A. A created the lowest need for recovery slow-wave sleep (S3). We learned more from the physiological measures used in this study than from the performance or subjective measures. We combined the results of this study with information available in the research literature about submarine watchstanding schedules, dating as far back as 1949. As a result, the A and several other schedules were recommended for further study in sea trials and for use in 24-h operations in geographically-confined, limited-crew-number situations.

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1069.U

Hospital Staff Nurses Regularly Report Fighting to Stay Awake on Duty

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Introduction: Although the hazards associated with sleep deprived house staff have been examined in over a dozen studies, little attention has been paid to the relationship between staff nurse fatigue and patient safety. Scheduled shifts may be 8, 10, or 12 hours, and sometimes even longer. Encouraging or even mandating overtime is not an uncomman practice for hospitals struggling with high patient acuities and insufficient numbers of registered nursesOne goal of this national study was to collect data about the hours currently worked by hospital staff nurses and to determine if nurses working extended shifts and/or overtime were more likely to have difficulties remaining awake on duty.
Methods: Three hundred ninety-one randomly selected nurses participated in this study. The majority of participants were female (93.2%), middle-aged (44.5 ± 9.2 years), and all working at least 36 hours/week. The majority of participants were married or living with a significant other (72.8%), and 46% had children under 18 years of age living at home.Data collected daily for 28 consecutive days included information about participants' sleep, mood, scheduled work hours, actual work hours, errors and near-errors, episodes of drowsiness and actual sleep on duty, and difficulties driving home due to drowsiness. Nurses also recorded when they worked overtime, whether the overtime was mandated or voluntary, and why the overtime was necessary.
Results: All nurses reported working longer than scheduled at least once during the 28-day data-gathering period, and 241 nurses (62%) reported working longer than scheduled on more than 10 days. Almost a quarter of the sample (22%) reported working for periods of 16 hours or more, and several nurses reported working three or four double (16-hour) shifts in a row. Data collected about 5282 work shifts revealed that one-quarter of the shifts (n=1320) exceeded 12 hrs 50 minutes. The longest scheduled shift was 22 hrs 30 minutes and the longest duration worked in a single day was 23 hrs 57 minutes. The majority of nurses (67.9%) reported struggling to stay awake at work at least once, and almost one-quarter of the participants (22.1%) actually fell asleep on duty. Although most reported drowsiness or falling asleep on duty only once during the four-week period, 70 nurses (17.9%) reported difficulties staying awake on more than 5 occasions, and 15 nurses reported falling asleep on more than 5 occasions.Drowsiness and falling asleep on duty was not confined to nurses working at night. Slightly more than half the episodes of drowsiness (n=502), and approximately one-third of the the episodes of falling asleep on duty (n=78) occurred between the hours of 0600 and 2400.

Conclusions: Although some drowsiness was expected among nurses working at night, the large numbers of nurses working during the daytime who also had difficulties remaining awake on duty was not expected.The number of nurses reporting difficulties remaining awake at work represents a serious risk to patient safety. Nurses cannot provide safe care for their patients, or recognize potentially dangerous errors in medications orders if they are struggling to stay awake.

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1070.U

Relationships Between Attachment Styles and Sleep Patterns

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Introduction: John Bowlby's attachment theory attempted to explain relationships between children and their caregivers and how this bond influenced subsequent personality development. Attachment styles and sleep patterns are conceived as developmentally organized systems. Yet, few studies have explored the link. Consistent with the observation that individuals with differing personality types exhibit differential sleep patterns, one might assume that persons with varying attachment styles might also show differential sleep patterns and might be more or less likely to report sleep complaints. This study sought to investigate the relations between attachment styles and sleep patterns in an older adult sample.
Methods: Seventy Blacks (59%) and Whites (41%) participated in the study; 73% were women and 27% were men. Their average age and BMI were 68.27 $\pm$ 5.97 years and 27.68 $\pm$ 5.72 kg/m2. Physical health was assessed with the Comprehensive Assessment and Referral Evaluation (CARE). Sleep complaints were assessed with the vision subscale of the CARE (a = 0.49). Additionally, sleep quality was obtained with the Pittsburgh Sleep Quality Index. Participants also wore an actigraph (Actiwatch-L, Mini Mitter Co., Inc., Sunriver, OR) at home to monitor sleep-wake activity for a week, yielding data on total sleep time, sleep onset latency, sleep efficiency, and a sleep fragmentation index. Attachment was measured utilizing the Relationship Style Questionnaire (RSQ). The RSQ consists of a 30-question, 5-point Likert scale, four-subcategory model from which secure (a = 0.54), preoccupied (a = 0.49), dismissing (a = 0.53), and fearful (a = 0.57) were derived.
Results: Partial correlations were used to assess associations between attachement styles and sleep patterns, controlling for ethnicity, age, sex, BMI, education, and income. These analyses showed that individuals scoring high on the preoccupied attachment dimension reported daytime napping (rsps = 0.33, $p < 0.05$) and took more sleep-inducing medications (rsps = 0.36, $p < 0.05$); a trend was also observed suggesting lower sleep duration among these individuals (rsps = -0.26, $p > 0.05$). Individuals scoring high on the dismissing attachment dimension demonstrated lower actigraphic onset sleep latency (rsps = -0.31, $p < 0.05$); a trend was noted suggesting greater sleep duration among these participants. No significant correlations were found for the secure and fearful dimensions, although individuals scoring high on the secure dimension may have had little difficulty initiating sleep (rsps = 0.23, NS).
Conclusions: The finding that individuals scoring high on the dismissing attachment dimension fell asleep faster suggests that they might ruminate less over problems, which is often observed among persons with insomnia. Conceivably, individuals scoring high on the preoccupied attachment dimension may have been taking sleep-inducing medications to improve their sleep. It remains unclear whether individuals napped more because they were preoccupied with life events or as a residual effect of sleep medications. Future studies are needed to broaden our understanding of the relationship between attachment styles and sleep patterns.

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1071.U

Sleep Characteristics of 40-45 year old Short, Medium and Long Sleepers in a Norwegian County

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Introduction: In a recent study from USA it was reported that subjects who slept between 6.5 and 7.5 hours per night had lower mortality rates than both shorter and longer sleepers. We studied sleep characteristics of short (less than 6.49h), medium (6.50h to 7.49h) and long (more than 7.50 h) sleepers in a material collected on 40-45 year olds in Hordaland county, Norway.
Methods: The study population included all individuals in Hordaland county born 1953-57 (29.400). A subgroup of 8860 persons (3531 men and 5329 women) answered a questionnaire with detailed information on sleep habits and problems. Sleep length was defined as reported rise time minus bedtime minus sleep latency. Subjects reporting shiftwork or being on call were excluded. Thus data from 2337 men and 3183 women were complete enough to be included in this material. Subject scored Morningness-Eveningness on a 5 point scale (clearly morningness =1, clearly eveningness =5), Sleep Satisfaction on a 5 point scale from very good =1 to very poor =5, and Sleepiness and Difficulty sleeping on a 5 point scale from never =1 to always =5.
Results: 569 men (24 %) and 485 women (15 %) were short sleepers, 1221 men (52 %) and 1484 women (47 %) were medium sleepers while 547 men (23 %) and 1214 women (38 %) were long sleepers (gender diff. Chi square $p< 0.0001$).Mean subjective sleep need reported by male short sleepers was one hour shorter than sleep need reported by long sleepers: 6.74 h (decimals), 95 % confidence interval 6.66-6.82, vs. 7.71 (7.66- 7.78)h, the medium length sleepers reporting intermediate values: 7.29 (7.25-7.33)h. Women in all three categories reported higher subjective sleep need than men in the same category: short sleepers 7.40 (7.30-7.50)h, medium length sleepers 7.65 (7.61-7.69)h, long sleepers 8.03 (7.98-8.07)h. Sleep latencies were significantly longer in short sleepers than in long sleepers (men 21.6 min vs. 15.6 min; women 30.0 min vs. 15.8 min). In medium length sleepers latencies were 15.8 min (men) and 17.1 min (women). Both male and female short sleepers scored significantly higher on the morningness-eveningness scale (more eveningness) than long sleepers. Male medium length sleepers did not differ from long sleepers in this respect, while women medium sleepers had an intermediate score. The scores for sleepiness and difficulty sleeping were significantly higher in short than in long sleepers in both genders and higher in women in all categories. Sleep satisfaction was higher in the medium and long sleepers that in the short sleepers of both genders but did not differ between the medium length and long sleepers.
Conclusions: Short sleepers differ from intermediate and long sleepers on several sleep characteristics. They report lower sleep need, longer sleep latency, more sleepiness and more difficulty sleeping. They are less satisfied with their sleep, and they tend to be evening persons.

1072.U

Cholinergic Activation of the Phasic Pontine-wave (P-wave) Generator Enhances Improvement of Learning Performance in the Rat

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Introduction: Recent studies have indicated that the well-documented

improvement in performance on learning tasks after REM sleep is due to increased P-wave generator activation during post-training REM sleep. However, no studies have yet determined the consequences of supplemental activation of the brainstem P-wave generator in relation to memory processing and improvement of learning. The aim of this study was to test the hypothesis that supplementary activation of the P-wave generator during REM sleep enhances consolidation and integration of memories, resulting in improved learning.

Methods: Experiments were performed on 18 male Sprague-Dawley rats, weighing between 300 and 350 g. To objectively measure states of sleep and wakefulness, rats were chronically implanted with electrodes to record cortical EEG, neck muscle EMG, EOG, hippocampal theta wave, and P-waves. In addition, a stainless steel guide tube was implanted for control saline or carbachol microinjections into the P-wave generator. After recovery and habituation trials, rats were trained on a two-way active avoidance learning task in the morning. Immediately after training, one group of rats received a carbachol microinjection into the P-wave generator, and the other group was microinjected with control saline into the same target area. After training trials and microinjections, rats were allowed a six-hour period of undisturbed sleep in the polygraphic recording chamber. At the end of six-hours of undisturbed sleep-wake recordings, rats were retested in a session of avoidance learning trials.

Results: After learning trials, the total percentage of time spent in REM sleep was significantly increased in both saline (15.36%) and carbachol (17.70%) microinjected rats. After learning trials, REM sleep P-wave density was significantly greater throughout the six-hour period of recordings in carbachol treated rats compared with the saline treated rats. In the retrial session, the improvement in performance was 22.75% higher in the carbachol-microinjected rats compared to the saline microinjected rats.

Conclusions: These findings show that the consolidation and integration of memories create a homeostatic demand for P-waves. In addition, these findings provide experimental evidence, for the first time, that supplemental activation of the P-wave generator may further enhance consolidation and integration of memories, resulting in greater improved performance on a recently learned task.

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1073.U

Post-training REM Sleep Deprivation-induced Learning Impairment in the Rat Can be Prevented by Activation of the Pontine-wave (P-Wave) Generator

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Introduction: Sleep and learning studies in animals and humans have demonstrated that post-training REM sleep deprivation can partially or even totally block improved task performance on subsequent retesting. In an earlier study, we demonstrated that learning trials increase P-wave density and that the improvement of learning performance in the retest session is proportional to the increased P-wave density in the post-trial REM sleep. The goal of the present study was to examine whether activation of the P-wave generator could prevent the learning impairment produced by post-training REM sleep deprivation.

Methods: Experiments were performed on 20 male Sprague-Dawley rats, weighing between 300 and 350 g. To objectively measure states of sleep and wakefulness, rats were chronically implanted with electrodes to record cortical EEG, neck muscle EMG, EOG, hippocampal theta wave, and pontine-waves (P-wave). In addition, a stainless steel guide tube was implanted for control saline or carbachol microinjections into the P-wave generator. After surgical recovery, habituation, and baseline recording, experimental recording sessions began. During the experimental recording day, all rats were subjected to 30 trials of a two-way active avoidance learning task (between 9:15 and 9:45 A.M.). Immediately after these learning trials, 10 rats received control saline (50 nl) and 10 rats received carbachol (50 ng in 50 nl) microinjection into the P-wave generator. After microinjection, rats were selectively deprived of REM sleep during a six-hour polygraphic recording session (10:00 A.M. to 4:00 P.M.). REM sleep deprivation was achieved by observing the ongoing polygraphic record and awakening rats within 2-3 seconds of the onset of each REM sleep episode. At the end of the six-hour polygraphic recordings, rats were retested for 30 learning trials (between 4:05 P.M. and 4:50 P.M.).

Results: Based on the polygraphic records, our sleep deprivation technique selectively eliminated 90-97% of REM sleep. In the retest trials, rats that received the control saline microinjection (SRD) did not show any learning improvement compared to their earlier test trials. In contrast, rats that received the carbachol microinjection (CRD) showed a significant improvement ($P<0.001$) in retest trials compared to their earlier test trials and the retest trials of the SRD group.

Conclusions: The results presented here demonstrate that post-training REM sleep deprivation impairs improvement of learning performance in retest trials. Most significantly, these results demonstrate, for the first time, that activation of the P-wave generator, by carbachol microinjection, prevented the memory impairing effects of post-training REM sleep deprivation. This evidence supports our hypothesis that activation of the P-wave generator during REM sleep deprivation enhances a physiological process of memorization that naturally occurs during post learning REM sleep.

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1074.U

Influence Of Different Novel Environments On Sleep in Mice

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Introduction: Novel environments elicit anxiety and/or exploratory behaviors that may vary depending on perceived threat or danger. REM sleep is decreased in the conditioned fear model of anticipatory anxiety (Sanford et al., Behav Genet 33: 43-58, 2003), but may be increased in paradigms involving contextual/spatial learning. C57BL/6J (B6) mice display less anxiety-like behaviors and exhibit longer lasting exploration in the open field (OF) compared to BALB/cJ (C) mice (Tang et al., Behav Brain Res 136: 555-69, 2002). B6 mice also show less reduction in REM after fear conditioning. The relative impact of anxiety and exploration on sleep is not known. We examined sleep in C and B6 mice after exposure to two novel environments (a brightly lit OF and a dimly lit enclosed chamber (EC)) that may induce different levels of anxiety while providing an opportunity for exploration.

Methods: Mice were implanted with transmitters (DataSciences ETA10-F20) for recording sleep via telemetry. After 48 hr baseline sleep recording, C (n=6) and B6(n=3) mice were exposed for 25 min to OF under normal room illumination (100 lux). Different C (n=5) and B6 (n=5) mice were exposed for 30 min to EC under lower illumination (< 10 lux). Both exposures were made 2 hr following lights on, and sleep was analyzed over the subsequent 10 hr. Wakefulness, NREM and REM were visually scored in 10 s epochs based on EEG and activity.

Results: C mice exposed to OF showed decreased REM over the subsequent 6 hr (-34% ± 5.8, p = .03), followed by a non-significant increase in REM over the next 4 hr (+32% ± 17, p = .09). B6 mice exposed to OF exhibited decreased REM for 3 hr (-40% ± 7, p = .05), followed by a non-significant increase in REM over the next 7 hr (+40% ± 23, p = .20). C mice exposed to EC exhibited reduced NREM (p=.002) and REM (p=.0002) in the first hr. A non-significant increase in REM that last approximately 4 hr was observed beginning after the 5th recording hr

(+56% ± 23, p = .09). B6 mice exposed to EC did not show decreases in either REM or NREM. Increases in REM were observed after 3 hr and lasted for 5 hr (+39% ± 16, p = .03).
Conclusions: Compared to B6 mice, C mice exposed to OF displayed longer periods of decreased REM, followed by shorter periods of relatively increased REM. After exposure to EC, reductions in sleep occurred only in C mice. Thus, both OF and EC appear to produce greater fear or anxiety in reactive C mice as indicated by greater REM suppression. The results suggest that the relative level of anxiety induced by an environment can influence the amount of exploration and the potential effects it has on sleep.

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1075.U

Influence Of Shock Training And Cued Fear On Sleep In Two 129 Mouse Strains

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Introduction: Mice of the 129 "family" are widely used in neuroscience research, particularly for the creation of gene "knockout" animals. However, there is considerable genetic variation among 129 strains, in particular between the 129X1/SvJ strain (129X1, formerly 129/SvJ) and related substrains compared to other 129 strains (e.g., 129P3/J (129P3, formerly 129/J)). The 129 strains also differ in measures of anxiety and may have low shock-avoidance learning. In conditioned fear, shock training (ST) and fearful cues (FC) associated with shock produce significant alterations in sleep. The alterations are mainly reductions in REM that are greater in more "anxious" animals. In this study, we examined sleep during baseline, after ST and after FC in 129P3 and 129X1 mice.
Methods: Male 129P3 (n=9) and 129X1 (n=9) mice (Jackson Laboratories) were intraperitoneally implanted with transmitters (DataSciences ETA10-F20) for recording sleep via telemetry. Sleep was visually scored based on EEG and activity. After recovery and baseline sleep recording, the mice were trained to associate an auditory cue with footshock on 4 consecutive ST days (ST1-ST4; 15 cue-shock pairings between 0800 to 0900 h). Five days later, the FC was presented to the mice in their home cage (prior to 1100 h). Sleep was recorded after ST and after FC. For analyses, ST data were divided into two 5-h Blocks (10 h light period recording) and three 4-h Blocks (12 h dark period recording). Sleep after FC was divided into five 4-h Blocks (8 h light period, 12 h dark period).
Results: In baseline recordings, 129P3 mice showed significantly less total sleep, less total NREM, fewer NREM episodes, less total REM and fewer REM episodes. Strain differences were observed mainly in dark period sleep. ST did not significantly alter NREM in either strain. In 129X1 mice, REM was significantly reduced during Block 1 on ST1 (total REM) and ST2 (total REM and REM%). In contrast, 129P3 mice exhibited reduced total REM and REM% during Block 1 on all training days. The FC produced a significant reduction in total REM during Block 1 in 129X1 mice and in total REM and REM% in 129P3 mice. After FC, NREM was reduced during Block 1 in 129X1 mice, but was not significantly altered in 129P3 mice.
Conclusions: There are significant differences in the baseline sleep of 129P3 and 129X1 mice. There are also strain differences in the effects of ST and FC on sleep. REM in 129X1 mice appeared to be more resistant to the effects of ST since it returned to baseline levels by ST3. REM in the more "anxious" 129P3 mice was reduced on all ST days; however, both strains exhibited significant reductions in REM in response to FC. Reports of low shock avoidance learning and the present results suggest that 129P3 and 129X1 mice may be useful for studying shock motivated learning and its relationship to sleep.

