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The 2005 Annual Meeting abstract supplement unites the Journal *SLEEP* and the science of the Associated Professional Sleep Societies in a convenient format. As in past years, this special issue will include all abstracts to be presented at the APSS 19th Annual Meeting, June 18-23, in Denver, Colorado. The supplement will provide all members, including those unable to attend the meeting, a brief glimpse into the new ideas and fresh research, which the APSS Annual Meeting provides.

Of the 1055 abstracts accepted, 228 will be presented in oral presentation format and the remainder as poster presentations. Similar to prior meetings, the Program Committee elected to:

1) Thematically group the posters presented at the meeting;
2) Display posters for one of the three scheduled poster days;
3) Most importantly, there will be a 90 minute block of time each day (Monday, Tuesday, and Wednesday, June 20, 21 and 22) between 1:30pm and 3:00pm that authors will be available for questions during poster viewing.

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:

Category A – Basic Neuroscience
Category B - General Physiology
Category C - Clinical Pharmacology
Category D - Dreams

Category E - Circadian Rhythms
Category F - Phylogeny
Category G - Pediatrics
Category H - Aging
Category I - Sleep Deprivation
Category J - Sleep Disorders - Breathing
Category K - Sleep Disorders - Narcolepsy
Category L - Sleep Disorders - Insomnia
Category M - Sleep Disorders – Parasomnias
Category N - Sleep Disorders – Movement Disorders
Category O - Sleep Disorders – Neurologic Disorders
Category P - Sleep in Medical Disorders
Category Q - Sleep in Psychiatric Disorders
Category R - Instrumentation & Methodology
Category S - Sleep Education
Category T - Molecular Biology & Genetics
Category U - Behavior & Cognition

Attendees of the APSS 19th Annual Meeting will experience a forum for the discussion of new ideas and key research in the field of sleep medicine and sleep research. Our hope is that this experience fosters an environment in which members and attendees obtain education on the latest basic science, clinical science and technologies in the sleep field, further promoting the recent growth trend in this field. We look forward to sharing in the success of this pivotal event.

David P. White, M.D.
Editor-in-Chief
<table>
<thead>
<tr>
<th>Category</th>
<th>Abstracts</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category A – Basic Neuroscience</td>
<td>0001 – 0107</td>
<td>1-35</td>
</tr>
<tr>
<td>Category B - General Physiology</td>
<td>0108 - 0129</td>
<td>36-43</td>
</tr>
<tr>
<td>Category C - Clinical Pharmacology</td>
<td>0130 - 0150</td>
<td>44-50</td>
</tr>
<tr>
<td>Category D – Dreams</td>
<td>0151 – 0161</td>
<td>51-54</td>
</tr>
<tr>
<td>Category E - Circadian Rhythms</td>
<td>0162 – 0215</td>
<td>55-73</td>
</tr>
<tr>
<td>Category F - Phylogeny (no abstracts in this category)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Category G - Pediatrics</td>
<td>0216 – 0316</td>
<td>74-107</td>
</tr>
<tr>
<td>Category H - Aging</td>
<td>0317 - 0353</td>
<td>108-120</td>
</tr>
<tr>
<td>Category I - Sleep Deprivation</td>
<td>0354 - 0452</td>
<td>121-153</td>
</tr>
<tr>
<td>Category J - Sleep Disorders – Breathing</td>
<td>0453 - 0632</td>
<td>154-212</td>
</tr>
<tr>
<td>Category K - Sleep Disorders – Narcolepsy</td>
<td>0633 - 0664</td>
<td>213-223</td>
</tr>
<tr>
<td>Category L - Sleep Disorders – Insomnia</td>
<td>0665 - 0764</td>
<td>224-256</td>
</tr>
<tr>
<td>Category M - Sleep Disorders – Parasomnias</td>
<td>0765 - 0780</td>
<td>257-262</td>
</tr>
<tr>
<td>Category N - Sleep Disorders – Movement Disorders</td>
<td>0781 - 0828</td>
<td>263-279</td>
</tr>
<tr>
<td>Category O - Sleep Disorders – Neurologic Disorders</td>
<td>0829 - 0854</td>
<td>280-288</td>
</tr>
<tr>
<td>Category P - Sleep in Medical Disorders</td>
<td>0855 - 0902</td>
<td>289-305</td>
</tr>
<tr>
<td>Category Q - Sleep in Psychiatric Disorders</td>
<td>0903 - 0937</td>
<td>306-317</td>
</tr>
<tr>
<td>Category R - Instrumentation &amp; Methodology</td>
<td>0938 - 0989</td>
<td>318-335</td>
</tr>
<tr>
<td>Category S - Sleep Education</td>
<td>0990 - 0998</td>
<td>336-338</td>
</tr>
<tr>
<td>Category T - Molecular Biology &amp; Genetics</td>
<td>0999 - 1013</td>
<td>339-343</td>
</tr>
<tr>
<td>Category U - Behavior &amp; Cognition</td>
<td>1014 - 1055</td>
<td>344-358</td>
</tr>
</tbody>
</table>