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1076.U

Cosleeping in School-aged Children

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Introduction: Cosleeping, the practice of parents and children sleeping together in body contact for all the night, is quite common in families with young children, mainly suffering from sleep disorders. Since few studies were specifically addressed to study cosleeping in this age group, we decided to investigate prevalence and predictors toward this sleep practice in a non clinical population.
Methods: We studied 1030 healthy children attending 5 public schools in the urban area of Rome. Parent reports on Children's Sleep Habits Questionnaire (Owens, 2000) and Child Behavior Checklist (Achenbach, 1991) were used to assess children's sleep and behavioral problems. Demographic information (age, sex, parity, marital status, SES), previous and current child's sleep problems, sleeping arrangements were collected. Unpaired t-test or Chi-square were used to test for groups (cosleepers vs solitary) as appropriate. To assess predictors of cosleeping logistic regression was perfomed.
Results: Data were available for 901 children (481 F 420 M, aged 6.1 –11.9; mean 8.4) Five per cent (3.1% F, 1.9% M) regularly has been cosleeping on average for 6,4 yr (range 4-10). Children started cosleeping at a mean age of 17 months (3-24). Prevalence of cosleeping declined with age during childhood (7,9 % at 6-7 and 3,5% at age 10-11 yr; p<001). Cosleepers reported more sleep problems before age 3 years than solitary sleepers (80% vs 20%; p<.001). Furthermore, cosleeping is more frequent in one-parent families (35% vs 9%; p<.001), in families with at least one parent shiftworker (35% vs 4%; p<.001) or who had coslept as a child (37% vs 6%; p<.001.Cosleepers rated higher on CSHQ (total score 61 vs 45; p<.001), Bedtime Resistance (15 vs 7 p<.001), Sleep Anxiety (10 vs 4 p<.001), Nightwakings (4 vs 3 p<.001) and Parasomnias subscales (10 vs 8 p <.001) than solitary, no significant differences were found regarding sleep duration and CBCL variables. Logistic regression results (Chi square 356,1; p<0001) were highly significant resulting in 86,6% classified correctly. Particularly, results showed that low SES (OR 3.72; p<.001), parent shifworker (OR 0.12; p<0.1), one-parent families (OR 11.5; p<.001) parent cosleeper as a child (OR 0.15;p<.01) prolonged breastfeeding (OR 0.52; p<.01), sleep problems before age 3 years (OR 1.61; p<.01), current sleep problems (CSHQ OR 0.48; p<01) significantly predicted cosleeping, while sex, parity, CBCL were not related to bedsharing.
Conclusions: Our results showed a relative high incidence of regular and long-lasting cosleeping in school-aged children. As already reported, cosleeping was significantly related to child's previous and current sleep problems, on the other hand the highest incidence of parents reporting having coslept as a child, suggests also a lifestyle choice. No significant behavioral problems were found in children cosleeping. Therefore bedsharing seems to reflect a parents' way to cope with sleep problems and the long persistance of this practice may be related to a lifestyle of families.

1077.U

Sleepiness in a Brazilian Truck Driver Population: Contributing Factors and Impact on Driving Performance

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Introduction: In Brazil, there are few data about sleepiness and the risk of road traffic accidents, specially regarding truck drivers.This study is

a part of a research project developed to determine the prevalence of sleepiness in a truck driver population in the South of Brazil, identify the contributing factors for sleepiness and its impact on driving performance.
Methods: Cross sectional study consisted of an application of a self-administrated questionnaire and the Epworth Sleepiness Scale(ESS). The questionnaire was composed of questions regarding professional data, sleep habits, nighttime symptoms, excessive daytime sleepiness and history of automobile accidents.
Results: A hundred eighty- two male drivers, age(mean ± sd) of 34.1 ± 9.6 years, were studied. Mean driving hours a day was 9.5pm 2.7 hours, mean driving hours at night shift was 4.3 pm 2.4 hours. Median distance performed weekly was 1200 kilometers(range 700 to 3000 kilometers). The ingestion of wake- promoting and sleeping pills was reported in 5% and 2% of participants, respectively. The most common sleep complaints were insomnia (31%), loud snoring (42%) and witnessed apnea (8%). Forty of 160 drivers (25%) reported fall asleep eventually while driving, 4 drivers (2.5%) reported fall asleep daily or almost daily. Seventy five drivers (41%) had been involved in a traffic accident, and 9 of 52 drivers (17%) indicated sleepiness as a contributing factor. The ESS was above 10 points in 57 (31%) of the interviewers.
Conclusions: The present data demonstrated that sleepiness is a prevalent symptom in a truck driver population in South of Brazil and is possibly related to accidents.

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1078.U

Gender Differences in Sleep-Wake Pattern and Daily Social Rhythm During Japanese Childbearing Family Transition
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Introduction: Although it is well known that the crucial period for disturbance in sleep-wake patterns in childbearing women is the first few months after delivery, few studies have focused on couples. Sleep patterns have been addressed in a few studies, but even fewer have examined how daily activities of women and men are altered by transition to parenthood. The purpose of this longitudinal study was to describe gender differences in sleep-wake patterns, daily social rhythms, and chronotype at 32-36 weeks of pregnancy compared with 4-5 weeks after the birth of their first child.
Methods: Data were collected from 62 healthy Japanese couples recruited from four maternal outpatient clinics in Kansai area of Japan and screened for medical, psychiatric, obstetrical complications. Couples completed a 7-day sleep/wake log to obtained sleep/wake pattern, and each recorded their activities and events every 15 minutes during the day. Autocorrelations (Ar) were calculated from the recorded bedtime and wake time daily with a 7-day lag. Daily social rhythm was measured with Monk's Social Rhythm Metric (SRM) and scores could range from 0 (no regular rhythm) to 7 (highly regular rhythm). The Morningness-Eveningness Questionnaire in Japanese (MEQ-J) was used to estimate chronotype; scores can range from 16 (definitely evening type) to 86 (definitely morning type). Repeated measures ANOVA tested between-subject differences by gender (mothers and fathers) and within-subject changes over time (pregnancy and postpartum) in Ar, SRM, and MEQ-J. Significance was set at $p < 0.05$.
Results: The age ranges for women (30 + 3.9 yrs) and men (M=31 + 4.6 yrs). Most (89%) were nuclear family structure. Feeding style were breast-feeding (47%), bottle feeding (6%), and mixed feeding (47%). Sleeping arrangements (who slept together with infant in the same room during postpartum) were varied: couple (53%), only women (24%), mixed during one week with couple or only women (16%), women and her own mother (5%), and infant only (2%). At both times, women's MEQ-J scores (55+8.07 and 53+9.1, respectively) were higher than men's (51.8+10.1 and 50.5+8.6, respectively); however, the differences were not significant (F = 3.6, p=.06). There was a gender-by-time interaction for Ar (F=5.3, p=0.02) with a lower Ar from pregnancy to postpartum (.56 to .38) for women but no change for men (.52 to .50). Women had a significant decrease in SRM from pregnancy to postpartum (3.6 to 3.3) but SRM increased significantly (3.6 to 4.1) for men (F=6.9; p=0.009).
Conclusions: The baby's birth had more disruptive effects on women's sleep-wake patterns and social rhythms than men's. Even though over half of the men slept with their infants, their sleep-wake patterns were not as disrupted as the women's. If anything, their social rhythms improved after the baby was born.

1079.U

Poor Driving Simulator Performance and Increased Alpha EEG Activity in Night and Day Hospital Shiftworkers
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Introduction: The National Sleep Foundation states that the population of shift workers are at risk for drowsy driving (2002). Total sleep time for night shift workers is typically reduced by 2-4 hours (Akerstedt, 1985). Gold et al. (1992) surveyed hospital nurses and found that night nurses and rotating nurses were more likely than day nurses to report nodding off at work and at the wheel. For this study, we examined performance differences between day shift and night shift hospital workers. We hypothesized that 1) night-shift workers, due to less sleep and possibly a circadian rhythm disturbance, would overall have greater lane position variability and greater alpha activity, and 2) the lane position variability and alpha activity would increase during the hour-long simulated drive.
Methods: The STISIM driving simulator, designed by Systems Technology, was used in this study. Participants included ten day shift workers and ten night shift workers, all hospital employees, between the ages of 18 and 35. The sample was comprised of 5 males and 15 females. Participants possessed a valid driver's license and had normal vision, or vision corrected to normal. Subjects were asked not to consume any nicotine or caffeine 3 hours prior to the drive. Following a 10-minute practice drive, participants completed a 1-hour highway-driving scenario between the hours of 1530 and 1700. We recorded relative EEG powers of alpha, theta and beta and lane position variability (ft). These measures were sampled continuously throughout the task and grouped data into 10-minute blocks.
Results: We computed a 2 (group) x 6 (time) ANOVA with repeated measures for time. Lane position variability increased during the drive, [F (1,90) = 2.589, p = .031], as did alpha activity [F (1,90) = 3.262, p = .009]. Lane position variability increased from a mean of 1.02 feet (SD = .26) to a mean of 1.40 feet (SD = 1.42). Alpha power increased from a mean of .085 (SD = .03) to a mean of .098 (SD = .04). There was no significant group effect for lane position variability [F (1,5) = .490, p = n.s.] or for alpha activity, [F (1,5) = .463, p = n.s.]. There was no group by time interaction for either measure.
Conclusions: The increase in lane variability and alpha activity over the simulated driving task indicates the presence of fatigue both in night and day shift workers. In other studies with highly selected control groups, neither lane variability nor alpha activity increased over time for the control groups (Risser et al., 2000, Freeman et al., 2002). This suggests that hospital day shift workers also accumulate a sleep debt from cramming a week's worth of work into 3-4 long days. Follow-up with sleep logs and actigraphy and comparison to other industries will help answer this question.

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1080.U

Experience-Dependent Reactivation of Declarative Memories During Human Slow Wave Sleep

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Introduction: Sleep is implicated in the plastic changes that underlie learning and memory consolidation. Accordingly, we have reported using positron emission tomography (PET) that the brain structures engaged in the implicit learning of a sequential material are re-activated during the subsequent REM sleep in healthy volunteers (Nature Neurosci. 2000 3:831-6). A further hypothesis is that experience-dependent cerebral reactivations predominate in different stages of sleep as a function of the nature of the prior learning process. Here, we predicted that explicit topographical learning would modulate regional cerebral blood flow (rCBF) variations during post-training slow wave sleep (SWS) in hippocampal and parahippocampal regions known to be involved in spatial learning (i.e., the animal precursor of human episodic memory).
Methods: Using PET and automated infusions of oxygen-15 labeled water, three groups of healthy volunteers were scanned respectively during (I) active exploration of a complex virtual 3D maze in which numerous cues were given by the environment: walls, background music, objects, … (n=12 subjects), (II) during all stages of sleep (SWS, stage 2, REM) after extensive learning on the same virtual maze (n=6), and (III) likewise during sleep but without prior learning (n=6). PET data were analyzed (SPM99) using a random effect model to ensure inter-individual consistency.
Results: In Group I, maze exploration (vs. tracking of scrambled moving scenes) activated bilateral parahippocampal, occipital, precuneal and posterior parietal regions (p-corrected value < .05). A conjunction analysis revealed that rCBF in the right parahippocampal gyrus was both (a) increased during maze exploration (Group I) and (b) significantly different during post-training SWS in trained than untrained subjects (i.e., a Group [II vs. III] by Condition [Wakefulness vs. SWS] interaction; p < .001). Other activation sites not predicted a priori in which rCBF varied in an experience-dependent manner during SWS were found in the bilateral temporal, right middle occipital and left fusiform gyri (p-corrected < .05).
Conclusions: Experience-dependent reactivations support the hypothesis that human slow wave sleep participates to the reprocessing and consolidation of recent declarative memory traces. Added to our prior finding of experience-dependent reactivations during REM sleep after an implicit learning episode, the present results suggest that reactivation of different types of memory traces (i.e., implicit vs. explicit) might be partially sleep state-dependent (REM vs NREM).

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1081.U

Diagonal Weight Shifts During Upright Stance Are Related To Sleep Apnea And Show Diurnal Variations

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Introduction: Circadian variations in postural control can affect the level of physical and mental functioning necessary for safe and efficient performance, especially on jobs involving stress and hazard. Measurement of postural control by computerized posturography is a simple, reliable, and non-invasive method that is widely used in clinical and rehabilitative medicine. The sensitivity of postural responses to circadian changes has been demonstrated in previous investigations that focused on the assessment of postural sway. In the present study the diurnal postural changes were measured by calculation of diagonal weight shifts (DWS) between heel and contralateral toes, a parameter hitherto not employed in such context, but already validated by two unpublished pilot studies. In addition, the relationship between the postural scores and polysomnography parameters was evaluated.
Methods: Subjects were 23 drivers, referred by the ministry of transportation for evaluation of sleepiness (mean age 35; mean BMI 29) with no musculoskeletal or neurological impairments. Posture was assessed by the four-plate (Tetraxiametric) Interactive Balance System (IBS), which measures independently the vertical pressure of heel and forefoot of each foot on four separate platforms and thereby enables the assessment of DWS. The following five positions, each to be maintained for 48 seconds, were tested: standing on solid surface, platforms on level, eyes open (1) and closed (2); standing on elastic pads, platform tilted forward 8 degrees, eyes open (3) and closed (4); and as in position 4 with head tilted back approximately 30 degrees (5). This posturographic examination was given 5 times at 10:00, 12:00, 14:00, 16:00, and 18:00 on the day following a full-night polysomnography.
Results: Preliminary statistical analysis revealed that left DWS (LDWS=% weight on left heel divided by % weight on right toe) in the second and third sessions (12:00 and 14:00) were significantly correlated with respiratory disturbance index (RDI) ($p<0.01$), number of oxygen desaturations ($p<0.01$), and minimum oxygen saturation ($p<0.05$). A MANOVA with a main factor of group (RDI¡Ý15/RDI<15) and a repeated measurements factor of session (time of day) yielded significant main effects of group ($F(1,120)=5.55$, $p<0.05$) with higher LDWS in subjects with RDI¡Ý15, as well as a significant main effect of session ($F(4,120)=3.15$, $p<0.05$) so that LDWS were lower at 14:00 and 16:00. No relationship was found between LDWS and BMI or MSLT scores.
Conclusions: This preliminary analysis indicates that subjects with higher RDI had higher postural shifts. Correlations with objective and subjective measurements of sleepiness as well as cognitive functioning are currently being explored. In addition, consistent with previous reports, diurnal variations in postural control were found. In another unrelated study, LDWS predicted the level of fighter pilot performance. Taken together, theses results may suggest posturographic evaluation as a supplementary diagnostic tool. The empirically assessed validity of this tool, however, requires further systematic research.

1082.U

Perceptual Learning after a Nap: The Mini-Me of Sleep

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Introduction: Learning on a variety of perceptual and motor tasks is enhanced by a night's sleep. Here we add a new dimension to our understanding of sleep-dependent learning by demonstrating a special role for daytime napping. We have previously shown that repeated, within-day testing on a texture discrimination task (TDT) produced retinotopically specific deterioration in performance; but an hour nap restored performance to baseline for two subsequent testing sessions. This improvement was related to an increase in slow wave sleep (SWS) in the experimental nap. In the current study, we investigated three questions: (1) Whether longer naps that include both SWS and rapid eye movement (REM) sleep produce improvement beyond baseline performance (i.e., learning), (2) whether this improvement is retinotopically specific, similar to the nocturnal sleep-dependent TDT learning, and (3) whether deterioration develops with the simple passage of time or depends on the amount of testing.
Methods: Nappers (n=18) performed the TDT at 9AM (Test 1) and 7PM (Test 2) on day one, and again at 9AM the following morning (Test 3). They also took a PSG-monitored nap (80 – 100min) between Tests 1 and 2. Non-nappers (n=28) were tested on the same schedule, but did not

nap. A Switch group (n=6) was tested in one visual quadrant at Test 1, then allowed to sleep for up to 90 min with PSG recording, and finally were tested in the contralateral visual quadrant at Test 2. A 24hour group (n=13) were tested at Test 1 and Test 3,with no nap or intervening test.
Results: Nappers showed within-day improvement on the TDT from Test 1 to Test 2 (t17=-2.22, p=.04) This learning was significantly correlated with the product of the amounts of SWS & REM in the nap (r=.64, p=.007). In the non-nappers, performance deteriorated, and by an amount previously seen for retesting after 2 hr. Thus, stimulus exposure rather than inter-test interval produced TDT deterioration. The switch group did not show transfer of learning across quadrants, suggesting that the nap-dependent learning occurred in areas of early visual cortex. Over-night improvement from Test 1 to Test 3 was examined and found that significantly greater for nappers than non-nappers(t43=-2.29, p=.02) In fact, improvement after a nap plus a night of sleep was equivalent to that previously reported after two nights of sleep.
Conclusions: Depending on sleep length, a nap can stabilize or reverse same-day, practice dependent, task deterioration. Our findings demonstrate that a longer nap, containing both SWS and REM, can induce actual improvement, similar to that previously reported for nocturnal sleep. This learning occurs in early visual processing areas, as also reported for nocturnal sleep. Further, subsequent nocturnal sleep appears to produce additive benefits, so that 24 hr improvement becomes as great as that normally seen only after 48 hrs.

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1083.U

Does Sleep Facilitate The Gain Of Explicit Knowledge Of A Hidden Rule In A Number Reduction Task?