**Author Index**

<table>
<thead>
<tr>
<th>Author</th>
<th>Abstract Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abaluck, B</td>
<td>529</td>
</tr>
<tr>
<td>Abbott, S M</td>
<td>171</td>
</tr>
<tr>
<td>Abe, M</td>
<td>698</td>
</tr>
<tr>
<td>Abe, P T</td>
<td>351, 353, 902</td>
</tr>
<tr>
<td>Acebo, C</td>
<td>188, 209, 310, 1025</td>
</tr>
<tr>
<td>Accurso, M</td>
<td>319</td>
</tr>
<tr>
<td>Ackerman, P</td>
<td>119, 122</td>
</tr>
<tr>
<td>Adams, T</td>
<td>613, 614</td>
</tr>
<tr>
<td>Adler, I</td>
<td>240</td>
</tr>
<tr>
<td>Adie, J</td>
<td>60, 61, 62</td>
</tr>
<tr>
<td>Ajagina, A</td>
<td>271, 274, 307</td>
</tr>
<tr>
<td>Albrecht, I</td>
<td>113, 854</td>
</tr>
<tr>
<td>Al-Shamma, H</td>
<td>5</td>
</tr>
<tr>
<td>Al-Shamrani, A</td>
<td>509</td>
</tr>
<tr>
<td>Alam, M</td>
<td>99</td>
</tr>
<tr>
<td>Allen, R</td>
<td>802, 883</td>
</tr>
<tr>
<td>Allen, R P</td>
<td>815, 826, 827, 828, 970</td>
</tr>
<tr>
<td>Aigbogun, A</td>
<td>842</td>
</tr>
<tr>
<td>Almeida, T</td>
<td>887</td>
</tr>
<tr>
<td>Almeida, T F</td>
<td>106, 666</td>
</tr>
<tr>
<td>Almeida, M</td>
<td>501, 503, 505, 506, 570, 574, 580, 623</td>
</tr>
<tr>
<td>Almeida, M S</td>
<td>557</td>
</tr>
<tr>
<td>Ainsworth, B</td>
<td>709</td>
</tr>
<tr>
<td>Aiolfi, S</td>
<td>500</td>
</tr>
<tr>
<td>Aisawa, R</td>
<td>641, 698</td>
</tr>
<tr>
<td>Aigbogun, J</td>
<td>932</td>
</tr>
<tr>
<td>Aikens, E</td>
<td>713, 916, 918</td>
</tr>
<tr>
<td>Ainsworth, B</td>
<td>46</td>
</tr>
<tr>
<td>Alerci, J</td>
<td>67, 412</td>
</tr>
<tr>
<td>Almeida, T</td>
<td>328</td>
</tr>
<tr>
<td>Alexandre, A</td>
<td>62</td>
</tr>
<tr>
<td>Alexander, R</td>
<td>709</td>
</tr>
<tr>
<td>Allan, S R</td>
<td>77</td>
</tr>
<tr>
<td>Allen, R P</td>
<td>713, 916, 918</td>
</tr>
<tr>
<td>Allen, R P</td>
<td>709, 707</td>
</tr>
<tr>
<td>Amin, D D</td>
<td>383, 392</td>
</tr>
<tr>
<td>Amin, D</td>
<td>242, 244</td>
</tr>
<tr>
<td>Amlaner, C J</td>
<td>46</td>
</tr>
<tr>
<td>Amin, D D</td>
<td>67, 412</td>
</tr>
<tr>
<td>Ancoli-Israel, S</td>
<td>243, 320, 322, 324, 325, 327, 335, 336, 472, 507, 514, 516, 561, 581, 857, 870, 872, 919, 1037</td>
</tr>
</tbody>
</table>

**SLEEP, Volume 28, Abstract Supplement, 2005**

**Key Word Index**

<table>
<thead>
<tr>
<th>Key Word</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep</td>
<td>154-212</td>
</tr>
<tr>
<td>Dreams</td>
<td>213-223</td>
</tr>
<tr>
<td>Narcolepsy</td>
<td>224-256</td>
</tr>
<tr>
<td>Insomnia</td>
<td>257-262</td>
</tr>
<tr>
<td>Movement Disorders</td>
<td>263-279</td>
</tr>
<tr>
<td>Neurologic Disorders</td>
<td>280-288</td>
</tr>
<tr>
<td>Medical Disorders</td>
<td>289-305</td>
</tr>
<tr>
<td>Psychiatric Disorders</td>
<td>306-317</td>
</tr>
<tr>
<td>Instrumentation &amp; Methodology</td>
<td>318-335</td>
</tr>
<tr>
<td>Sleep Education</td>
<td>336-338</td>
</tr>
<tr>
<td>Molecular Biology &amp; Genetics</td>
<td>339-343</td>
</tr>
<tr>
<td>Behavior &amp; Cognition</td>
<td>344-358</td>
</tr>
</tbody>
</table>