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Introduction: Repeated training on a task may eventually lead to explicit recognition of hidden rules underlying the task structure. By reprocessing and integrating newly acquired memories with old ones, sleep may facilitate this process. Here, we investigated the effects of sleep on the acquisition of explicit knowledge in a paradigm, which allows for a suddenly occurring insight into a hidden structure, leading to immediately improved task performance. We hypothesized that sleep related memory processing would support this transition.
Methods: 48 healthy participants (24 female, 24 male) performed a number reduction task (NRT). In this task, subjects have to transform a string of eight digits into a string of seven digits by applying two simple rules. The transformation is achieved in seven steps, each generating one digit of the new string. The seventh digit of each response string represents the solution of this sequence. With increasing practice, performance becomes faster, indicating the gradual acquisition of implicit knowledge. However, subjects can also acquire explicit knowledge about a hidden rule of the task that is embedded in each response string they generate, namely that the second input always equals the seventh input (i.e., the solution of the string). The time point when subjects acquire explicit knowledge about this hidden rule can be determined exactly, because with this knowledge subjects can arrive at the solution after only two steps instead of seven and therefore, according to instructions, cut short sequential responding. All subjects first performed three blocks of the NRT (with 30 sequences in each block) and, after an eight-hour retention interval, another twenty blocks. Each subject was assigned to a Sleep group (retention interval from 2300h to 0700h, filled with sleep), a Wake/Night group (retention interval from 2300h to 0700h, filled with wakefulness), or a Wake/Day group (retention interval from 1100h to 1900h, filled with wakefulness). Analyses of variance comparing the three groups were performed for the number of blocks required after the retention interval until the gain of explicit knowledge of the hidden rule (as indicated by cutting short sequential responding). Subjects who acquired explicit knowledge of the rule already before the retention interval were excluded.
Results: Preliminary results show that subjects in the sleep condition needed fewer blocks to gain explicit access to the hidden rule than subjects in the wake conditions ($p<0.05$). This sleep specific effect tended to be more pronounced in men than women.
Conclusions: Results are consistent with the hypothesis that sleep related memory processing facilitates the gain of explicit knowledge of a hidden rule in the NRT. This outcome suggests that sleep not only consolidates pre-existing memory traces but can also produce qualitative changes in the access to these traces.

1084.U

The Relationship Between Laboratory and Self-Rated Sleep Characteristics in Childhood and Adolescent Depression

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Introduction: Previous work has attempted to quantify the relationship between objective polysomnographic measures and subjective assessment of sleep based on self-report. Strong correlations were reported between subjective and objective sleep measures in healthy controls and unmedicated outpatients. A strong interconnection between sleep disturbance and MDD in adulthood has been more difficult to establish in childhood depression. The purpose of the present study was to examine the relationship between subjective and objective sleep in children and adolescents with MDD compared to healthy normal controls.
Methods: The present study evaluated subjective and objective sleep measures in 59 depressed children and adolescents 8-17 years of age (34 males, 25 females) compared to 30 healthy controls in the same age range (16 males, 14 females). All patients were symptomatic and unmedicated at the time of study. All study participants maintained regularized sleep schedules for 5 days prior to the sleep study, verified by actigraphy, and followed by 2 consecutive nights in the sleep laboratory. MANOVAs contrasted the group and sex effects separately for objective and subjective sleep measures and on the difference between comparable measures. Pearson's product moment correlations were completed between all subjective and objective sleep measures separately for group (NC or MDD), and sex. Stepwise regressions were then performed to determine which objective sleep measures best predicted subjective sleep, separately in each of the four groups.
Results: No significant group or gender main effects or interactions were obtained in any of the objective or subjective sleep measures by MANOVA. However, the difference between objective and subjective measures showed a significant group by gender interaction for total sleep time (TST) and for sleep latency. Girls with MDD were most accurate in rating sleep latency, but over estimated TST by more than 30 minutes. Males with MDD only slightly underestimated TST (<5 minutes), but overestimated sleep latency by 9 minutes. Overall, the MDD groups were more accurate at rating sleep than the NC groups, with the exception of total sleep time in NC girls who underestimated by less than 10 minutes. Correlations indicated that the interrelationships between subjective and objective sleep measures differed by group and gender. The MDD males also had the highest number of significant correlations between subjective an objective sleep measures, followed by the MDD females and then the NC groups which both had the same number of significant correlations.
Conclusions: The relationship between subjective and objective sleep did show a significant influence of group and gender, but not the individual measures. Moreover, the MDD group was reasonably accurate in estimate sleep measures, contrary to expectation. These results suggest

that the variables that children and adolescents use to judge sleep quality and depth depend on gender and diagnostic group and may have implications for perceived antidepressant effects on sleep.

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1085.U

The Role of REM Sleep and Gender in Overnight Regulation of Anxious Mood

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Introduction: Significant gender differences have been reported in both anxiety symptomatology and sleep disturbance, with females consistently at a higher risk for both. Even in non-clinical or "normal" populations, females are more likely to experience both anxious mood and sleep disturbance than men. The present investigation examined explicitly the overnight mood regulation function of sleep as an explanatory mechanism in the relationships among gender, anxious mood, and sleep disturbance. Specifically, this study addressed three questions: 1) Does sleep actively regulate "normal" levels of tension/anxiety in a non-clinical population? 2) Is REM sleep the factor responsible for this regulatory function? 3) Do females have increased levels of pre-sleep tension/anxiety to regulate?, and 4) Do females show a smaller decrease in anxious mood following sleep - before and after controlling for pre-sleep level of tension/anxiety? Thus, females might be more vulnerable to anxiety, in part, because they are less effective at regulating anxious mood overnight.
Methods: 60 volunteers were recruited for a 2-night sleep study. Respondents were screened to rule out: 1) past or current Major Depressive Episodes, 2) current use of medication that might influence sleep architecture, and current pathology as evidenced on the SCID-NP, Hamilton Depression Rating Scale (> 10), and the Beck Depression Inventory (> 14.) Participants were instructed to regularize their sleep to an 11:00 P.M. to 7: 00 A.M. schedule for two weeks prior to their first laboratory night. The POMS, the PANAS, and the BDI were administered 10 minutes prior to lights out (11:00 P.M.). Participants were allowed eight hours of bedtime per night. Participants were then woken at 7:00 A.M. and given another POMS and PANAS. Participants (n=31) who scored less than 3 on the POMS Tension/Anxiety factor were excluded from analyses that assessed overnight mood change.
Results: A repeated measures analysis of variance indicates significant decreases in pre-sleep anxious mood from night to morning for both men and women. However, as predicted, pre-sleep to morning changes in anxious mood specifically were greater for men (mean change score =-5.2) than for women (mean change score = -2.2); (t=-2.018; p<.01) with the interaction of night-morning x gender significant at p<.05 (F=4.1). Gender differences were also found in REM latency (mean REML-men = 108 minutes; mean REML-women=127 minutes; (t=-1.53; p< .05), but not in REM %, total REM minutes, and REM density. Interestingly, when those subjects with significant pre-sleep anxiety were examined separately, gender differences were found in eye movement density (mean EMD-men=1.9; mean EMD-women=2.2; (t= -.93; p< .05,) but not in REM %, total REM minutes, or REM latency.
Conclusions: These results support the idea that REM sleep contributes to the regulation of anxious mood in a manner similar to the overnight regulation of depressed mood. These results also substantiate the hypotheses that there are gender differences in this process, and that this process will occur even when there are non-pathological levels of anxiety to regulate.

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1086.U

Reduced Power After A Power Nap

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Introduction: Afternoon "power naps" may improve subsequent performance. Yet potential benefits of a nap may not be realized immediately, because awakening is accompanied by a period of impaired performance known as sleep inertia. Sleep inertia is exacerbated by prior sleep deprivation but also occurs after nighttime sleep in nondeprived individuals. Sleep inertia can last minutes to hours, partly depending on the task and the dependent variables used to assess it. In many experimental paradigms waking control conditions are not feasible, rendering it impossible to assess changes in performance that are not due to inertia (e.g., learning or boredom). To control for these factors, we used waking and rest control groups. We investigated sleep inertia over the course of an hour following a 2-hour afternoon experimental manipulation (sleep, wake, or rest) in individuals who maintained a regular 8-hour nighttime sleep schedule before the study.
Methods: Fifty healthy subjects aged 18-28 years were assigned to sleep (n=18), wake (n=16), or rest (n=16) groups. The sex of subjects and experiment time (13:55-15:55 or 15:55-17:55) were balanced across groups. Sleep inertia was assessed using a 3-minute addition task that required summation of pairs of 2-digit numbers; the dependent variable was the number of sums attempted. The task was practiced before the study. The experimental day included a pre-experimental baseline session and 5 evenly spaced sessions in the hour immediately following the manipulation. Performance in these 5 sessions was expressed relative to baseline and submitted to repeated measures ANOVA with the factors group, time, and session.
Results: Performance on the addition task showed a significant group*session interaction ($F(8,176) = 2.12$, $p=0.036$). One-way ANOVAs indicated a significant main effect of session in the sleep ($F(4,68)=12.13$, $p<0.001$) and rest ($F(4,60)=4.11$, $p=0.005$) groups, whereas performance did not change across sessions in the wake group ($F(4,60)=1.86$, $p=0.13$). In the first session after the manipulation, the sleep group performed worse than the wake group ($t=2.41$, $p=0.02$), whereas the other groups did not differ significantly. Performance increased from session 1 to session 2 in the sleep group ($t=3.28$, $p=0.005$) and in the rest group ($t=2.74$, $p=0.02$) but not in the wake group. By the last session, all groups reached a similar level of performance that significantly exceeded baseline ($t=3.78$, $p<0.001$).
Conclusions: "Power" or cognitive throughput as assessed by speed of calculation was significantly reduced immediately following a two-hour afternoon sleep opportunity. A rest group that was required to lie in the dark without sleeping also showed inertia that was less pronounced than in the sleep group, suggesting that darkness and a supine position are sufficient to diminish performance. Speed of calculation recovered within an hour and reached a level significantly above baseline, demonstrating that learning occurred. The degree of learning did not differ between groups, indicating no beneficial effects of the nap.

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1087.U

The Objective Alerting Effects of Brief Naps Following Eight Hours of Nocturnal Sleep

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Introduction: Recent research indicates that brief naps can effectively ameliorate the negative effects of mild nocturnal sleep reduction. The

current investigation extended this research to individuals obtaining a more normal sleep duration prior to the naps. Brief naps of varying lengths were compared in order to determine the optimal nap length for improving objective alertness following a nocturnal sleep of about eight hours.

Methods: Participants were 24 self-reported good sleepers (M=22.71 yrs, SD=5.41) who participated in a repeated-measures design with five napping conditions: no-nap and 5, 10, 20 and 30 mins of polysomnographically defined sleep. All naps were scheduled to terminate at approximately 15:00 hrs. Prior nocturnal sleep was permitted between 22:00 and 07:00 hrs and was confirmed by sleep diary and activity monitor (M=8.08 hrs, SD=0.35). Objective alertness, indexed by sleep latency, was assessed pre-nap, and at 65, 125 and 185 mins post-nap.

Results: Each of the 5, 10, 20 and 30-min naps showed significant improvements of sleep latency compared to no-nap (i.e., improved objective alertness) at all of the post-nap testing times. The 10-min nap produced significantly longer sleep latency than the 5-min nap, 65-mins after napping, while the 20 and 30-min naps produced significantly longer sleep latencies than the 5-min nap, both 65 and 125 mins after napping. There were no significant differences in sleep latency between the 10 and 20-min nap conditions at any post-nap interval, nor were there significant differences between the 20 and 30-min nap conditions. However, across the three post-nap testing times, the 30-min nap produced significantly greater improvements in objective alertness than the 10-min nap.

Conclusions: The 5, 10, 20 and 30-minute naps all significantly improved objective alertness for at least 3 hrs in the afternoon. The pattern of findings also indicated a dose-dependent relationship between nap duration and post-nap benefit such that the longer the nap, the greater the increase of sleep latency. Accordingly, of those nap lengths examined in this study, the 30-min nap appears to improve objective alertness the most following a nocturnal sleep of at least eight hours.

1088.U

Sleep Behavior And Social Rank In Gelada Baboons

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Introduction: Sociality is one of the most striking features in the lives of many primates. The social rank of individuals within a social group may be reflected in the individual's sleep. Dominant animals could perceive less risk of being attacked by group members than subordinates, and therefore exhibit longer, more intense and less fragmented sleep. Alternatively, dominant animals could be more alert to be able to control group processes, leading to less intense and more fragmented sleep than in subordinates.

Methods: We investigated the relationship between social rank and sleep in 10 gelada baboons living in a zoo (2 adult and 2 subadult males, 3 adult females and 3 juveniles). Sleep behavior was continuously recorded with infrared video systems for 11 consecutive nights. Sleep behavior was scored based on body postures and movements. The states awake, transitional sleep, relaxed sleep, and the number of awakenings per night were determined for 1-min epochs. Transitional sleep was scored when resting animals were sitting on the sleeping board with the head held upright, gradually sinking towards the chest. Relaxed sleep was scored when the head rested on the chest or was bent towards the side or backwards. Social rank was determined by direct daytime observations of interactions between individuals over several weeks. Significances between sleep variables, social rank and age was determined with the Page test, and their relation with Spearman's correlations.

Results: Sleep duration was 686±31 min (mean of 10 individuals), and correlated negatively with age ($p=0.033$, $r_s=-0.709$). Sleep duration was not related to social rank in the males (11 nights, $n=4$, $p>0.1$), while in the 3 females and in the 3 juveniles it increased with decreasing rank ($n=11$, $p<0.001$, $p<0.01$, respectively). Relaxed sleep comprised 88±12.0 % of total sleep in males and 98±0.8% in females. Relaxed sleep increased with decreasing rank in both males and females ($p<0.001$ for each). Transitional or "light" sleep decreased with decreasing rank in the 3 males ($n=11$, $p<0.001$), while no such relation was found in females. Transitional sleep, but not relaxed sleep correlated positively with age in the adults ($n=6$, $r_s=0.899$, $p<0.02$; juveniles were excluded because they were not always visible). The frequency of awakenings per night was 42.2±7.0 ($n=6$), and was affected neither by rank nor by age.

Conclusions: Our data indicate that some aspects of sleep of gelada baboons are related to their social life within the group. Sleep duration was related to rank in the 3 females and the 3 juveniles. Transitional sleep and relaxed sleep were inversely related to social status, whereas sleep fragmentation was independent of rank. The dominant males spent less time in relaxed sleep, i.e. in deeper sleep than subordinates. This result is consistent with the hypothesis that dominants are more alert at night, enabling them to keep control and to react more quickly to adverse stimuli.

1089.U

Day-to-day Determinants of Sleepiness – A Longitudinal Diary Study

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Introduction: Few studies have explored the determinants of daytime sleepiness in real life conditions using a non-epidemiological approach. The aim of the present study was to investigate the determinants of daytime sleepiness on a day-to-day basis, using diary data and calculating intraindividual correlations.

Methods: The sample consisted of 43 individuals (17 males and 26 females; mean age: 42 years, range: 18-69 years), who filled out a sleep/wake diary during 6 weeks. A majority of the subjects was working regular daytime hours (e.g. 08-17h). The sleep/wake diary included questions of sleep, health, stress, sleepiness, coffee consumption and alcohol. The sleepiness ratings were made every second hour (08, 10, 12h etc.) using the Karolinska Sleepiness Scale (KSS; 1 very alert – 9 very sleepy). The following determinants of daytime sleepiness were used in the statistical analysis: health (1 very poor-7 excellent), stress (1 very low-9 very high), sleep length, bedtimes, napping (0/1=yes), ease falling asleep, how did you sleep, restless sleep, refreshed from sleep, sufficient sleep, premature awakening, ease waking-up, depth of sleep (the response scale was 5-graded for the sleep questions, 5 meaning good sleep/lack of problems), spontaneous awakening (0-1 yes), weekday (0-1 weekend), coffee (no. of cups), alcohol (1-4 high amount) and previous day KSS (lagged). The data was pooled (no. of data points=1465). Each individual was dummy coded and forced into the analysis in order to remove the interindividual variance. A stepwise multiple regression analysis was also carried out with daytime sleepiness as the dependent variable.

Results: A mean KSS between 06h and 24h was calculated across days. The mean KSS was 4.3 (sd=0,9) and the mean range (within individuals) was 3.6 (sd=1.4). The strongest significant correlation coefficients was found for "health" ($r=-0.42$, $p<0.001$), "refreshing sleep" ($r=-0.35$, $p<0.001$), "ease waking-up" ($r=-0.31$, $p<0.001$), "sufficient sleep" ($r=-0.24$, $p<0.001$), "sleep length" ($r=-0.20$, $p<0.001$) and "napping" (0.18, $p<0.001$). The remaining independent variables were also significant, with the exception of "alcohol", although the correlation coefficients were weak. 7 predictors became significant in the multivariate analysis; "health" (R2 change=+8.6%, beta for the last step=-0.28), "refreshing sleep" (+3.3%, -0.12), "napping" (+0.6%, 0.08). "Bedtime" (+0.6%, 0.11), "ease waking-up" (+0.6%, -0.12), "KSS, previous day" (+0.4%, 0.11) and "sufficient sleep" (+0.1%, -0.04). The total amount of explained variance was 14.2%. Thus, a high level of daytime sleepiness was determined by poorer health, non-refreshing sleep, napping, late

bedtime, difficulties waking-up, high level of sleepiness on the previous day, and insufficient sleep.
Conclusions: The results show that the rating of health was closely related to sleepiness. Among the sleep variables, ratings related to the awakening (refreshing sleep, ease waking-up) showed the strongest associations with daytime sleepiness. Sleep ratings related to insomnia and sleep length, as well as coffee, alcohol and weekday, were only weakly associated with sleepiness. In conclusion, self-rated health was the strongest determinant of sleepiness.