**Next Page**
<table>
<thead>
<tr>
<th>Author</th>
<th>Page Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cook</td>
<td>658, 659</td>
</tr>
<tr>
<td>Constantino, M J</td>
<td>677</td>
</tr>
<tr>
<td>Consens, F B</td>
<td>759, 780, 801</td>
</tr>
<tr>
<td>Chong, M S</td>
<td>327</td>
</tr>
<tr>
<td>Choo, I H</td>
<td>1045</td>
</tr>
<tr>
<td>Chouinard, S</td>
<td>1048</td>
</tr>
<tr>
<td>Chrispin, F S</td>
<td>604</td>
</tr>
<tr>
<td>Chrousos, G P</td>
<td>602</td>
</tr>
<tr>
<td>Chu, T T</td>
<td>633</td>
</tr>
<tr>
<td>Chung, A</td>
<td>647</td>
</tr>
<tr>
<td>Chung, F</td>
<td>466</td>
</tr>
<tr>
<td>Chung, S A</td>
<td>193, 195, 924</td>
</tr>
<tr>
<td>Chung, Y</td>
<td>273</td>
</tr>
<tr>
<td>Churchill, G A</td>
<td>1006</td>
</tr>
<tr>
<td>Churchill, L</td>
<td>64, 70</td>
</tr>
<tr>
<td>Ciafaloni, E</td>
<td>843, 844, 845</td>
</tr>
<tr>
<td>Cintra, F</td>
<td>893</td>
</tr>
<tr>
<td>Cirelli, C</td>
<td>13, 1000, 1001</td>
</tr>
<tr>
<td>Cirignotta, F</td>
<td>695</td>
</tr>
<tr>
<td>Clark, C P</td>
<td>921</td>
</tr>
<tr>
<td>Claustrat, B</td>
<td>395</td>
</tr>
<tr>
<td>Clerici, S</td>
<td>159</td>
</tr>
<tr>
<td>Claydts, R</td>
<td>172</td>
</tr>
<tr>
<td>Cochen, V</td>
<td>848</td>
</tr>
<tr>
<td>Coelho, C F</td>
<td>770</td>
</tr>
<tr>
<td>Coffey, M J</td>
<td>486, 879</td>
</tr>
<tr>
<td>Cogliati, C</td>
<td>394</td>
</tr>
<tr>
<td>Cohen, A</td>
<td>832</td>
</tr>
<tr>
<td>Cohen-Zion, M</td>
<td>243</td>
</tr>
<tr>
<td>Cole, C S</td>
<td>341, 349</td>
</tr>
<tr>
<td>Cole, K</td>
<td>416</td>
</tr>
<tr>
<td>Colella, I</td>
<td>282, 283</td>
</tr>
<tr>
<td>Coleman, C</td>
<td>275</td>
</tr>
<tr>
<td>Colletti, L M</td>
<td>173, 197, 1038, 1050</td>
</tr>
<tr>
<td>Colligan, E</td>
<td>971, 972</td>
</tr>
<tr>
<td>Collin, H</td>
<td>951</td>
</tr>
<tr>
<td>Collins, N S</td>
<td>662</td>
</tr>
<tr>
<td>Collins, S D</td>
<td>662</td>
</tr>
<tr>
<td>Collop, N</td>
<td>619</td>
</tr>
<tr>
<td>Collop, N A</td>
<td>889</td>
</tr>
<tr>
<td>Colombo, P C</td>
<td>968</td>
</tr>
<tr>
<td>Colrain, I M</td>
<td>128, 299</td>
</tr>
<tr>
<td>Combs, A</td>
<td>726</td>
</tr>
<tr>
<td>Conduit, R</td>
<td>1053, 1054</td>
</tr>
<tr>
<td>Conduro, R</td>
<td>805</td>
</tr>
<tr>
<td>Conley, Y P</td>
<td>627</td>
</tr>
<tr>
<td>Connolly, H</td>
<td>229, 300</td>
</tr>
<tr>
<td>Connolly, H V</td>
<td>288, 289, 290</td>
</tr>
<tr>
<td>Conroy, D A</td>
<td>773</td>
</tr>
<tr>
<td>Conroy, D A</td>
<td>740</td>
</tr>
<tr>
<td>Consedine, N</td>
<td>690</td>
</tr>
<tr>
<td>Consens, F</td>
<td>598, 740</td>
</tr>
<tr>
<td>Consens, F B</td>
<td>486, 487, 777, 784, 879</td>
</tr>
<tr>
<td>Constantino, M J</td>
<td>677</td>
</tr>
<tr>
<td>Conway, S</td>
<td>590</td>
</tr>
<tr>
<td>Cook, H</td>
<td>658, 659</td>
</tr>
<tr>
<td>Cook, S R</td>
<td>288</td>
</tr>
<tr>
<td>Cooke, J</td>
<td>445</td>
</tr>
<tr>
<td>Cooke, J R</td>
<td>322, 335</td>
</tr>
<tr>
<td>Cooper, B</td>
<td>261</td>
</tr>
<tr>
<td>Copa, A</td>
<td>137</td>
</tr>
<tr>
<td>Corbin, R</td>
<td>467</td>
</tr>
<tr>
<td>Cordero, J M</td>
<td>612</td>
</tr>
<tr>
<td>Corey-Bloom, J</td>
<td>325</td>
</tr>
<tr>
<td>Corona, A</td>
<td>159</td>
</tr>
<tr>
<td>Corso, M M</td>
<td>273</td>
</tr>
<tr>
<td>Cortesi, F</td>
<td>226</td>
</tr>
<tr>
<td>Coste, O</td>
<td>395</td>
</tr>
<tr>
<td>Cote, K A</td>
<td>347</td>
</tr>
<tr>
<td>Cotton, D</td>
<td>483</td>
</tr>
<tr>
<td>Cottrell, K A</td>
<td>487</td>
</tr>
<tr>
<td>Cousins, J C</td>
<td>189, 751</td>
</tr>
<tr>
<td>Cousens-Read, M E</td>
<td>437, 977</td>
</tr>
<tr>
<td>Coyle, M</td>
<td>131</td>
</tr>
<tr>
<td>Coyle, M A</td>
<td>721</td>
</tr>
<tr>
<td>Crabtree, V</td>
<td>254, 298</td>
</tr>
<tr>
<td>Crabtree, V M</td>
<td>260</td>
</tr>
<tr>
<td>Craddock, A J</td>
<td>895, 897</td>
</tr>
<tr>
<td>Cramer Bornemann, M A</td>
<td>773</td>
</tr>
<tr>
<td>Cramer-Bornemann, M</td>
<td>579</td>
</tr>
<tr>
<td>Cramer-Bornemann, M A</td>
<td>583</td>
</tr>
<tr>
<td>Crawford, L</td>
<td>864</td>
</tr>
<tr>
<td>Cresswell, P</td>
<td>656, 961</td>
</tr>
<tr>
<td>Crochet, S</td>
<td>52</td>
</tr>
<tr>
<td>Croford, L J</td>
<td>881</td>
</tr>
<tr>
<td>Crompton, M</td>
<td>339</td>
</tr>
<tr>
<td>Crosby, B</td>
<td>277</td>
</tr>
<tr>
<td>Crowder, C</td>
<td>519</td>
</tr>
<tr>
<td>Crowell, D H</td>
<td>951</td>
</tr>
<tr>
<td>Crowley, S J</td>
<td>188</td>
</tr>
<tr>
<td>Crudele, C P</td>
<td>383, 392</td>
</tr>
<tr>
<td>Cruz, C</td>
<td>133, 134</td>
</tr>
<tr>
<td>Cruz, N</td>
<td>742</td>
</tr>
<tr>
<td>Cuevas, R</td>
<td>313</td>
</tr>
<tr>
<td>Culp, E</td>
<td>96</td>
</tr>
<tr>
<td>Curcio, G</td>
<td>4</td>
</tr>
<tr>
<td>Czeisler, C A</td>
<td>174, 175, 190, 202, 212, 364, 365, 818</td>
</tr>
</tbody>
</table>