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1090.U

Driving Impairment Due To Sleepiness Is Exacerbated By Low Blood Alcohol Concentrations (BACs)
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Introduction: Sleepiness causes around 10% of UK road crashes; a high percentage of which are either fatal or result in serious injury. Given that alcohol has some soporific effect, then combining sleepiness with alcohol, even at low doses may increase the risk of a crash. None of the studies investigating this combination have looked at this interaction during sustained driving, and with low BACs. We investigated BACs of 30-40 mg% (£ half the UK legal driving limit) on driving performance in moderately sleepy, young men (the most at risk group of drivers).
Methods: Twelve men (av 22.7y), drove for a 2-hour simulated drive (14:00-16:00h) in each of 4 conditions: normal sleep + no alcohol (BASE), sleep restriction + no alcohol (SR), normal sleep + alcohol (ALC), sleep restriction + alcohol (SR+ALC). Sleep restriction was to 5h (02:00-07:00h) the previous night. 30min before each drive, drivers consumed 375ml orange juice, containing 75ml 37.5% proof vodka in ALC and SR+ALC, or with nil alcohol for other conditions. They drove an immobile, full size, interactive car simulator, on a dull, monotonous, dual carriageway. Sleep-related lane drifting indicated driving impairment and was identified as "sleep-drifting". Objective and subjective sleepiness were measured via EEG (4-11Hz) and the Karolinska Sleepiness Scale respectively. Data were analysed in 30min epochs using two-way repeated measures ANOVAs with Tukey post hoc tests.
Results: Over the drive mean BACs fell from 30.75mg% to 0.42mg%. There was a significant between-condition effect for all indices ($p<0.02$). SR and ALC each caused significant deterioration in all indices, with mean total sleep-drifting for the whole drive rising from BASE by 227% and 194% respectively. Sleep-drifting worsened significantly with SR+ALC, producing a 515% and 88% increase from BASE and SR respectively, indicating an ADDITIVE EFFECT. The worst impairment during SR+ALC was in the 2nd 30min of the drive (around the circadian trough), when total sleep-drifting increased 1056% above BASE and 252% above SR. Compared with SR, the effect of SR+ALC was also significant in the EEG, but not with subjective sleepiness; i.e. – when combining alcohol with sleep restriction, subjective sleepiness did not reflect the increases (from sleep restriction alone) in sleep-drifting and objective sleepiness.
Conclusions: Modest and apparently "safe" levels of alcohol intake exacerbate driving impairment due to sleepiness. Although our sleepy drivers acknowledged greater subjective sleepiness after alcohol intake, they apparently failed to realise the extent of their marked driving impairment. This worsened ability to drive was reflected in clear EEG changes. Legally acceptable levels (for most countries) of alcohol consumption at lunchtime present an increased risk when driving under dull, monotonous conditions during the afternoon circadian trough. This risk is greatly enhanced if the driver had a restricted night's sleep previously.

Research supported by UK Department for Transport

1091.U

The Effect of Residual Alcohol on Sleepy Drivers in the Afternoon
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Introduction: We have recently shown that low alcohol intake at lunchtime (well below "warning" levels for UK roadside breathalysers) increases afternoon sleepiness and impairs driving performance in an interactive car simulator during a 2-hour simulated drive. This effect was enhanced when drivers were already sleepy, following a night of reduced (5h) sleep. However, blood alcohol concentration (BAC) is not a good indicator of impairment, as there can be residual impairment long after BACs have reached zero. This study extended our previous work, by assessing whether near-zero BACs at the beginning of the same 2-hour afternoon drive continued to impair driving, EEG and subjective sleepiness in young men (the most at risk group for sleep-related road crashes).
Methods: Twelve men drove from 14:00h to 16:00h during each of 4 conditions; normal sleep + no alcohol (BASE), sleep restriction + no alcohol (SR), normal sleep + residual alcohol (RESALC), sleep restriction + residual alcohol (SR+RESALC). Sleep restriction was from 02:00h to 07:00h (5h) the previous night. 90min before each drive, for RESALC and SR+RESALC participants drank 375ml orange juice, containing 75ml 37.5% proof vodka, Vs nil alcohol for the other conditions. They drove an immobilised, full size, interactive car simulator, on a dull, monotonous, dual carriageway. Sleep-related lane drifting indicated driving impairment and was identified as "sleep-drifting". Objective and subjective sleepiness were measured via EEG (4-11Hz) and the Karolinska Sleepiness Scale respectively. Data were analysed in 30min epochs using two-way repeated measures ANOVAs with Tukey post hoc tests.
Results: BACs were close to zero at the beginning of the drive. There was a significant between-condition effect for both sleep-drifting ($p<0.05$) and subjective sleepiness ($p<0.001$). Compared to BASE, RESALC caused no increase in any index. SR, as expected, led to increases in all indices. SR+RESALC produced interesting trends. In the 1st hour of the drive the combined effect caused an apparent increase in sleep-drifting compared to SR, however, during the 2nd hour, this reversed, as SR+RESALC led to less sleep-drifting than SR alone. This apparent arousing effect may be due to an alcohol rebound. This trend is also evident in both the subjective sleepiness and EEG.
Conclusions: Residual alcohol appears to have little effect on driving performance and sleepiness levels during a monotonous afternoon drive, unless the driver is already sleepy, when even a zero BAC may produce some residual impairment. However, later in the afternoon, in already sleepy drivers, this may lead to a rise in alertness, indicating perhaps a rebound ("withdrawal") effect, or even a phase advance of the late-afternoon circadian peak.

Research supported by UK Department for Transport

1092.U

Sleep Related Vehicle Crashes – Effect of Traffic Density
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Introduction: In the UK 16-20% of collisions on monotonous major roads are due to driver sleepiness. It is generally accepted that the greater the traffic density the greater the number of collisions in general, but it is not clear whether this applies to sleep related vehicle crashes (SRVCs), especially as these tend to occur at times of the day with low traffic flow. Nothing is known about the proportion of SRVCs on roads with differing 24h traffic volumes.

Methods: We undertook in-depth analyses of police accident files on collisions causing death or injury during a two-year period on 6 sections of motorways (three lane, dual carriage highways) as well as more minor roads in the UK. Motorways had differing 24h traffic flows and ranged from 60,000 to 114,000 (both directions) vehicles/24h. The following criteria identified SRVCs: (a) good weather and clear visibility; (b) breathalyser below the legal driving limit; (c) no mechanical defects; (d) elimination of speeding and driving too close to the vehicle in front; (e) no causal medical disorder/medication; (f) vehicle either ran off road or hit another vehicle/object clearly visible for several seconds beforehand, sufficient to exclude momentary distraction; (g) no emergency swerving/braking. The driver may not admit to being asleep.
Results: Neither total numbers of motorway crashes (all causes) nor SRVCs were significantly correlated with traffic density, although there was a near significant trend for the former. Interestingly, though, the proportion of SRVCs in relation to total crashes showed a significant negative correlation ($r = -0.84$ $p<0.05$) with traffic density. When we looked specifically at early morning hours (02:00-06:00h), again there was no significant association between traffic density and total crashes or SRVCs, but there was a near significant trend for the former. However, during this period, the inverse relationship between traffic density and SRVCs as a proportion of all crashes, was highly significant ($r = -0.98$ $p<0.002$). That is, whereas around 60% of all early morning crashes on motorways with very low traffic density were SRVCs, with a higher traffic density, the trend for increasing numbers of crashes were increasingly likely to be due to other causes.
Conclusions: The influence of traffic density on numbers of SRVCs on monotonous highways is not straightforward as there are opposing influences, especially during early morning hours, with the circadian trough. For example, and within certain limits, increasing traffic density introduces more sleepy drivers on the road. On the other hand, the greater the number the vehicles provides more stimulation for these sleepy drivers, thus helping to counteract sleepiness. The net effect is that although there is some increase of SRVCs with increasing traffic density, there is a decreasing likelihood of a crash being sleep related.

Research supported by UK Department of Transport

1093.U

Road Lighting Does Not Decrease Sleep Related Road Crashes at Night

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Introduction: When traffic density is controlled for, more vehicle collisions occur on major roads at night than in the day. Studies comparing lit and unlit sections of roads claim that improved lighting reduces nighttime collisions. However, such claims may be confounded by underlying circadian rhythm effects. We investigated the occurrence of sleep related vehicle crashes (SRVCs) during the night on lit Vs unlit roads with similar traffic flow rates.
Methods: We undertook in-depth analyses of police accident files on collisions causing death or injury during a two-year period on 2 sections of motorways (three lane, dual carriage highways) in the UK, one lit the other unlit. Both sections were rural, similar in distance and traffic flow (around 80,000 vehicles/day). The following criteria identified SRVCs: (a) good weather and clear visibility; (b) breathalyser below the legal driving limit; (c) no mechanical defects; (d) elimination of speeding and driving too close to the vehicle in front; (e) no causal medical disorder/medication; (f) vehicle either ran off road or hit another vehicle/object clearly visible for several seconds beforehand, sufficient to exclude momentary distraction; (g) no emergency swerving/braking. The driver may not admit to being asleep.
Results: Over 24h, during daylight and darkness combined, the proportion of SRVCs on the unlit road was 30%, compared with 20% on the lit road. Ostensibly, this points to lighting being effective. However, during darkness, proportionately more SRVCs (50%) occurred on the lit compared with the unlit road (38%) during the same hours. 36% of the SRVCs on the lit road resulted in death or serious injury Vs 29% for the unlit road.
Conclusions: Whilst road lighting may appear to reduce SRVCs when assessed over the 24h period, this only applied to daylight hours. It is unclear why lit roads at night seem to lead to proportionately more SRVCs. For example, vehicles may travel faster on these roads because of better visibility, with the drivers having less time to wake up or respond to hazards when dozing off. This may also account for why SRVCs on lit roads seem more likely to result in death or serious injury. Our findings fail to support the belief that lighting reduces all traffic collisions, and supports the view that circadian factors are more likely to be the cause of SRVCs at night/in the early hours than the absence of road lighting.

Research supported by UK Department for Transport

1094.U

Waking 7-8 Hz "Thinking" Activity is Linked to Sleep 0.5-1 Hz "Recovery" Activity in the Left Frontal EEG

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Introduction: Functional imaging shows delta sleep activity reflects daytime 'brainwork', especially within the prefrontal cortex (PFC). Other findings report that delta activity (0.75-4.5Hz) during the first nonREMP positively correlates with daytime theta activity (5-8Hz). However, the latter findings were derived from a monopolar (Cs4s-As2s) EEG derivation, using only broad delta and theta frequency bands. Can one now be more specific: (i) with cortical region; (ii) delta frequency in non-REM; (iii) theta frequency during waking? We have shown recently that for the left frontal area, 0.5-1.0Hz in the first nonREMP is related to waking PFC performance in healthy, older people. Sleep <1Hz EEG activity may well reflect cortical re-organisation of waking circuits. Using 0.5-1.0Hz sleep delta activity as a reference, we report on a link with a specific waking theta activity, indicative of "thinking".
Methods: Twelve right-handed, healthy, good sleeping older adults (mean $67.3y \pm 1.2y$ SEM, range 61-75y) without daytime sleepiness (<2naps/month and KSS screening over 3 days), were recruited. Waking EEGs under different eyes closed "thinking" conditions (in a soundproof booth) were recorded during the daytime (10.30h-11.00h), and usual sleep EEGs recorded at night. We also analysed the pre-sleep period after "lights out" but preceding signs of drowsiness (e.g. eye rolling). All EEGs comprised four bipolar derivations (Fps1s-Fs3s; Fps2s-Fs4s; Os1s-Ps3s; Os2s-Ps4s). Power spectra of 30s epochs for 0.5-1Hz were computed for the first NREMP, and power spectra of 5s epochs for four 1Hz frequency bins, ranging from 4-8Hz, were computed for the waking EEG. Power data were standardised within subjects to remove individual differences.
Results: 7-8Hz was the only morning waking theta frequency significantly correlated with sleep 0.5-1.0Hz activity ($r=0.67$ df. 10 $p<0.02$), and this was only evident in the left frontal EEG. No other EEG quadrant or waking theta frequency produced significant outcomes. Interestingly, 7-8Hz pre-sleep wake EEG showed an even higher correlation with sleep 0.5-1.0Hz ($r=0.81$ df. 10 $p<0.001$), but again only for the left frontal EEG and for no other theta frequency bin. 7-8Hz activities for morning Vs pre-sleep were correlated significantly ($r=0.75$ df. 10 $p<0.008$). This 7-8Hz activity was not associated with sleepiness as spectral analysis showed increasing sleepiness to be distinctly different and linked with 4-6Hz power.
Conclusions: In these older people, quiet, relaxed thinking, particularly during the settling down period between lights out and drowsiness, is

linked to 7-8Hz activity from the left frontal region. This is probably the frontal "kappa" EEG activity described by others. We also find that it is associated with local 0.5-1.0Hz activity during the first non-REMP, which possibly reflects normal cortical recovery from wakefulness. Thus, for this cortical area, it seems that the more active is waking thinking, the more there is recovery or cortical reorganisation during the first nonREMP.

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1095.U

Time of Day and Peripheral Cytokines Impact Extinction of Cocaine-induced Conditioned Place Preference

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Introduction: Evidence implicates the brain cytokine network and sleep regulation in learning and memory consolidation. In humans, motor skill learning improves during sleep and in both humans and rodents, sleep deprivation interferes with learning. Central administration of the cytokine, interleukin 1b (IL1b) interferes with memory consolidation for context conditioning in rats. Since brain cytokine mRNA levels are higher after light onset and lower prior to dark onset in rats, we evaluated the impact of time of day on conditioning, extinction and reinstatement of cocaine-induced conditioned place preference (CPP). Also we evaluated whether peripheral administration of IL1b, using a dose that promotes sleep, would alter extinction or reinstatement.
Methods: Cocaine-induced CPP was produced by 5 daily injections of cocaine (15mg/kg, ip) followed by placement into the rat's non-preferred compartment (n=8 at AM and n=8 at PM) for 30 min. A 2nd injection, saline was given to each rat 12h later and the rats were then placed into their preferred compartments. The cocaine-induced CPP and extinction (presentation of the CPP environment without cocaine) were evaluated over 15 min and assessed by the time spent in the cocaine-paired chamber at either AM or PM. After the rats reached extinction criteria (2 adjacent days significantly different from the cocaine test), they were tested for reinstatement of CPP with cocaine at 5 mg/kg, ip. In a second independent experiment, rats were conditioned in the PM and then saline or human recombinant IL1b (0.5 mg/kg, ip) (n=8 for each) was injected 1.5 h prior to extinction. The number of entrances into the cocaine-paired side was evaluated as a measure of activity for the treated rats.
Results: No significant differences were observed in time spent in the cocaine-paired environment between AM and PM groups in the conditioning test. However, extinction of cocaine-induced CPP reached criteria faster (2-3 days) for the PM than for the AM group (5-6 days). No significant differences were observed in cocaine reinstatement when tested at their extinction time. Peripheral administration of IL1b decreased the number of entrances into the cocaine-paired chamber and produced a large variation in the time spent on the cocaine-paired side. Although the rate of extinction was similar between saline and IL1b-treated rats, IL1b-treated rats did not express extinction when tested without IL1b injections while saline-treated rats maintained their extinguished responses without injections.
Conclusions: These data suggest that time of day impacts the extinction rate: extinction in the AM takes longer than in the PM. Peripheral administration of IL1b in the PM at a dose that promotes sleep also decreases the retention of extinction learning. The higher levels of brain cytokine mRNA levels in the AM (see abstract—Cearley et al.) may interfere with extinction learning..

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1096.U

Time of Day Impacts Cytokine mRNA Levels after Extinction of Cocaine-induced Conditioned Place Preference

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Introduction: The brain cytokine network and sleep regulation are implicated in learning and memory. Learning improves during sleep and sleep deprivation attenuates learning. Gene expression of the sleep regulatory substances, such as the cytokines interleukin 1b (IL1b) and tumor necrosis factor a (TNFa), is higher in the AM than in the PM in specific brain regions of rats. This diurnal rhythm in cytokines is implicated in sleep regulation. We hypothesized that the higher levels of cytokines in the AM makes learning more difficult. Our evidence to support this hypothesis includes our findings that time of day decreases the rate of extinction for cocaine-induced conditioned place preference (CPP), and that administration of IL1b in the PM decreases the retention of extinction learning (see accompanying abstract, Churchill et al.). We evaluated the diurnal levels of the cytokine mRNA in rats that had been trained for cocaine-induced CPP, extinguished, reinstated, and then subjected to a final extinction test.
Methods: Cocaine-induced CPP was produced by 4 daily injections of cocaine (15mg/kg, ip) (see abstract by Churchill et al.). Within 2 hours after a final extinction (2 days after the last cocaine exposure), the rats were sacrificed, brain regions were dissected, and total RNA was isolated using a TRIzol reagent. First strand cDNA was synthesized using reverse transcription and aliquots were amplified using Real-Time polymerase chain reaction (PCR).
Results: There were significantly higher mRNA levels for TNFa ($p<0.05$) in the AM group in comparison with the PM group in the somatosensory cortex, hypothalamus, prefrontal cortex, and nucleus tractus solitarius (NTS). A trend toward significance ($p<0.06$) was observed in TNFa mRNA levels in the amygdala and locus coeruleus. Also, significantly higher mRNA levels for IL1b ($p<0.05$) were found in the AM group compared with the PM group in the prefrontal cortex, amygdala, and NTS.
Conclusions: Diurnal rhythms in cytokine mRNA levels are evident in rats after cocaine-induced CPP, extinction, reinstatement and a subsequent extinction trial. In general, sleep during the day reduced TNFa and IL1b mRNA levels in specific brain regions and increased the rate of extinction. Perhaps, behavioral treatments to enhance sleep might improve the rate of extinction in cocaine addicts.

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1097.U

Assessing the Cognitive Consequences of Drowsiness with EEG and Working Memory Task Performance Measures

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Introduction: To better understand the impact of drowsiness on neurocognitive function, we performed an experiment in which healthy young adults were kept awake overnight performing tasks at periodic intervals. The tasks required sustained attention and made varying demands on working memory (WM), the limited capacity to hold information in mind for several seconds and use it to guide behavior. WM is a critical resource for higher cognitive processes, and impairments in WM functions adversely affect performance across a wide array of activities. We recorded EEG during task performance because neurophysiological measures are sensitive to changes in both ongoing attentional effort and transient attentional processes, and thus may provide a more

comprehensive view of the neurocognitive effects of drowsiness than that obtainable from task performance measures alone (Gevins et al Cerebral Cortex, 1997; Neuropsychopharm, 2002; Smith et al, Sleep, 2002).
Methods: Sixteen healthy young adults participated in several daytime baseline sessions and an overnight session in which they remained awake performing a battery of tasks at periodic intervals from 11:00PM until 6:00AM. At each interval, subjects completed subjective sleepiness questionnaires. EEGs were recorded while they performed low and high load versions of a spatial WM task and while they rested quietly. Data from the overnight session were compared to data from the daytime baseline sessions. EEG power spectra computed over the resting periods and over the 4-minute WM task blocks were analyzed along with the amplitude of averaged event-related potentials (ERPs) time-registered with WM task stimulus presentation.
Results: Subjective drowsiness increased gradually and linearly across the overnight session, as did EEG measures of drowsiness during the passive resting conditions. EEG indicators of sustained attentional effort, including frontal midline theta band and parietal alpha band EEG power during WM task conditions did not significantly change across the night. Task performance and transient, attention-related N100 & P300 ERP components decreased rapidly between 11:00PM and 1:30AM, and then remained at that depressed level throughout the rest of the night.
Conclusions: Drowsiness can significantly disrupt the neurophysiological circuits underlying the transient focusing of attention (ERP measures), resulting in impaired performance of a demanding task. Such problems can occur despite a sustained effort to perform well (EEG measures). Drowsiness thus has differential impacts on an individual's subjective sleepiness and passive EEG measures, motivation and effort, neurocognitive function, and overt performance. Assessing such diverse effects with a multifaceted, multivariate approach, such as that of the current experiment, may facilitate research on the neurocognitive consequences of problem drowsiness associated with lifestyle factors or sleep disorders.

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1098.U

Influence Of A Tricyclic Antidepressant On The Learning And Memory Trace Consolidation In The Rats

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Introduction: Introduction: The functional essence of the paradoxical sleep (PS) is often linked to the memory processes organization. At the same time, the depressive patients, in the sleep-wakefulness cycle (SWC) of which an excessive amount of PS is observed, are characterized with significant deterioration of the memory. It is known also that during PS the monoaminergic systems are inactivated in the brain, and that an essence of the antidepressant action lies in suppression of PS and in elevation of the monoaminergic function. The present work deals with an assessment of effects of the antidepressant-induced modulation of the amines' function in the learning and memory trace consolidation.
Methods: Methods: Experiments were carried out in adult male rats (250-300 g). Influence of amitryptilin hydrochloride (8 mg/kg, i.p.) on the learning and memory trace consolidation was studied in the active avoidance test, in the one-session (120 trials) learning paradigm. Prior to the experiments the rats were selected according to their fear/exploration ratio indices. In both active (n=30) and passive (n=30) rats the three subgroups were allocated – controls, pre-, and post-session-injected ones. The pre-session injection of the drug was made one hour prior to the beginning of the active avoidance acquisition. The post-session injection was made immediately after the test acquisition. Considering the clinical observation that significant factors in the depression are the concomitant phobic state and decreased motor activity, the passive animals were conditionally considered as those inclined to depression. The data were evaluated statistically (by the Student's t-test).
Results: Results: 1) The pre-session administration of amitryptilin into the passive animals resulted in an obvious facilitation of the learning process, while in the active animals – contrariwise, the number of trials to reach the criterion of the test acquisition was higher than in the control animals. As to the number of trials to reach the criterion of reproduction of the acquired active avoidance performance (on the second day after the learning session), in the passive animals this index was again reliably lower (against the controls), while in the active ones – higher.2) The post-session administration of amitryptilin did not exert any significant influence on the reproduction (on the second day after the learning) of the already acquired active avoidance response in either subgroup.
Conclusions: Conclusions: The optimal concentration of the monoamines in the brain should play a significant role in the learning processes' organization but not in the memory trace consolidation. These results once again point at importance of correct dosage choice in order to achieve an optimally positive clinical effect.

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1099.U

The Interactive Effects Of Task Demand And Prolonged Wakefulness On Simulated Steering And Secondary Task Performance

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Introduction: A greater theoretical understanding of the mechanisms underlying sleepy driving is a prerequisite to the development of methodologies aimed at detecting driver drowsiness. This study employed a dual-task paradigm to test a compensatory model of sleepy driving that posits basal sleepiness/alertness and the mobilization of cognitive resources as two independent factors that interact to produce manifest driving performance. The model dictates that the extent to which driving performance deteriorates under conditions producing sleepiness is dependent upon the amount of reserve cognitive capacity available to the driver. This reserve can be drawn upon to offset the influence of increasing basal sleepiness.
Methods: Participants were 24 healthy male university students (mean age 19.1 years) who, after two training sessions, underwent one night of prolonged wakefulness in which they completed testing sessions at 2400, 0300, and 0600. During each session, participants completed two tasks simultaneously: 1) a visual tracking task that required the participant to use a steering wheel to keep a target inside a set of moving parallel lines; 2) a continuous auditory signal detection task that was used as a measure of reserve capacity. Participants were instructed to give priority to the tracking task. Each session was carried out in three 10-minute blocks in which the tracking task was completed under differing conditions of demand (Easy, Moderate, Difficult) in a counterbalanced order. Following each block, the Stanford Sleepiness Scale and scales assessing self-reported workload were completed.
Results: Repeated-measures ANOVAs were performed with Time of Night and Task Demand extracted as sources of variance. Consistent with predictions derived from the model, the total amount of steering task error time increased over the course of the night ($F(2,46) = 23.61$, $p < .001$) and as a function of Task Demand ($F(2,46) = 47.29$, $p < .001$). Most importantly, there was a significant interaction between Time of Night and Task Demand such that steering performance deterioration was greatest under the Difficult condition and least under the Easy con-

dition ($F(4,92) = 5.33$, $p < .01$). Signal detection errors also increased during prolonged wakefulness ($F(2,46) = 8.39$, $p < .01$); a significant interaction between Time of Night and Task Demand ($F(4,92) = 2.80$, $p < .05$) indicated that detection errors increased only under the Easy and Moderate conditions but not under the Difficult condition. A similar pattern was observed for self-reported workload, however the interaction was not significant ($F(2,46) = 2.26$, $p = .08$).

Conclusions: The results of the present study support a model of sleepy driving in which the driver can compensate for increases in basal sleepiness by deploying more cognitive resources toward driving safely. The reliability and validity of on-line drowsiness detection may be enhanced by developing methods of monitoring both sleepiness and the availability of compensatory mechanisms to the driver.

1100.U

Simulated Driving Impairments Following Heavy Call And Alcohol In Pediatric Residents: Preliminary Findings

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Introduction: Chronic and acute sleep loss experienced by medical trainees adversely impacts mood, neurobehavioral functioning, and performance of professional duties. Self-report studies have documented fatigue-related driving impairments in residents, including increased motor vehicle accidents and falling asleep at the wheel post-call. No study has compared such decrements to an accepted standard of functional impairment, such as a moderately elevated blood alcohol concentration. We compared simulated driving performance and the ability to self-monitor performance under four conditions: rested (Light Call; LC), sleep loss (Heavy Call; HC), Rested + Alcohol (LC/Alcohol) and Sleep Loss + Placebo (HC/Placebo).

Methods: Residents were tested during two separate sessions beginning at 1500 hours: after a month of light or no call (LC, LC/Alcohol) and post-call after a month of heavy (q 4 or q 5) call (HC, HC/Placebo). Sleep was monitored by actigraphy and sleep diary for the week before each test session. Participants performed a battery of neurobehavioral tasks, including a 30-minute simulated driving task, twice at each session. The driving task instructions are to stay centered in the right hand lane and maintain the posted speed. Alcohol was administered as .6 g/kg for men (.55 g/kg for women) mixed with tonic water in a 1:5 ratio after completion of the first neurobehavioral battery in the LC condition. The placebo—tonic water with three drops of vodka—was administered after the first neurobehavioral battery in the HC condition.n. Participants rated their performance after each 30-minute driving task on a 1 (extremely good) to 7 (poor) scale. Dependent variables on the driving task were lane position variability, speed variability, and off-road incidents.

Results: Fifteen residents (mean age 29.8 years (sd 3.5), 8 women, 2 PL-1, 9 PL-2, 4 PL-3) have completed the study. Lane position variability was significantly worse in the HC and LC/Alcohol conditions compared to the LC condition [$F(3,39)=5.71$, $p<.01$]. Speed variability was worse in both HC conditions than in either the LC or LC/Alcohol conditions [$F(3,39)=5.59$, $p<.001$]. No significant differences were found for off-road incidents. No main effects of sex nor significant interactions were found. Significant correlations between actual and predicted performance occurred for LC ($r=.66$, $p<.01$), HC ($r=.61$, $p<.05$), and HC/Placebo ($r=.53$, $p<.05$) conditions, but not for the LC/Alcohol condition ($r=.18$, $p>.05$).

Conclusions: Preliminary results suggest that residents' impairments under real-life conditions of call-related sleep deprivation are equivalent to or worse than the level of impairment associated with moderate alcohol intoxication. In contrast to alcohol, however, residents are aware of these fatigue-related decrements. These findings have significant implications for resident safety and programs to address resident sleepiness.

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1101.U

Morning Presentation Of An Auditory Stimulus Disrupts Subsequent Nighttime Sleep

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Introduction: Evening presentation of an auditory stimulus promotes subsequent sleep by increasing SWS duration, increasing sleep efficiency, and decreasing WASO compared with a control stimulus. In addition, several studies suggest that the timing of behavioral and sensory demands during prior wakefulness differentially affects subsequent nighttime sleep. For example, morning presentation of exercise or body heating produces different effects on nighttime sleep than evening presentation. Therefore, this study investigated the effects of a two-hour nonphotic auditory stimulus presented in the morning upon awakening on subsequent nighttime polysomnographic sleep. A second aim was to compare the results with a previous study that used the same stimulus presented in the evening to assess the role of auditory presentation time on sleep.

Methods: Subjects were seven women and one man, ages 19 to 63 (mean age ± SD, 31.0 ± 18.9 y), in good physical and psychological health without sleep disturbance. CNS medication usage or extreme morningness/eveningness were exclusionary. Subjects completed two four-day, four-night sleep laboratory sessions in constant dim light (<20 lux) conditions. They received either a two-hour auditory stimulus (presented at 60 decibels) or a control stimulus from 0600 h-0800 h on both the second and third mornings. Presentation order of the stimulus/control sessions was counterbalanced. Subjects remained awake during presentations; infrared cameras and polysomnography monitored compliance. Sleep was polysomnographically recorded on all nights. Records were scored in 30-second epochs using Rechtschaffen and Kales' standard scoring criteria. Paired t-tests examined differences in sleep measures between each corresponding night in the control and stimulus conditions. Data are presented as mean ± SEM; $p< .05$ was considered significant.

Results: The auditory stimulus significantly increased total wake time (25.81 ± 6.17 vs. 11.56 ± 5.38; $t7=2.88$, $p<.03$), decreased sleep efficiency (92.53% ± 1.80% vs. 96.53% ± 1.51%; $t7=2.69$, $p<.03$) and increased REM latency (123.00 ± 24.87 vs. 81.69 ± 15.12; $t7=3.47$, $p<.01$) compared to the control on the first night following morning presentation. On the second night following presentation, the auditory stimulus significantly decreased total wake time (22.69 ± 7.06 vs. 45.63 ± 12.35; $t7=2.80$, $p<.03$) compared to the control. By contrast, sleep measures did not differ significantly between the stimulus and control conditions on the two nights without corresponding morning presentation.

Conclusions: Morning presentation of an auditory stimulus impedes sleep by increasing total wake time, decreasing sleep efficiency, and increasing REM latency compared with a control stimulus. The results are limited to the first night following exposure only, suggesting adaptation to the auditory stimulus by the second night. These findings contrast the sleep-promoting effects produced when the same auditory stimulus is presented immediately before sleep. However, the results are similar to other studies that have shown differential effects of behavioral stimuli on sleep as a function of presentation time. The results of this study have significance for determining the appropriate stimulus administration time necessary for producing disruptive or soporific effects on sleep.

1102.U

An Olfactory Stimulus Modifies Subsequent Sleep In Men and Women

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Introduction: Nonphotic stimuli, including stress and auditory cues modify subsequent sleep when presented before sleep. By contrast, little is known about whether olfactory stimulus exposure before sleep affects nighttime sleep. A few studies found that lavender increases total sleep time and decreases wake time. These studies, however, used small samples and uncontrolled testing conditions. In addition, women consistently surpass men in odor detection and discrimination tests. Therefore, this study investigated the effects of an olfactory stimulus presented before bedtime on subsequent polysomnographic sleep. We also investigated gender differences in such effects.
Methods: Subjects were 15 women and 10 men, ages 18-30 (mean age ± SD, 20.8 ± 2.5 y), in good physical and psychological health without sleep disturbance. CNS medication usage or extreme morningness/eveningness were exclusionary. Subjects completed three consecutive overnight sessions: one adaptation night, one stimulus night and one control night (stimulus/control night order was counterbalanced). Subjects received an intermittent presentation (first two minutes of each ten-minute period) of an olfactory (lavender oil) or a control (distilled water) stimulus from 2310 h-2340 h. Sleep was polysomnographically recorded from 0000 h-0800 h. Records were scored in 30-second epochs using Rechtschaffen and Kales' standard scoring criteria. Repeated measures analyses of variance, with gender as a between-subjects factor, examined differences in sleep measures between the control and stimulus sessions. Data are presented as mean ± SEM; $p < .05$ was considered significant.
Results: The olfactory stimulus significantly increased stage 3 % SPT (5.47% ± .48% vs. 4.70% ± .57%; $F1,23 = 4.78$, $p<.05$) and SWS duration (33.69 ± 4.35 vs. 28.38 ± 4.41; $F1,23 = 5.92$, $p<.05$) compared to the control. Women showed a longer non-REM duration in the stimulus than control session (356.33 ± 7.76 vs. 346.87 ± 7.91), while men showed a shorter duration (342.75 ± 9.51 vs. 359.30 ± 9.69; $F1,23 = 4.74$, $p<.05$). By contrast, men showed a shorter REM latency in the stimulus than control session (105.65 ± 15.83 vs. 150.30 ± 19.65), whereas women showed a longer latency (101.77 ± 12.93 vs. 95.30 ± 16.04; $F1,23 = 4.22$, $p=.05$). Overall, women showed a significantly longer SPT (470.33 ± 3.55 vs. 457.03 ± 4.35; $F1,23 = 5.61$, $p<.05$), shorter TWT (12.37 ± 4.49 vs. 29.50 ± 5.50; $F1,23 = 5.83$, $p<.05$), shorter sleep onset latency (7.55 ± 3.36 vs. 22.05 ± 4.11; $F1,23 = 7.46$, $p<.05$), shorter stage 2 latency (11.62 ± 3.49 vs. 25.33 ± 4.28; $F1,23 = 6.16$, $p<.05$) and better efficiency (97.32% ± .95% vs. 93.87% ± 1.16%; $F1,23 = 5.32$, $p<.05$) than men.
Conclusions: Lavender presentation before bedtime produces soporific effects by increasing SWS duration. Furthermore, lavender differentially affects non-REM duration and REM latency in men and women. Overall, women showed better sleep quality than men, with shorter onset latency, less wake and better sleep efficiency. Lavender presentation before bedtime may serve as a nonpharmacologic alternative for promoting sleep in men and women.

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1103.U

The Frequency and Associated Factors of Excessive Daytime Sleepiness in Korean Young Men

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Introduction: This epidemiologic study was to ascertain the prevalence of daytime sleepiness and to investigate the associated factors with daytime sleepiness in korean young men.
Methods: 1) 6,143 subjects was examined among military recruits in Seoul Regional Military Manpower Administration, from April. 2000 to November. 2000.2) Epworth Sleepiness Scale and Stanford Sleep disorders Questionnaire were used in this study. 3) Multiple regression analysis was used to find out sleep variables associated with Epworth Sleepiness Scale.
Results: 1) Individuals who had 11 or more ESS(Epworth Sleepiness Scale) score were taken to represent excessive daytime sleepiness. Total 1,392 subjects(23.4%) of all subjects met this criteria of excessive daytime sleepiness. 2) Mean ESS score of excessive daytime sleepiness group was 12.92¡¾2.17. 3) Symptoms of cataplexy, symptoms of sleep apnea, restless leg symptoms, frequency of awakening during night, and frequency of nap were shown to have a significant correlation with increased ESS scores.
Conclusions: 1) 23.4% of Korean young men had excessive daytime sleepiness which is associated with various clinical correlates, notably with symptoms of cataplexy.2) Further research is needed to investigate the relationship between excessive daytime sleepiness and clincal correlates, especially symptoms of cataplexy, in the general population.

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1104.U

An Investigation of Information Processing Upon Arousal From Sleep

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Introduction: Arousal from sleep is associated with a large transient surge in cardiovascular activity. Increased activity in brain structures that are associated with vigilance, sensory receptiveness and motor responsiveness, such as locus coerulus and dorsal raphe nuclei, also occurs at this time. It has been proposed that this reflex-type response results in a heightened state of activation in which individuals are more receptive to incoming sensory information than during relaxed wakefulness. The N1 evoked potential is sensitive to changes in levels of attention and arousal and may be used to assess the degree of attention-related activation at wake onset. Previously our laboratory has shown that during sleep onset, periods of wakefulness are associated with an N1 amplitude that is significantly smaller than that seen in wakefulness. However, this study did not target the period immediately following wake onset. The current study tested the hypothesis that, upon arousing from stable sleep, N1 amplitude will be greater than that seen during relaxed wakefulness.
Methods: Four participants were run over two nights in wake and sleep conditions. Measures collected included 12 channel EEG, EMG, EOG and ECG. In each condition participants were presented with a sequence of three tones, S1:80dB,1000Hz,50ms(followed by 2sec interval), S2:80dB,1000Hz,3sec(followed by 2sec interval) and S3:80dB,1000Hz,50ms. In the wake condition, sequences were presented with a random ISI of 10-20s, while in the sleep condition presentation occurred during stage 2 sleep. In the sleep condition the function of S2 was to arouse the participant, therefore the intensity of this tone was adjusted between 70-100dB to produce an arousal. In the sleep condition S3 was timed to occur within the arousal response to S2, while in wake it occurred during continual wakefulness. Data are presented representing the averaged responses to S3 under three conditions: wakefulness, sleep followed by an ASDA arousal and sleep followed by an arousal that did not meet ASDA criteria.
Results: Results indicated a substantial P50-N1 component to S3 during wakefulness at Cz (mean=-9.98mV, sd.=2.01). The P50-N1 to stimuli

following an ASDA arousal was slightly reduced relative to that seen in wakefulness (mean=-7.92mV, sd.=1.74), and did not differ to that seen in the average of responses to stimuli presented where an ASDA arousal to S2 could not be detected (mean=-8.62mV, sd.=6.0). Non-parametric analysis indicated no significant differences between the three values (Kendall's W=0.75, Chi Square(2)=3, p>0.05).
Conclusions: These results suggest that at wake onset, as defined by the presence of an ASDA arousal, N1 amplitude is not augmented. In addition, as indexed by N1 amplitude, there is no difference in level of cortical activation between arousals that meet ASDA criteria and those that do not. The data are not consistent with the hypothesis that the cortex is in a hyper-aroused state following an ASDA arousal.