**D**

<table>
<thead>
<tr>
<th>Author</th>
<th>Page Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>D'Alessandro, R</td>
<td>657</td>
</tr>
<tr>
<td>D'Almeida, V</td>
<td>411, 569</td>
</tr>
<tr>
<td>D'Andrea, L A</td>
<td>990</td>
</tr>
<tr>
<td>Dahi, H</td>
<td>219, 519</td>
</tr>
<tr>
<td>Dahlgren, A</td>
<td>196</td>
</tr>
<tr>
<td>Dahlgren, A K</td>
<td>1042</td>
</tr>
<tr>
<td>Daigle, A</td>
<td>228</td>
</tr>
<tr>
<td>Dailey, D E</td>
<td>261</td>
</tr>
<tr>
<td>Daisy, Y</td>
<td>286</td>
</tr>
<tr>
<td>Dalal, B</td>
<td>474</td>
</tr>
<tr>
<td>Daley, M E</td>
<td>735</td>
</tr>
<tr>
<td>Daley, T M</td>
<td>1051</td>
</tr>
<tr>
<td>Dalton, J</td>
<td>876</td>
</tr>
<tr>
<td>Dampier, C</td>
<td>275</td>
</tr>
<tr>
<td>Dandrow, C</td>
<td>228</td>
</tr>
<tr>
<td>Dang-Yu, T</td>
<td>663</td>
</tr>
<tr>
<td>Daniel, J</td>
<td>799</td>
</tr>
<tr>
<td>Daniel, L C</td>
<td>302</td>
</tr>
<tr>
<td>Daniels, S</td>
<td>242, 244</td>
</tr>
<tr>
<td>Author</td>
<td>Pages</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>--------------------------------------</td>
</tr>
<tr>
<td>Deurveilher, S</td>
<td>41</td>
</tr>
<tr>
<td>Dessange, A</td>
<td>699</td>
</tr>
<tr>
<td>Darabi, F P</td>
<td>154, 914</td>
</tr>
<tr>
<td>Dautovich, N D</td>
<td>271, 274, 307, 352, 760</td>
</tr>
<tr>
<td>Dauvilliers, Y</td>
<td>663</td>
</tr>
<tr>
<td>Davidson, J R</td>
<td>717</td>
</tr>
<tr>
<td>Davies, C</td>
<td>996</td>
</tr>
<tr>
<td>Davies, D R</td>
<td>354</td>
</tr>
<tr>
<td>Davies, G</td>
<td>196</td>
</tr>
<tr>
<td>Davies, C R O</td>
<td>55</td>
</tr>
<tr>
<td>Davila, D G</td>
<td>957</td>
</tr>
<tr>
<td>Davis, C J</td>
<td>435, 1011</td>
</tr>
<tr>
<td>Davis, H C</td>
<td>261</td>
</tr>
<tr>
<td>Davis, J</td>
<td>149</td>
</tr>
<tr>
<td>Davis, K F</td>
<td>264</td>
</tr>
<tr>
<td>Davenport, L R</td>
<td>854</td>
</tr>
<tr>
<td>Dauvuluri, V K</td>
<td>420, 421</td>
</tr>
<tr>
<td>Dawson, D</td>
<td>192, 217</td>
</tr>
<tr>
<td>Dawson, J</td>
<td>140</td>
</tr>
<tr>
<td>De, A</td>
<td>93</td>
</tr>
<tr>
<td>De Gennaro, L</td>
<td></td>
</tr>
<tr>
<td>de Grandmont, P</td>
<td>769</td>
</tr>
<tr>
<td>de Haas, S</td>
<td>832</td>
</tr>
<tr>
<td>De Koninc, J</td>
<td>153, 443, 864</td>
</tr>
<tr>
<td>de la Eva, R</td>
<td>315</td>
</tr>
<tr>
<td>de Lacy, S</td>
<td>642</td>
</tr>
<tr>
<td>de Leera, L</td>
<td>29, 49, 97</td>
</tr>
<tr>
<td>de Noord, I</td>
<td>910</td>
</tr>
<tr>
<td>De Paola, A</td>
<td>893</td>
</tr>
<tr>
<td>De Valck, E</td>
<td>172</td>
</tr>
<tr>
<td>De Volder, I</td>
<td>172</td>
</tr>
<tr>
<td>de Weerd, A</td>
<td>808, 832</td>
</tr>
<tr>
<td>Deacon, S</td>
<td>715</td>
</tr>
<tr>
<td>Dean, D A</td>
<td>205</td>
</tr>
<tr>
<td>Dean, G</td>
<td>875</td>
</tr>
<tr>
<td>Deb, P</td>
<td>924</td>
</tr>
<tr>
<td>Decary, A</td>
<td>318, 465, 765</td>
</tr>
<tr>
<td>Decker, M J</td>
<td>849, 851</td>
</tr>
<tr>
<td>Decker, P A</td>
<td>634</td>
</tr>
<tr>
<td>DeFinis, A L</td>
<td>760</td>
</tr>
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<td>Del Felice, A</td>
<td>468</td>
</tr>
<tr>
<td>Deline, A</td>
<td>881</td>
</tr>
<tr>
<td>Dement, W C</td>
<td>109, 781</td>
</tr>
<tr>
<td>DeMasse, S</td>
<td>479, 480</td>
</tr>
<tr>
<td>den Hertog, H</td>
<td>636</td>
</tr>
<tr>
<td>Dennis, C</td>
<td>267</td>
</tr>
<tr>
<td>Derchak, P</td>
<td>131, 721</td>
</tr>
<tr>
<td>DeRosa, P</td>
<td>618</td>
</tr>
<tr>
<td>DeRoshia, C W</td>
<td>173</td>
</tr>
<tr>
<td>Desautels, A</td>
<td>785</td>
</tr>
<tr>
<td>Descarrecaux, C</td>
<td>158, 776</td>
</tr>
<tr>
<td>Deshields, T</td>
<td>886</td>
</tr>
<tr>
<td>Deshpande, A</td>
<td>799</td>
</tr>
<tr>
<td>Deurveilher, S</td>
<td>41</td>
</tr>
<tr>
<td>DeViva, J C</td>
<td>762</td>
</tr>
<tr>
<td>Devlin, C</td>
<td>726</td>
</tr>
<tr>
<td>Devlin, C M</td>
<td>955</td>
</tr>
<tr>
<td>Dhamija, R</td>
<td>567</td>
</tr>
<tr>
<td>Di Perri, C</td>
<td>805</td>
</tr>
<tr>
<td>Diallo, A</td>
<td>1002</td>
</tr>
<tr>
<td>Diesem, R</td>
<td>536, 584</td>
</tr>
<tr>
<td>DiFazio, M</td>
<td>806</td>
</tr>
<tr>
<td>Dijk, D</td>
<td>425</td>
</tr>
<tr>
<td>Dikmen, S</td>
<td>838</td>
</tr>
<tr>
<td>DiLeo, H A</td>
<td>939</td>
</tr>
<tr>
<td>Dimsdale, J</td>
<td>320</td>
</tr>
<tr>
<td>Dimsdale, J E</td>
<td>472, 507, 560, 561, 1037</td>
</tr>
<tr>
<td>Ding, M</td>
<td>6, 999, 1005</td>
</tr>
<tr>
<td>Dinges, D</td>
<td>384</td>
</tr>
<tr>
<td>Dinges, D F</td>
<td>143, 146, 197, 378, 379, 380, 383, 386, 390, 392, 400, 407, 508, 738, 1028, 1029, 1030, 1033, 1043, 1050</td>
</tr>
<tr>
<td>Dingwall, K</td>
<td>551, 553</td>
</tr>
<tr>
<td>Dinner, D S</td>
<td>812</td>
</tr>
<tr>
<td>DiPalma, J</td>
<td>690</td>
</tr>
<tr>
<td>Djolagic, I</td>
<td>1026</td>
</tr>
<tr>
<td>Dodd, D</td>
<td>253</td>
</tr>
<tr>
<td>Dodd, M J</td>
<td>1021</td>
</tr>
<tr>
<td>Doerr, C</td>
<td>539</td>
</tr>
<tr>
<td>Dong, S</td>
<td>297</td>
</tr>
<tr>
<td>Dong, C</td>
<td>524</td>
</tr>
<tr>
<td>Dopp, J M</td>
<td>601</td>
</tr>
<tr>
<td>Dorris, L</td>
<td>218</td>
</tr>
<tr>
<td>Dorsey, C</td>
<td>451</td>
</tr>
<tr>
<td>Dostie, V</td>
<td>1044, 1046</td>
</tr>
<tr>
<td>Douglass, J L</td>
<td>594</td>
</tr>
<tr>
<td>Douglass, A B</td>
<td>718</td>
</tr>
<tr>
<td>Dover, L</td>
<td>512, 534, 554, 600</td>
</tr>
<tr>
<td>Dowling, G</td>
<td>164</td>
</tr>
<tr>
<td>Doyon, J</td>
<td>1044, 1046</td>
</tr>
<tr>
<td>Drake, A L</td>
<td></td>
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<tr>
<td>Drake, C</td>
<td>660, 710, 711, 748</td>
</tr>
<tr>
<td>Drake, C L</td>
<td>330, 721</td>
</tr>
<tr>
<td>Drapeau, C</td>
<td>124, 148, 342</td>
</tr>
<tr>
<td>Dreisbach, J K</td>
<td>256, 298</td>
</tr>
<tr>
<td>Drozd, J</td>
<td>217</td>
</tr>
<tr>
<td>Drum, W</td>
<td>795</td>
</tr>
<tr>
<td>Drummond, S</td>
<td>381, 438, 440, 901, 1041</td>
</tr>
<tr>
<td>Drummond, S A</td>
<td>964</td>
</tr>
<tr>
<td>Drummond, S P</td>
<td>387, 433, 442, 514, 516, 1019, 1052</td>
</tr>
<tr>
<td>Duane, D D</td>
<td>633</td>
</tr>
<tr>
<td>Dube, B</td>
<td>126</td>
</tr>
<tr>
<td>Dubuc, M</td>
<td>920</td>
</tr>
<tr>
<td>Duffy, J F</td>
<td>818</td>
</tr>
<tr>
<td>Dugovic, C</td>
<td>84, 88, 94</td>
</tr>
<tr>
<td>Duke, R L</td>
<td>522</td>
</tr>
<tr>
<td>Dumont, M</td>
<td>167, 168, 200, 785</td>
</tr>
<tr>
<td>Dunai, A</td>
<td>195</td>
</tr>
<tr>
<td>Dunbar, S B</td>
<td>869</td>
</tr>
<tr>
<td>Dunlop, L</td>
<td>539</td>
</tr>
<tr>
<td>Dunsley, S</td>
<td>147, 539, 814, 886, 965</td>
</tr>
<tr>
<td>Dunsley, S P</td>
<td>67, 412, 459, 980, 983</td>
</tr>
<tr>
<td>Dupuis, A</td>
<td>124</td>
</tr>
<tr>
<td>Duran, R</td>
<td>882</td>
</tr>
<tr>
<td>Durance, A</td>
<td>486, 879</td>
</tr>
<tr>
<td>Duricka, D</td>
<td>1009</td>
</tr>
<tr>
<td>Dwyr, P C</td>
<td>1051</td>
</tr>
<tr>
<td>Dyche, J</td>
<td>1049</td>
</tr>
</tbody>
</table>
Harrell, D B ........................................ 938
Harrington, J J .................................. 333, 996
Harris, J K ........................................... 720
Harris, S ........................................... 136, 313, 332, 501, 505, 570, 580
Harris, S G ......................................... 314
Harris, S L ........................................... 503, 506, 574
Harris, T ........................................... 348
Harrison, T B ...................................... 514, 516
Harsh, J ............................................ 119
Harsh, J R .......................................... 277, 645
Hart, I K ........................................... 656, 961
Hart, R W ........................................... 609
Harten, L ........................................... 565, 588
Hartley, J ........................................... 579
Hasan, R ............................................ 841
Hashidume, Y ..................................... 515
Hasler, B P ........................................ 189, 922
Hassan, R ........................................... 885
Hassani, O .......................................... 76
Hassett, B ......................................... 726, 955
Hassoun, P ........................................ 889
Hawkins, B J ...................................... 614
Hawkins, G A ..................................... 1002
Hayaishi, O ........................................ 41
Hayashida, K ..................................... 562