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1105.U

Internal State Versus Behavioral Approach To Subjective Sleepiness
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Introduction: Subjective sleepiness is a complex phenomenon that is not yet well understood. One way to further examine sleepiness may be to use Lang's tripartite model of emotional responses. Lang proposes that there are three emotional response systems: internal states, physiological states, and behavioral changes. Several common measures of sleepiness such as the Stanford Sleepiness Scale (SSS), the Epworth Sleepiness Scale (ESS), the Profile of Mood States (POMS) and visual analogue scales (VAS) assess sleepiness in ways that may allow a comparison based on Lang's theory. The SSS, POMS, and VAS assess an internal feeling of sleepiness. In contrast, the ESS assesses a more behavioral component of sleepiness. The purpose of this study was to examine whether the subjective measures assessed sleepiness in different ways and as such whether sleepiness could be seen as consisting of at least two components, an internal state and a behavioral assessment, as suggested by Lang's theory.
Methods: The participants were 184 college students. The students completed the SSS, ESS, POMS, and VAS. The order of the scales was counterbalanced between participants. Correlations between the four measures and a principle components factor analysis were completed on the data to examine how the different scales were related to each other. The factor analysis used a specification of 2 factors and a Varimax rotation.
Results: The ESS resulted in relatively weak correlations (.17 to .32) with the other measures of sleepiness, whereas the correlations between the SSS and the other measures, except the ESS, were moderate to high (.41 to .79). The factor analysis indicated that the SSS, POMS, and VAS loaded highly into Factor 1 and accounted for 54.6% of the total variance across the measures of sleepiness. In contrast, the ESS alone loaded highly into Factor 2, with only minor contributions from the other sleepiness scales. Furthermore, Factor 2 accounted for only 17.0% of the variance across all measures.
Conclusions: The current results indicate that the ESS may be assessing sleepiness in a different manner than the SSS, POMS, and VAS. The SSS, POMS, and VAS were moderately to strongly correlated and loaded strongly on one factor. In contrast, the ESS had relatively weak correlations with the other scales and loaded on a separate factor. These findings indicate that the ESS may be assessing a different component of subjective sleepiness than the other scales, a behavioral component. In contrast, the SSS, POMS, and VAS seem to be assessing an internal state of subjective sleepiness. These results support the application of Lang's theory to subjective sleepiness and furthermore suggest that researchers and clinicians should consider using both types of sleepiness scales to obtain a more complete assessment of subjective sleepiness.

1106.U

Differential Effects of Sleepiness, Measured By Multiple Sleep Latency Test (MSLT) and Stanford Sleepiness Scale (SSS), on Psychomotor Vigilance Test (PVT)
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Introduction: The clinical and public health importance of excessive daytime sleepiness has been increasingly recognized. It has been hypothesized that sleepiness is multidimensional. Understanding which aspects of sleepiness compromise the ability to sustain alertness remains to be seen. The purpose of this study was to compare the relationships of perceived sleepiness and propensity to fall asleep, each of which may reflect different dimensions of sleepiness, with vigilance.
Methods: The study sample comprises 394 subjects enrolled in the Wisconsin Sleep Cohort Study. The measures, obtained during a daytime protocol, included the MSLT, SSS, and the PVT. To assess the differential effects of sleepiness, measured by the MSLT and SSS on the PVT outcomes, the sleepiness and the PVT variables were transformed to standard deviation units and the GLM procedure of SAS was performed on individual PVT outcomes, adjusting for SDB, gender, age, body mass index, educational status. P-value <0.05 was considered statistically significant
Results: The MSLT score was significantly, but not strongly, associated with diminished psychomotor vigilance measured by the PVT domains, including median reaction time (effect size (ES) = 0.12), fastest 10% (ES = 0.12), slowest 10% (ES=0.11), and lapse (ES=0.10), except for time on task decrement (ES = 0.05) and false response (ES = 0.03). The SSS score was significantly, but not strongly, related to median reaction time (ES = 0.14), slowest 10% (ES=0.12), and lapse (ES=0.14), except for fastest 10% (ES = 0.05), time on task decrement (ES = 0.09), and false response (ES = 0.06).
Conclusions: Both objective and subjective dimensions of sleepiness were significantly associated with most of the PVT domains. However, sleepiness, measured by the MSLT and the SSS, may act differently in influencing "optimal response" domain of vigilance.

1107.U

Acute and One Week of CPAP Withdrawal Impairs Driving Performance
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Introduction: Nasal CPAP improves a range of neurobehavioural performance in patients with obstructive sleep apnea, including simulated driving. However, the impact of driving performance following acute and short-term withdrawal of CPAP has not been previously investigated. Many patients in Australia cease CPAP for short vacation periods involving substantial rural driving as they may be camping or engaged in other activities precluding CPAP use. We hypothesised that driving performance will be affected when regular CPAP treatment is temporarily removed from OSA patients.
Methods: AusEd driving simulator was performed in 5 patients who underwent 7 nights of CPAP withdrawal after at least 12 months of therapy (minimum compliance > 4 hours/night and RDI < 10). The AusEd driving simulator is a tool that assesses driving performance, in particular, steering, speed and reaction time variables. It is designed to simulate nighttime monotonous driving scenarios. The subjects were asked to drive for 30 mins, keeping the speed between 60-80km/hr and to maintain the vehicle in the middle of the left hand lane. The driving sessions were performed at approximately 8:30PM and 08:30AM on each of 4 days. Day 1 – last night on CPAP, Day 2 – following acute (1 night) CPAP withdrawal, Day 8 – following chronic (7 nights) CPAP with-

drawal and Day 9 – following acute (1 night) CPAP reinstitution. Recordings were performed without light and noise controlled environment.
Results: For these 5 patients, there were no changes over the one week period in velocity deviation or reaction time. There was trend (P<0.2) in increased crashes at day 2. The main change over time was a decrease in steering performance. Standard Deviation From Median Lane Position (SdMLP) and Average Steering Deviation From Median Lane (AvSDML) were both impaired at Day 2 (acute withdrawal). However Day 8 results for steering performance were not different from baseline.
Conclusions: Driving performance is immediately affected by acute (one night) removal of CPAP treatment. Although the sample size is small, it is possible that the absence on Day 8 changes from baseline (7 days off CPAP) reflects on an adaptive response to recurrent OSA.

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1108.U

Sleep And Arousal Components Of Sleepiness: An Intra-Familial Study

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Introduction: An intra-familial questionnaire study on sleep/wake habits and sleepiness/arousal was designed to test a state-trait sleepiness model, comprising both a sleep and a wake drive. First, it was hypothesized that sleepiness partly represents a stable, personal characteristic, determined by genetic and stable environmental factors (trait sleepiness). This would be reflected in resemblances in sleepiness level within families. Secondly, this model conceptualized sleepiness as resulting from 2 opposing drives, a sleep drive and a wake drive or physiologic and behavioral arousal.
Methods: Within each of the 219 families studied, a parent between 46 and 74 years (M=59.2; SD=7.4) and one child between 21 and 51 years (M=32.9; SD=6.1) completed the Epworth Sleepiness Scale (ESS), the Hyperarousal Scale (HS), the Pittsburgh Sleep Quality Inventory (PSQI), the Pre-Sleep Arousal Scale, the Sleep-Wake Activity Inventory, the Profile of Mood States and the Athens Insomnia Scale.
Results: Multilevel Analysis (random intercepts model with 2 levels: persons within families) indicated that 19% of the variance in ESS-scores could be attributed to commonalities within families (Ssm0s2=2.478; p<.05). Including the ratio between the average total sleep time and the self-estimated sleep need as a predictor variable, a trend was found for ESS-scores to increase as the extent to which one gets sufficient sleep decreased (bs1s=-.033; p<.06). In contrary to what was expected, ESS-scores increased with higher HS-scores (bs2s=.092; p<.001). Selecting the extreme hyperaroused respondents (HS > 1 SD above the mean), it was found that the ratio sleep/sleep need nor the HS-score were related to the ESS-score (bs1s=-.009; n.s.; bs2s=.032; n.s.). Using evening sleep onset latency as the dependent variable, regression analysis gave following results: sleep latency significantly increased as the HS-score increased (bs2s=.520; p<.0001), while the ratio sleep/sleep need did not have a significant effect (bs1s=-.054; n.s.). A higher arousal score was significantly associated with a shorter sleep duration (average sleep time in PSQI) (r=-.29; p<.001) and a poorer sleep quality (total PSQI) (r=.61; p<.001).
Conclusions: Genetic and stable environmental factors shared within families significantly contribute to daytime sleepiness as measured with the ESS, confirming the concept of trait sleepiness. In everyday life the ability to fall asleep at night (sleep latency) showed to be particularly hampered by high arousal levels (wake drive). The ability to stay awake during the daytime seems to be sensitive to an insufficient amount of sleep at night (sleep drive). We hypothesize that the unexpected positive link between arousal and daytime sleepiness is in part mediated by the negative impact of arousal on the quality and duration of sleep at night, which increases daytime sleep pressure. Results suggest that it is only in extreme aroused persons that the impact of the heightened arousal is present during the daytime as well, cancelling out the net effect of poor nocturnal sleep on daytime sleepiness.

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1109.U

The Influence of Sleep on Memory: An Event-Related Potential Study

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Introduction: Behavioral and electrophysiological studies have shown that cognitive processes active in the awake state are also active during sleep, allowing memory consolidation during sleep and improved performance the following day. There is little information, however, on the nature of the mechanisms involved. The aim of the present study was to use cognitive evoked potentials (ERPs) in order to characterize some of the cognitive processes involved in the facilitation of recognition performance by sleep.
Methods: Ten healthy participants (5 females, 5 males) aged between 18 and 39 years were asked to keep regular sleep-wake schedules before coming to the laboratory, and filled an agenda during the course of the experiment. Each session comprised of two phases. During the acquisition phase, participants were presented on a computer screen with a series of stimuli (faces) and asked to memorize them. Either 8 hours of nocturnal sleep or 8 hours of daytime awakening elapsed between the two sessions. At the recognition phase, participants were presented with the 40 previously learned "old" stimuli mixed with 40 "new" faces never learned and asked to recognize the learned faces while ERPs were recorded. All participants contributed to both conditions, in a counterbalanced fashion, with no more than one week between sessions. ERP data was analyzed using a 2 (night/day) x 2 (old/new) x 3 (Fz, Cz, Pz) ANOVA with repeated measures (subjects).
Results: Participants correctly recognized 74.4±9.9% the faces following nocturnal sleep vs. 64.4±13.9% following daytime wake. Reaction times for correct responses were not different. Analysis of the N200 showed a main effect of recording site (p = .007) and a significant session x repetition x site interaction (p = .04). The ANOVA performed on the P300 data revealed a main effect of site (p = .03) and a significant session x repetition x site interaction (p = .03). N200 and P300 results reflected a larger day/night effect over Fz for the session following nocturnal sleep. The P600 results showed a session x site interaction (p = .03), corresponding to a larger day/night effect over Pz for the session following nocturnal sleep.
Conclusions: The effect of sleep on recognition performance using ERP measures is made of early frontal and late parietal processes that could respectively represent a facilitation of familiarity assessment and of trace access, following a night of sleep. These results are consistent with the role of sleep in memory consolidation.

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1110.U

Is BMI A Good Predictor For Sleepiness In Applicants For Commercial Vehicle License?

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Introduction: Obstructive Sleep Apnea (OSA) is thought to be related to excessive daytime sleepiness. Several studies have proved a relationship between OSAS and sleepiness related accidents among commercial drivers. Following this conclusion, the Israeli Ministry of Transportation Medical Wing decided to refer obese (BMI >32) applicants for a commercial vehicle driver's license to undergo polysomnography and MSLT assessment, in order to determine their suitability for safe driving.
Methods: Subjects: 69 men and 1 woman, applicants for commercial driving license, mean age: 47± 11 yrs., mean BMI 38 ± 7 kg, without reported daytime sleepiness. Procedure: Subjects underwent full polysomnography including: EEG, EOG, submental EMG , nasal flow, snoring, chest respiration belt, abdominal belt, EKG and pulse oximitry. The following day they underwent 5 trails of MSLT at two-hourly intervals beginning at 10 am. The results were analyzed according to Rechtshaffen guidelines.
Results: Seventy-eight percent were diagnosed as having OSAS (RDI = 39.8 ± 34); 11.5% without any sleep disorder and 10.5% with other sleep disorders. MSLT scores were as follows: 14.3% less than 5 min., 24.3% between 5-10 min. and 22.8% between 10-15 min. Significant correlation (Pearson) between nocturnal sleep latency and mean sleep latency in MSLT [$r = 0.274$, $p<0.05$] and between RDI and mean sleep latency in MSLT[$r = -0.214$, $p<0.05$]. In addition, significant correlations between BMI and RDI ($r=0.295$, $p<0.05$) and between BMI and the number of desaturations ($r=0.252$, $p<0.05$) were found. No significant correlation was found between mean sleep latency in MSLT and the following variables: REM latency, REM%, SWS%, number of arousals, number of awakenings, sleep efficiency, number of desaturations, age and BMI.
Conclusions: In sleep medicine MSLT is considered as the gold standard test for sleepiness. Mean latency of less than 10 min indicates pathological sleepiness. In our study 38.6% of the subjects with BMI over 32, who did not complain of sleepiness fell into this category. Obviously the applicants tested were highly motivated to overcome their sleepiness, in order to ensure their receiving a commercial driving license. Therefore, if we also include the whole group whose latency in MSLT is less than 15 min, 61.4% of the subjects showed pathological sleepiness. When screening the sleepiness of applicants for commercial driving, their subjective reports are totally unreliable. Weighing and measuring height is a very simple procedure to calculate the BMI. This study suggests that the cut off point of BMI 32 is a competent prediction for risk of OSAS [78%] and pathological sleepiness (61.4%). Although BMI in this study has been found to be a good predictor for sleepiness in commercial vehicle drivers, further analysis taking into account other objective parameters, would enable determination of the relative weight of each parameter in predicting sleepiness in this population

1111.U

Three Components of Human Motor Memory Plasticity: Stabilization, Enhancement and Recollection Labilization

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Introduction: Memory consolidation has generally been defined as a time-dependent process involving the stabilization of learned information. Recent studies have shown that episodes of wake (Muellbacher et al. 2002) and sleep (Walker et al. 2002) are important for memory formation, yet the consequences of each of these respective brain states in producing distinct forms of consolidation remains unknown. It is also unknown whether the recall of information previously consolidated by episodes of wake and sleep in humans, can result in a memory representation returning to an unstable form.
Methods: Sixty-four subjects were tested on a sequential finger-tapping motor-skill task. Two unique motor sequence patterns were used ("Seq-I" and "Seq-II") in counter-balanced order. Subjects were trained (x12 trials) either on only one sequence or on both sequences, and subsequently retested (x3 trials) in five different protocols.
Results: Subjects in group-1 learned only one motor sequence (Seq-1) on day-1 (1PM). When retested 24hrs later, normal overnight improvements in speed and accuracy developed, as previously reported (Walker et al. 2002). Subjects in group-2 learned Seq-I on day-1 (1PM) and, after 10min, learned Seq-II. When retested 24hrs later, overnight improvements in accuracy occurred only for Seq-II (learned last), with improvement blocked for Seq-I. Subjects in group-3 learned Seq-I at 10AM day-1, and were trained on Seq-II 6hrs later (4PM). When retested on day-2 (1PM), normal overnight improvements had developed for both sequences. Subjects in group-4 trained only on Seq-1 on day-1 (1PM), and when retested 24hrs later on day-2, normal overnight improvements were seen. After this retest on Seq-I, subjects were trained on Seq-II. When retested after a further 24hrs, on day-3 (1PM), normal overnight improvements were seen for Seq-II, while the accuracy improvements that had been achieved by day-2 on Seq-I were now reversed, returning close to post-training values. Subjects in group-5 also trained on Seq-1 on day-1, but they were not retested during day-2. Instead, they simply trained on Seq-II on day-2. In contrast to group-4, retesting on day-3, after a further 24hrs, showed normal delayed improvements for both sequences.
Conclusions: We conclude that (1) an initial 6hr post-training waking period results in a process of memory stabilization for this task, but without enhancing performance; (2) sleep subsequently triggers a distinctly different process, which produces additional performance gains overnight in the absence of additional rehearsal; and (3) despite the occurrence of both stabilization and enhancement, the subsequent reenactment of the motor pattern once more renders the memory representation vulnerable to interference from a competing motor pattern and can lead to a reversal of previously learned aspects of the task. All three of these phenomena may represent elements of a more inclusive model of memory consolidation.