Hayashida, K ..................................... 1022
Hayes, A M ......................................... 1017
Hayes, J ............................................ 257, 284
Haynes, P ........................................... 919
Haynes, P L ....................................... 751
Hayrapetyan, L .................................. 369, 371
Hays, R D ........................................... 748
He, Q ............................................... 524
He, Z ................................................... 524
Hedner, J ........................................... 523
Hegel, M ........................................... 907
Hegeman-Kleinn, I M ............................ 636
Heims-Penokie, P C ................................ 634
Heimbucher, G E .................................. 633
Heinzer, R .......................................... 534
Heitkemper, M E .................................. 758
Helman, J I ......................................... 487
Hemm, J ............................................ 244
Henderson, J ..................................... 882
Henderson, L ..................................... 279
Hendricks, J C .................................... 38
Hening, W ......................................... 815
Hening, W A ..................................... 826
Hennen, J .......................................... 451
Henny, P ........................................... 85
Henriksen, S J ..................................... 49, 103, 104
Herbert, W G ..................................... 614
Herer, P ............................................. 194, 469
Hering, E ........................................... 237
Hernandez, B ..................................... 672
Hershey, C O ....................................... 971, 972
Hesla, P ........................................... 655
Heslegrave, R J .................................... 426
Heumann, M ....................................... 777
Hicks, A A .......................................... 824
Hicks, R A .......................................... 912, 931
Higami, S .......................................... 573
Higami, Y .......................................... 573
Hilbert, J .......................................... 843, 845
Hill, F ............................................... 483
Hill, S ............................................. 1001
Hill, S L ............................................ 14
Hilton, M F ........................................ 211, 213, 215, 1036
Hiltunen, J ........................................ 374
Himanen, S ........................................ 368
Hindmarch, I ..................................... 140, 425, 729, 731
Hirota, Y ........................................... 1039
Hirshkowitz, M ................................... 531, 624, 741
Hirvonen, K ....................................... 368, 788
Hishikawa, Y ..................................... 698, 724
Hitchcock, S E .................................... 585, 849, 851
Hoffman, J M ...................................... 1030
Hoffman, L A ...................................... 627
Hoffmann, R ...................................... 114, 263, 856, 1027
Hoffmann, R F ................................... 740
Hofman, W F ...................................... 526
Hog, N ............................................. 415
Hogli, B ............................................ 808, 816, 817
Hodlerman, D .................................... 751
Holm, A ............................................ 374
Holman, E ......................................... 926
Holsten, F ......................................... 913
Honda, M .......................................... 655
Honda, Y ........................................... 655
Hong, M ............................................ 498
Hong, S ............................................ 648, 952
Hope, C R .......................................... 645
Hornyak, M ........................................ 676, 796, 808
Horowitz, T S .................................... 190, 1036
Hoskere, G ......................................... 576
Hossain, N .......................................... 169, 924