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1112.U

The Time Course of Sleep-Dependent Motor-Skill Learning

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Introduction: Growing evidence suggests that sleep plays an important role in the process of procedural learning. Previously we have shown that motor-skill learning continues to develop only across a night of sleep, correlating strongly with stage-II NREM (Walker et al. 2002). However, the temporal evolution of motor learning before and after sleep, the effects of different training regimens, and the long-term development of learning across multiple nights of sleep remain unknown.
Methods: Here we report data for forty subjects, in four groups, trained and retested on a sequential finger tapping motor-skill task across multiple days. Group-1 investigated differences in the profile of motor learning across the first 12hrs of wake prior to a night of sleep compared to the learning profile across 12hrs of wake following a subsequent night of sleep. Group-2 examined the development of learning after one night of sleep following a single training session, while Group-3 investigated the development of learning after one night of sleep following two suc-

cessive training sessions. Subjects in Group-4 received one training session, as in Group-2, but were retested only 72hrs later after three intervening nights of sleep.
Results: Following initial training in Group-1, small practice-dependent improvements were seen before, but not following, the large practice-independent gains which developed across the intervening night. In a comparative analysis between Group-2 and Group-3, doubling the quantity of training did not diminish or increase the amount of subsequent overnight sleep-dependent learning. Relative to Group-2, the additional nights of post-training sleep in Group-4 led to further improvement, although the majority of sleep-dependent learning appeared to develop during the first night of sleep following training. Finally, the amount of practice-dependent learning achieved during training did not correlated with the amount of delayed (practice-independent) sleep-dependent learning that subsequently developed.
Conclusions: Following initial training, small amounts of practice-dependent learning remain possible prior to a night of sleep. But after the normal overnight gains in performance subsequent rehearsal produces no significant improvement. Multiple nights of sleep do confer further improvements, but the greatest sleep-dependent improvement occurs across the first night of sleep. While doubling the number of trials in the initial training sessions offers modest continued improvement, observable during the session, it does not alter the magnitude of overnight sleep-dependent learning, suggesting the existence of two discrete motor learning processes. This hypothesis is further supported by the lack of correlation bewteen the amount of learning achieved during training and the amount of subsequent overnight learning. These sleep-dependent findings may have important implications for the efficient learning of skilled actions in humans, and hopefully for the recovery of motor skills following insults to the motor system such as stroke and brain damage, as well.

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1113.U

Early Morning Shifts (Short Sleep) and Long Distance Between Stops Increase Sleepiness in Train-Drivers

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Introduction: The main objective of this study was to experimentally evaluate the effects of early morning shifts on sleep, sleepiness and objective performance for train drivers during normal working conditions. The present paper presents subjective data on sleep and sleepiness.
Methods: 18 male train drivers, mean age 50 years (44–60), were studied during a drive from Stockholm to Malmö and back to Stockholm again. The drive to Malmö was 4h 27min (10 stops) and was followed by a 2h 28min rest before the return to Stockholm. The study involved three conditions: an early morning shift that started 5:49 (train departed 6:18) and ended 17:41, a day shift (7:49-19:41) and an evening shift (9:49-21:41). Subjects were scheduled to the three conditions with one week in between in a counter balanced order. Subjects were guaranteed at least a 12-hour rest before, and remained on their normal working schedule in between. Before leaving Stockholm, subjects completed a questionnaire about sleep the previous night. At every stop, subjects rated sleepiness using the Karolinska Sleepiness Scale (KSS, 1=very alert, 9=very sleepy, fighting sleep, difficulty staying awake). Ratings were retrospective and in addition to mean sleepiness (since the last stop) they also estimated the peak in sleepiness during the drive.
Results: Sleep length varied across conditions ($p<.001$) and was longest before the evening shift (7.7h/pm.13 sem) and shortest before the early morning shift (5.6/pm.22) with the day shift in between (6.7/pm.19). There were no difference in sleep quality or disturbed sleep between conditions but the ratings of insufficient sleep was more pronounced before the early shift ($p=.020$). There was an effect on sleepiness during driving and this was especially true for ratings of the maximum peak in sleepiness. A three factor repeated measures ANOVA showed that there was an effect of shift ($p=.011$) and time ($p=.026$) but no effect of direction ($p=.144$) and no interaction effects. Descriptive data show that there were peaks in sleepiness during the early shift when the drives between stops (inter-stop segments) were long and dips in sleepiness when inter-stop segments were short. To test the effect of inter-stop segment length, means were calculated for short inter-stop segments (11-15min) medium segments (24-37min) and long segments (57-58min). Segment length was entered as a factor in an ANOVA. The results shows that there was an effect of segment ($p=.017$), shift ($p=.003$) and an interaction segment*shift ($p=.048$). For the early shift, longer inter-stop segments increased sleepiness, but for day and evening shifts, segment length had no effect.
Conclusions: The results suggest that early morning shifts reduce sleep length and increase the susceptibility to sleepiness in train drivers. The increase in sleepiness was more pronounced during long drives between stops, which suggest an interaction between early morning shifts (short sleep) and long distance between stops (monotony) on sleepiness.

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1114.U

Statistical Modeling Of Responses Over Time In Sleep Restriction Protocols

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Introduction: Inter-individual differences in response to sleep loss are substantial. Sleep deprivation protocols often involve neurobehavioral and physiological testing over multiple days. Traditional analyses of longitudinal data rely on univariate or multivariate repeated measures ANOVA that ignore inter-individual variability in time trajectories and thereby underestimate standard errors. This results in overestimated statistical significance and undersized confidence intervals. There is need for conceptually simple, yet quantitatively valid statistical methods that avoid this problem by capturing inter-individual variability. Preferred methods should accommodate assay-specific non-linearity of time trajectories. To identify an optimal statistical approach to sleep deprivation time series data, three statistical techniques for estimating the parameters of a simple non-linear mixed effects regression model were compared using data arising from two experiments. The first study examined the effects of a 2h nap scheduled every 24h, with and without a once-daily dose of modafinil, during 88h of simulated sustained operations in the laboratory. The second involved a 14 day sleep restriction protocol comparing 4 hr, 6 hr and 8 hr time-in-bed conditions.
Methods: The proposed non-linear mixed effects regression model expresses change in response from baseline as a function of a subject-specific (non-linear) slope multiplied by elapsed time raised to a curvature parameter (theta) plus random error. The subject-specific slopes are assumed to arise from condition-specific normal distributions. The time exponent reflects curvature in the growth curves. When theta is 1, the model reduces to subject-specific simple linear regressions with no intercept. We estimated theta; the within-condition mean and standard deviations of the subject-specific slopes; and residual standard deviation using Standard Two-Stage (STS) least squares regression; Restricted Maximum Likelihood (REML) of a linear mixed model; and Maximum Likelihood (MLE) estimation of the non-linear model treating theta as an unknown parameter. For STS and REML, grid searches were used to identify optimal thetas that minimized mean squared error. Outcomes included measures from a psychomotor vigilance task, a probed memo-

ry recall task, a digit symbol substitution task, and the Karolinska Sleepiness Scale.
Results: Grid search identified the same optimum thetas for STS and REML. As theory predicted, condition-specific mean values were the same for balanced designs with REML producing slightly smaller (and more accurate) estimates of between-subject variance. Grid search identified optimal curvatures arbitrarily close to MLE. In a few cases, the MLE model failed to converge, but solutions were found using the STS and REML approaches. Specific-specific non-linear slopes were very useful in describing between-subject variability in the responses to sleep restriction.
Conclusions: The proposed simple non-linear mixed effects model is statistically valid, conceptually simple, allows focus on subject-specific differences, permits non-linear trends in growth curves, and may be estimated by iterative applications of least squares regression using elementary statistical software. We encourage its use in studies of responses to sleep restriction over time.

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1115.U

Suppression of REM Sleep in Rats Recorded in a Fearful Context
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Introduction: Fear conditioning in rats has been used to investigate the mechanisms through which fear and anxiety influence behavior. We previously demonstrated that presenting multiple footshocks to rats selectively suppresses REM sleep (REM) over the subsequent 2-3 hrs. Through fear conditioning, the context in which shock is presented can later produce effects similar to the shock itself. To examine the influence of a fearful context on REM, we recorded sleep in rats in the same conditions in which they had received shock.
Methods: Subjects were 90-day old, male Sprague-Dawley rats (N = 7) on a 12-hr. L:D schedule. They were surgically implanted with EEG, EMG, and pontine electrodes and allowed to recover for one week. After habituation to a chamber (24 Lux) and to the recording procedure for 4 hrs. over 3-5 days, a 4-hr. baseline sleep recording was obtained in this chamber on the next day. One day later, animals received 5 footshocks (0.5 mA, 0.5 sec, inter-shock interval 3-5 mins.) through the grid floor of a cage placed in a different chamber (75 Lux). The next day sleep was recorded for 4 hrs. in the brighter chamber. Animals were transported to the recording room by a different path on the shock and post-shock days compared to the habituation and baseline days. Sleep efficiency (time spent asleep/total recording period) and REM and non-REM (NREM) measures (percent, average episode duration, no. episodes) were calculated. The data were analyzed with a 2 (Day) X 4 (Hour) repeated measures ANOVA.
Results: While sleep efficiency was not significantly changed in the threatening context, REM percent was reduced compared to baseline (16.0 + 2.7 vs. 13.4 + 17.5), $F(6,1) = 6.67$, $p < 0.05$. The number of REM episodes was not influenced by the conditioning procedure, but the average REM episode duration (mins.) was considerably shortened (2.0 + 0.5 vs. 1.2 + 0.5), $F(6,1) = 14.86$, $p < 0.01$. The number and average duration of NREM episodes were not significantly reduced.
Conclusions: Rats conditioned to fear a specific transport path and recording chamber showed a suppression of REM when they were transported by this path and then recorded in this chamber one day later. The reduction in REM percent was due to a reduction in average REM episode duration. Sleep efficiency was unchanged, and the average duration of a bout of NREM was not significantly decreased. These findings are consistent with our previous observations in rats recorded for 4 hrs. immediately after receiving a series of footshocks and suggest that contextual conditioning of sleep/wake in rats persists for at least one day. The mechanisms controlling REM, compared to NREM, episode continuity were specifically affected by contextual fear conditioning. The duration of the effect and the extent of its dependence on the specific path/chamber context are currently under investigation.

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1116.U

Seasonality Score Index (SPAQ) And Morningnesss/Eveningness In Chilean University Students
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Introduction: It has been suggested that Morningness/Eveningness preferences are determined by genetic and life styles factors. A polymorphism in the human gene clock has been related to lark phenotype whereas reports on isolated pre-modern populations reported large asymmetries in the distribution of Horne-Ostberg score. On the other hand Seasonal Pattern Assessment Questionaire (SPAQ) relates seasonality to latitude, suggesting that the photoperiod is the main factor determining circannual rhythms in mood, appetite, etc. These evidences place circadian factors as a common causative mechanism for seasonality and Morningness/Eveningness preference. If it is true, larks and owls should show different seasonal vulnerability.
Methods: We studied a random sample of medical students (n=52; 26 males, 26 females; age: 19-26 yr.). A self-response questionnaire was developed concerning (i) sleep habits (school and weekend days); (ii) Morningness/Eveningness preference; and (iii) the SPAQ developed by Rosenthal et al. The questionnaire was applied during October of 2002 (Southern Hemisphere spring). School and weekend daily bed and rise time, wake preference profile, best and worst performance and mood timing, contributed to obtain Morningness/Eveningness categories: M/E1 (n=18); M/E2 (n=20) and M/E3 (n=14) that represent the low, intermediate and high score tercile respectively. Seasonality score index (SSI) was obtained by assessing SPAQ variables (sleep, social activity, mood, body weight, appetite and energy). Terciles for SSI scores determined the categories: SSI_1 (SSI<11, n=18); SSI_2 (SSI 11-13, n=19) and SSI_3 (SSI>14, n=15). Chi-square and non-parametric statistics were applied.
Results: Distribution of M/E score (range 6-29) show positive skewness with mode at 10 median at 13 and mean at 15. M/E1 and M/E3 show typical owl and lark patterns for performance, mood and wake hour preference respectively. As expected, M/E1 group reports larger total sleep time differences between weekend and school days, and more naps than M/E3. On the other hand, SSI distribution was normal with mean (SEM) at 11.7 (0.5) and median and mode at 12. SSI categories display typical seasonal pattern (worsening mood and energy and body weight gain during Southern Hemisphere winter months). Contingency tables show high consistency among the six variables. M/E categories show no difference in SSI scores. Significant difference among M/E categories was found only for seasonal mood change, where 100% of M/E3 report moderate to extremely large change in contrast to 61 and 55% of categories M/E 1 and M/E2 respectively.
Conclusions: Morningness/Eveningness categories obtained in our sample display similar SSI distributions. Individuals with lark profiles show more vulnerability to seasonal mood changes, with worsening during winter months. Our results suggest that specific circadian processes regulating mood are more prone to be affected by photoperiod.

1117.U

Sound Discrimination During Sleep

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Introduction: During sleep, humans continue to monitor their environment for cues indicating the need to awaken. By processing the information we receive during sleep, our brains are able to decide which sounds deserve our attention (by waking up) and which are best left ignored so that sleep may be preserved. In 1966, Wilson & Zung found that humans showed greater EEG arousal to target sounds versus nontarget sounds, but they did not counterbalance sounds with target status. The study presented here further tested human information processing during sleep by completely counterbalancing the presentation of sounds and by asking subjects to wake up to a category of sounds (either animal or machine sounds) rather than to specific sounds.
Methods: A total of 35 subjects (16 men, 19 women) from the Introduction to Psychology pool were recruited. Average age of the recruited subjects was 18.8 years (SD=0.8 years; ages 18-21). In this experiment, subjects took two afternoon naps. During each nap, subjects heard four sounds (two animal, two machine) while in Stage 2 sleep. Subjects were instructed to wake up to either animal sounds or machine sounds and sleep through other noises. Sounds and target status were completely counterbalanced across the two naps. Subjects' sleep was monitored objectively using polysomnography. Subjects were instructed to provide a subjective measure of awakening by saying, "I'm awake," when they heard a target sound; subjects were instructed to remain silent if they heard a nontarget sound, even if they found that the noise had awakened them.
Results: The interaction between subject gender and sound goal (whether a sound was a target or not) was significantly associated with EEG arousal ($p=0.05$). Based on their EEG, women were more likely to awaken to target sounds while men were more likely to awaken to nontarget sounds. In addition, all subjects were able to correctly identify target sounds that awakened them by saying, "I'm awake" ($p<0.01$).
Conclusions: The results of the present study indicate that women, but not men, are able to awaken to the target category of sounds heard during Stage 2 sleep. One possible explanation for the ability of women to wake up more frequently to target sounds is that they have been biologically programmed to respond to sounds during the night due to their need to attend to young children. However, we cannot rule out the possibility that women were more compliant than men with the experimenter's instructions. We also found that subjects, both women and men, were overwhelmingly successful in saying "I'm awake" only to target sounds. This is an impressive finding in that subjects were able to accurately remember which category of sound was the target, correctly identify the sound, and verbally state that they were awake, all while emerging from sleep.

1118.U

Sleep Disruption in Fathers and Mothers Before and After Childbirth

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Introduction: A number of studies have documented the sleep disruption that commonly occurs among women during pregnancy and the postpartum period. Yet fathers are also at risk for sleep disruption during this time. Few studies have included both parents and none have studied couples postpartum or used an objective estimate of sleep. The purpose of this longitudinal study was to describe the sleep of both parents before and after the birth of their first child.
Methods: As part of an ongoing randomized clinical trial, data are collected from childbearing couples during their last month of pregnancy and first three months postpartum. This study reports on couples assigned to the control group and includes data from their last month of pregnancy and first month postpartum. Wrist actigraphy (Ambulatory Monitoring, Inc., Ardsley, NY) was used to estimate sleep for 48 hours at both time points. Data from the second 24-hour period were analyzed. The 21-item General Sleep Disturbance Scale was also included. Repeated measures analyses of variance were used to test within-subject effects of time and parent on time in bed (TIB), total sleep time (TST), sleep efficiency (SE), wake after sleep onset (WASO), duration of wakings (DUR), and perceived sleep disturbance.
Results: To date, there are 28 control couples with complete actigraphy data and 30 with complete sleep disturbance ratings. SE decreased from 85.9 ± 9.7 during pregnancy to 71.5 ± 11.0 postpartum for mothers and from 87.1 ± 9.8 to 81.0 ± 10.8 for fathers. SE decreased over time for both parents ($Fs_{1,27s}=27.7$, $p<.001$), but decreased more for mothers than fathers ($Fs_{1,27s}=7.7$, $p=.01$). Similarly, WASO and DUR increased over time for both parents ($Fs_{1,27s}=44.3$, $p<.001$, $Fs_{1,27s}=29.8$, $p<.001$, respectively), but increased more for mothers than fathers ($Fs_{1,27s}=11.0$, $p=.003$, $Fs_{1,27s}=9.5$, $p=.005$). TIB increased from 8.7 to 9.5 hrs for mothers and from 7.7 to 8.2 hrs for fathers, yielding main effects for time ($Fs_{1,27s}=8.4$, $p=.007$) and parent ($Fs_{1,27s}=16.5$, $p<.001$). TST (6.8 hrs) did not change over time and did not differ for mothers and fathers. Self-reported sleep disturbance increased from 42.4 ± 16.7 to 52.8 ± 17.3 for mothers and from 26.0 ± 18.8 to 40.7 ± 15.1 for fathers, yielding main effects for time ($Fs_{1,29s}=20.0$, $p<.001$) and parent ($Fs_{1,29s}=17.6$, $p<.001$).
Conclusions: While mothers experienced more sleep disruption than fathers, both parents experienced significant postpartum sleep disruption. Total sleep time did not decrease, suggesting that the necessary wakings for infant care had a larger effect on sleep quality than on sleep quantity. Most fathers in this study (93%) had returned to work postpartum, compared to only a few (8%) of the mothers. Poor sleep quality is likely to be of particular concern to working parents. Future research is needed to explore the duration of these sleep changes, to evaluate their effect on psychosocial functioning and job performance, and to develop interventions for improving the sleep of new parents.

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1119.U

Schizophrenic Patients Do Not Show Sleep-Dependent Motor Skill Learning

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Introduction: Sleep plays a critical role in several forms of learning and memory consolidation. Perhaps the clearest evidence in humans lies in the enhancement of procedural skill performance following a night of sleep, an effect that has been seen for both visual and motor tasks. Such improvement can be blocked by sleep deprivation the night after training, and is not recovered with subsequent nights of sleep. Schizophrenia is characterized by diverse cognitive deficits that extend to learning and memory. The generality of these deficits has led to the proposal that they reflect deficient automation of task performance. Whether these deficit might be related to sleep dependent processes has not been investigated.
Methods: We studied 10 medicated schizophrenic patients on a motor skill finger tapping task that has previously been shown to have both practice-dependent and sleep-dependent components. Subjects were trained during twelve 30-sec trials, separated by 30-sec rest periods. During test trials, subjects typed the sequence 4-1-3-2-4 on a standard

keyboard "as quickly and accurately" as they could. Twenty-four hours later, they returned and were tested with an identical twelve trials over 12 minutes. Subjects were also trained on two additional tasks, a visual texture discrimination task, and the Sternberg Item Recognition Paradigm. We present the results of the motor skill learning task only.

Results: While schizophrenic patients performed more poorly than healthy young adult on day 1, the overall learning curves for the two groups were virtually identical. Schizophrenics showed an 82% (vs. 60% in healthy subjects) improvement across the 12 trials, with 57% (vs. 65%) of their improvement occurring during the second and third trial, and only 4.2% (vs. 2.9%) seen across the last two trials. In contrast to their apparently normal learning curve, patients retested 24 hrs later, after a night of sleep, showed an average decrease in speed of 6.9% vs. a 20.5% increase in the healthy subjects, during two test trials [$F(1,23)=14.1$, $p=0.001$]. Not one of the schizophrenic subjects approached a normal level of improvement. The additional 10 trials provided the schizophrenic subjects yielded no net improvement from day one, with the final trial on day 2 averaging only 3% faster than at the end of day 1.

Conclusions: The overnight deterioration in motor performance seen in this schizophrenic sample is in striking contrast to the highly consistent increase seen in healthy subjects. This is despite a normal learning curve seen across twelve trials on the first day. It is unclear whether this reflects medication effects on learning or sleep,or a core deficiency in sleep-dependent brain processes. Additional studies will be presented to help resolve this issue.

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1120.U

MSLTs in Young People as a Function of Parental History of Alcohol Abuse or Dependence: Preliminary Findings

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Introduction: The microstructure of sleep in adult humans changes in association with alcohol use, abuse, withdrawal, and abstinence. With the exception of work examining the likelihood of alcohol use resumption in abstinent alcoholics, few studies have assessed the predictive association of sleep-wake patterns and alcohol use. We have started to examine whether parental history of alcohol–related difficulties may predict sleep-wake patterns of offspring and ultimately whether sleep patterns may predict initiation of alcohol use. Here we present preliminary analyses of MSLT findings in youngsters with (PH+) and without (PH-) a parental history of alcohol abuse or dependence.

Methods: Children ages 9/10 years and adolescents ages 15/16 years were recruited. History of alcohol abuse or dependence among biological parents was determined using a structured clinical interview for DSM-IV criteria. Participants were excluded for: personal or family history of a sleep, psychotic, or genetically-transmitted neurologic disorder; personal history of epilepsy or metabolic disorder, chronic illness, mental retardation or other pervasive developmental disorder; current use of medications affecting sleep or biological rhythms, recent travel beyond 2 times zones; illness, serious injury, or physical handicap at the time of assessment. Twenty-seven participants have been evaluated: 7 children (4 m; 4 PH+) and 20 adolescents (9 m; 6 PH+). Children were Tanner stages 1 (n=4), 3 (n=2), or 4 (n=1); adolescents were Tanner stages 3 (n=1), 4 (n=3), or 5 (n=16). One week of actigraphy under self-selected conditions preceded a stabilization sleep schedule at home for 9 to 16 nights (mean =11), with compliance checked by diary, phone calls, and actigraphy. An adaptation and baseline in-lab night were followed by MSLT performed from 0900 to 1700 at 2-hour intervals. Participants were permitted to sleep for up to 20 minutes; SLTs were scored in 30-second epochs according to standard criteria.

Results: Assigned time in bed was significantly longer ($t = 13.91$; $p<.001$) in children (mean = 10.1 hr) than adolescents (mean = 9 hr), with significantly earlier bedtime (2111 vs. 2134; ($t = -2.24$; $p<.05$)) and later rising time (0717 vs. 0636 ($t = 4.27$; $p<.001$)) in children than adolescents. Results to date show no difference in MSLT pattern as a function of parental alcohol history. Age group (all children vs. all adolescents), however, showed significant differences in sleep latencies across the day. Mean sleep latencies on tests beginning at 0900 for children were: 20, 20, 19.9, 19.9, and 20 minutes; for adolescents were: 14.3, 13.9, 10.4, 15.6, and 16 minutes.

Conclusions: MSLT data from this preliminary data set showed no differences as a function of parental history of alcohol abuse or dependence. Age group differences may reflect the known reorganization of sleep tendency during puberty and/or the significant difference of stabilization sleep schedules. Larger sample sizes will permit more definitive assessment of the impact of parental history.

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1121.U

Olfactory Arousal Threshold in Stage 2, Stage 4, and REM Sleep in Comparison to an Auditory Signal

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Introduction: Although the assessment of human olfaction during wakefulness is a growing area of research, few studies have examined olfaction during sleep. The comparatively strong mediating influence of cognitive processes in waking olfactory perception relative to audition makes a contrast of olfactory and auditory perception interesting to study during sleep. To assess olfactory and auditory perception during sleep, we compared pyridine and peppermint at various intensities to one strong-intensity auditory tone.

Methods: Three men and 3 women ages 20-25 years participated. Peppermint and pyridine were presented for 15 seconds using an air-dilution olfactometer via intranasal cannulae at 100% concentrations and three successive one-third dilutions prepared in diethyl pthalate. The 'Up-and-Down' threshold-detection method of Zepelin was used. If behavioral arousal threshold to an odor was not achieved for a series, a 5-second 800 Hz tone was played at the mean stimulus strength effective in waking young adults from previous research (range = 78 to 105 dB). Behavioral arousal threshold from sleep was measured by the participant pressing a button and saying "I smell (hear) something." Physiological arousal was measured by polysomnography including central and occipital EEG, EOG, EMG, breathing, and EKG during stages 2, 4 and REM.

Results: Waking intensity was consistently greater for pyridine than peppermint. During sleep, 21 arousal series were completed for peppermint: 8 s tage 2, 8 stage 4, 5 REM sleep. No behavioral arousals occurred to peppermint; EEG activation occurred 5 times (strengths 1 and 3) in stage two, once at strength 4 in stage 4, and at least once to each strength in REM sleep. The tone produce behavioral arousals on 6 trials in stage 2, 7 in stage 4, and 4 in REM sleep, with EEG activation on the other tone trials. For pyridine, 25 arousal sleep series were completed: 11 stage 2, 8 stage 4, 6 REM sleep. Arousal threshold to pyridine occurred in 5 stage 2 trials (strengths 1, 2 (n=3), and 3), one stage 4 trial (strength 3), and 2 REM trials (strengths 1 and 2). EEG activation without behavioral arousal occurred once in stage 2, 4 times in stage 4, and three times in REM sleep. The tone produced behavioral arousals on all but one trial for each sleep stage, with EEG activation occurring on trials without behavioral arousal.

Conclusions: More frequent arousal to pyridine than peppermint likely

results from differences in stimulus intensity, although hedonic (pyridine is unpleasant) differences cannot be excluded. Stage 4 sleep was most resistant to odor arousals. Although EEG activation to odors may convey a level of sensory perception, human olfaction appears insufficiently sensitive during sleep to act as a sentinel system. Auditory signals, by contrast, were successful in arousing participants in all stages.

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1122.U

Sleep Behaviour and Driver Safety Knowledge in Australian Drivers

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Introduction: Road statistics in NSW suggest that 18% of all fatal accidents and 30% of fatal accidents in rural areas are attributable to driver fatigue with an overrepresentation of young drivers. There is little data available on sleep behaviour in different age groups in Australia. Previous work suggests sleep health knowledge in pre-driver Australians is poor but no data is available in the driver age group. The aim of this survey was to examine both sleep behaviour and sleep health knowledge in drivers of different ages.
Methods: A 42-question survey was mailed to 10000 respondents (aged 18-64 years) who were randomly selected from the New South Wales electoral roll. Questions were included on sleep behaviour and sleep knowledge. Respondents were divided into groups of young participants (18-24 years) and older participants (25-64 years). Overall, 3304 people (56.9% female; mean age of 35.5 years) responded. The response rate varied (younger 30.6%; older 40.5%).
Results: Significant differences for a number of sleep outcomes were found between younger and older participants. Total Sleep Time (TST) was significantly longer for younger participants compared with older participants for weekdays ($p< 0.00$) and weekends ($p<0.00$). Sleep latency times for both weekdays ($p<0.00$) and weekends ($p< 0.03$) were longer in the younger age group compared with the older age group. Fewer younger participants reported difficulties either initiating or maintaining sleep compared with older participants ($p< 0.00$). Younger participants who experienced sleep difficulties were significantly less likely to either consult a doctor ($p< 0.00$) or take prescription medication ($p< 0.00$) when compared to older participants. Of those individuals who napped, younger participants were more likely than older participants to nap for longer both on weekdays ($p< 0.01$) and weekends ($p< 0.01$). Younger participants were significantly less informed than older participants about sleep health knowledge related to safe driving ($p< 0.01$). Drivers in the 25-40 and > 40 age groups had similar sleep health knowledge. Females had superior knowledge ($p < 0.01$). More of the younger drivers were unsure about the effects of alcohol ($p<0.03$) and lack of sleep ($p<0.00$) than older drivers. People with poor sleep health knowledge had shorter TST, longer sleep latencies, shorter w/e naps, fewer people with 'excellent' health and more sleeping difficulties (all $p < 0.01$).
Conclusions: Younger participants slept longer, napped longer, reported fewer insomnia symptoms and were less likely to see their doctors or take prescribed medications than older participants. Younger participants were less informed about safe sleep health and driving practices than older drivers. Subjects with poor sleep health knowledge appeared to have more sleep difficulties. Such findings suggest that targeted educational measures are necessary to improve sleep health knowledge in young drivers, especially in relation to the combined effects of alcohol and lack of sleep

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1123.U

Fatigue and Exposure to Cigarette Smoke

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Introduction: The causes of chronic fatigue remain to be determined. In this study, we explored the possibility that levels of fatigue might be related to cigarette smoke.
Methods: Participants for this study were selected from a large group of university undergraduates who responded either high in fatigue (> 80th %ile) or low in fatigue (< 20 %ile) on the short-form version of the Fatigue Impact Scale (i.e., the FIS-10). These groups were balanced for sex, i.e., 50 men and 50 women in each group and were matched as closely as possible for age and ethnicity. For these groups, we scored their responses to a set of items that measured their exposure to cigarette smoke and its consequences.
Results: In response to the question "Do you smoke cigarettes?", we found that the High and Low Fatigue Groups were identical, i.e., 10 people in each group smoked cigarettes. However, in response to the question "Are you regularly exposed to cigarette smoke?", 52 people in the High Fatigue Group and 35 people in the Low Fatigue Group responded yes. The difference in the yes-no frequencies distributions to this question are significant ($x21 = 5.88$, $p < .025$, $f2 = .03$). The data indicate that the students in the High Fatigue Group were 1.49 times more likely to be exposed regularly to cigarette smoke than were the students in the Low Fatigue Group. Finally, we examined the difference between the High and Low Fatigue Groups for each item of the Smoking Symptoms Scale that we used in this study. These results clearly demonstrate that the High Fatigue Group reported significantly higher levels of symptoms than the Low Fatigue Group.
Conclusions: From these correlational data it is difficult to know if exposure to cigarette smoke increases fatigue. While this should be considered as a possibility, we are more inclined to believe the hypersensitivity to stimuli that may accompany fatigue caused the exposure of the High Fatigue Group to cigarette smoke to have a more salient effect on the smoking-related symptoms than was the case for the Low Fatigue Group. Regardless of the explanation, these data make it clear that exposure to cigarette smoke should be avoided, especially by those with high levels of fatigue.

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1124.U

Sleep Behaviour and Health in Australia

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Introduction: There is little data available on sleeping patterns, and we currently have no data on sleep and health in a representative population in Australia.
Methods: A 42-question survey was mailed to 10000 participants (aged 18-64 years) who were randomly selected from the New South Wales, Australia electoral roll. Overall, 3304 people (response rate: 35.6%) responded (56.8% female) with a mean age of 35.5 years.
Results: Most participants (58.8%) described their general health as good and slept for an average of 7.4 hours during the week. During weekends total sleep time increased by an average of 14 minutes. 14.2% of respondents reported napping on a regular basis with a mean napping time of 43 minutes on weekdays, increasing to 57 minutes on the weekend. 30.6% of respondents reported difficulties initiating or maintaining sleep, or a combination of both. Of these, most (71.7%) had experienced the symptoms for longer than 12 months. 39.7% of respondents reported insomnia symptoms, according to the Athens Insomnia Scale (AIS), while 19.6% exhibited possible insomnia, and 40.7% had no evidence of

insomnia. Those who reported sleeping difficulties scored significantly higher on the AIS (mean difference 5.7; P< 0.00) than those who reported no difficulties. Only 20.4% participants had visited their doctor for help for sleep difficulties, with only 18.2% of those choosing to take medication for their sleep problems. 42.2% of respondents reported family members who experienced similar sleeping difficulties. Those individuals reporting difficulties initiating or maintaining sleep experienced significantly longer sleep latency times on weekdays (mean difference 34mins; P< 0.00) and weekends (mean difference 26 mins; P< 0.00) compared with those individuals with no sleeping difficulties. Significant daytime sleepiness was reported by 11.1% of respondents who scored >10 on the Epworth Sleepiness Scale (ESS). 44.5% of respondents reported slight mood disturbance measured by a reported inability to keep up enthusiasm for getting things done – however only 3.6% considered this a very big problem. 4.8% of participants had visited their doctor to specifically discuss snoring or sleep apnea symptoms.
Conclusions: Most respondents in this survey were healthy and slept regularly for over 7 hours per night. However, almost one third of individuals reported insomnia symptoms with over 71% experiencing these difficulties for greater than 12 months. There was a 9% increase in the insomnia rate with the AIS, suggesting a possible overestimation of insomnia with this scale. It would appear that higher than expected number of Australians had consulted doctors about snoring. Follow up research is being conducted on the non-responders in this survey.

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1125.U

Patient Perception Of Sleep Quality And Quantity After Overnight Polysomnography

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Introduction: It is generally accepted that sleep quality and quantity are adversely affected by sleeping in the laboratory during a polysomnogram (PSG), a phenomenon which is commonly referred to as first night effect (FNE). Findings suggestive of FNE include reduced sleep efficiency, prolonged sleep and REM latency, reduced slow wave sleep (SWS) and decreased REM percentage. However, the accuracy of patient estimations of these parameters is uncertain. Patients commonly misperceive sleep quality and quantity after a PSG.
Methods: We analyzed PSG data and responses from a morning-after questionnaire from subjects referred to the Sleep Disorders Center over a one month period as part of an ongoing study. Only subjects who had never had a PSG and who had completed questionnaires were included. PSG variables included total sleep time (TST), sleep efficiency (SE), sleep latency (SL), REM and SWS percentage. Questionnaire variables included estimated SL and TST.
Results: Data from 53 subjects (33 men) were included. Mean age was 49 yrs (range 30-79). Fifty-one subjects were referred to the laboratory for sleep disordered breathing (96%), and 2 subjects were referred for movements in sleep (4%). Mean PSG data were: TRT: 391.4, TST: 293.2, SE:73.6, SL: 29.9 min, REM%: 11.2, SWS%: 10.4. The mean subject estimated SL was 54.1 minutes, and the mean subject estimated TST was 168.4 minutes. Further analysis of SL subject estimates revealed that 75% of subjects overestimated SL by more than 10 minutes, while 22% underestimated it by more than 10 minutes. The remaining subjects (15%) estimated SL accurately within 10 minutes. For TST, 50% of subjects underestimated TST, while 15% overestimated TST, and 35% accurately estimated TST within 30 minutes. SL and TST subject estimates correlated positively in that patients who overestimated SL (N=40) were more likely to underestimate TST (63%) than overestimate TST (0.5%). Similarly, subjects who underestimated SL (N=12) were more likely to overestimate TST (42%) than underestimate it (17%). When stratified into overestimators, underestimators and accurate estimators of SL, daytime sleepiness as measured by the Epworth Sleepiness Scale was not different among the groups, and SWS and REM sleep percentages were similar. However, more subjects in the group that underestimated SL reported dreaming (42%) than in accurate SL estimators (13%) and SL overestimators (1%).
Conclusions: Subject perceptions are relatively inaccurate when estimating SL (only 15% accurately estimated SL) and TST (35% accurately estimated TST) after a PSG. Subjects overestimated SL by 80%. More striking was that subjects underestimated TST by a mean of 43% . Interestingly, subject perceptions of SL, TST and dreaming were consistent in that those reporting longer SL reported lower TST and absence of dreaming, suggesting poor sleep, while those reporting shorter SL reported higher TST and dreaming, suggesting more consolidated sleep. While this study cannot determine the extent of FNE, it appears that subject perception of sleep quality and quantity is worse than the polysomnographic data.

1126.U

Epworth Sleepiness Scale in 2,117 Brazilians

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Introduction: The authors report on the mean ESS scores determined in a healthy population sample from urban communities in Brazil.
Methods: ESS was applied to 2,117 healthy individuals. 15 consecutive five-year age interval groups ranging from 15 through 84 years were created. Distribution of study population sample was balanced against the June 2000 Brazilian National Population Sensus (see graph 2)
Results: Graph 1: male and females ESS mean scores $\pm$ SD Table 1 : Results of ESS found in the sample
Graph 2 : Distribution of age-ranges in sample and in the population
Conclusions: Females in the age range 15 through 19 present a statistically higher ESS scores than males in the same age range. Increased ESS-measured degree of sleepiness in young females is in keeping with a need for longer sleep in young pre-menopausal females. Males in the age range 45-49 and 55-59 present a statistically (p<1,1%) significant higher ESS scores than females in the same age range. Higher prevalence of sleep-related breathing disorders in middle-age in males, hormonal changes brought about by menopause and insomnia in females may account for findings. Males and females in the 50-54 years age range showed non-statistically different ESS scores.