Hotta, S ............................................ 811
Hou, Y ............................................... 52
Houghton, W ..................................... 658, 659
Howard, E .......................................... 845
Howard, S K ....................................... 391, 958
Howarth, A ....................................... 218
Hozumi, S .......................................... 724
Hsiao-Hsui, L .................................... 160
Hsieh, J ............................................ 69, 198
Hsu, S ............................................... 737
Hsu, T ............................................... 150
Huang, J S ......................................... 674
Huang, M I ......................................... 906, 908, 911
Huang, X ........................................... 924
Huang, Y .......................................... 708
Huang, Z ........................................... 41
Huang, y ............................................ 830, 831
Hubbard, E M .................................... 164
Hubbard, J ......................................... 294
Huber, R ........................................... 13, 121, 1001
Huicron-Resendiz, S ............................. 49, 103, 104
Hull, F P ........................................... 424
Hull, S ............................................... 682
Hummers, L ....................................... 889
Hunter, J A ........................................ 616, 629
Hunter, M D ....................................... 861
Huntley, E .......................................... 1047
Huntley, E D ........................................ 235
<table>
<thead>
<tr>
<th>Name</th>
<th>Page Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jensen, E</td>
<td>451</td>
</tr>
<tr>
<td>Jenny, N</td>
<td>544</td>
</tr>
<tr>
<td>Jenni, O G</td>
<td>249</td>
</tr>
<tr>
<td>Janssen, I</td>
<td>868</td>
</tr>
<tr>
<td>James, J A</td>
<td>671</td>
</tr>
<tr>
<td>Jakus, R</td>
<td>120</td>
</tr>
<tr>
<td>Jakub, A</td>
<td>377</td>
</tr>
<tr>
<td>Jahn, S</td>
<td>89, 768, 894</td>
</tr>
<tr>
<td>Hyrup, J</td>
<td>891</td>
</tr>
<tr>
<td>Hwang, H K</td>
<td>344</td>
</tr>
<tr>
<td>Hyde, M E</td>
<td>377</td>
</tr>
<tr>
<td>Hyde, P R</td>
<td>109, 781</td>
</tr>
<tr>
<td>Ibrahim, S M</td>
<td>496</td>
</tr>
<tr>
<td>Ichiki, K</td>
<td>654</td>
</tr>
<tr>
<td>Ihlenfeldt, K</td>
<td>370</td>
</tr>
<tr>
<td>Iijima, S</td>
<td>641</td>
</tr>
<tr>
<td>Im, M</td>
<td>647, 950, 953</td>
</tr>
<tr>
<td>Imeri, L</td>
<td>2, 22</td>
</tr>
<tr>
<td>Inanawi, C</td>
<td>641</td>
</tr>
<tr>
<td>Ingebrigtsen, H B</td>
<td>452</td>
</tr>
<tr>
<td>Ingravallo, F</td>
<td>657</td>
</tr>
<tr>
<td>Inoue, Y</td>
<td>178, 562, 641, 847, 884</td>
</tr>
<tr>
<td>Iaichimescu, O</td>
<td>1034</td>
</tr>
<tr>
<td>Iranzo, A</td>
<td>775</td>
</tr>
<tr>
<td>Ironson, G</td>
<td>882</td>
</tr>
<tr>
<td>Irwin, M R</td>
<td>129</td>
</tr>
<tr>
<td>Ishihara, K</td>
<td>280</td>
</tr>
<tr>
<td>Ishizuka, T</td>
<td>54</td>
</tr>
<tr>
<td>Isojima, Y</td>
<td>178</td>
</tr>
<tr>
<td>Itoh, H</td>
<td>562</td>
</tr>
<tr>
<td>Itoh, H</td>
<td>1022</td>
</tr>
<tr>
<td>Iturbe, J</td>
<td>866</td>
</tr>
<tr>
<td>Itzhaki, S</td>
<td>575</td>
</tr>
<tr>
<td>Ivanenko, A</td>
<td>273</td>
</tr>
<tr>
<td>Jablonski, M</td>
<td>107</td>
</tr>
<tr>
<td>Jacobs, D</td>
<td>1053</td>
</tr>
<tr>
<td>Jahan, S</td>
<td>39</td>
</tr>
<tr>
<td>Jain, S</td>
<td>876</td>
</tr>
<tr>
<td>Jain, S R</td>
<td>883</td>
</tr>
<tr>
<td>Jain, S S</td>
<td>557</td>
</tr>
<tr>
<td>Jakus, R</td>
<td>120</td>
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<td>Jallad, R</td>
<td>885</td>
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<td>Jama, L</td>
<td>788</td>
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<tr>
<td>James, F O</td>
<td>203</td>
</tr>
<tr>
<td>James, J A</td>
<td>671</td>
</tr>
<tr>
<td>James, S P</td>
<td>131</td>
</tr>
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<td>Jamous, A</td>
<td>557</td>
</tr>
<tr>
<td>Jamous, A K</td>
<td>471</td>
</tr>
<tr>
<td>Janisse, J J</td>
<td>317</td>
</tr>
<tr>
<td>Jankelson, D</td>
<td>988</td>
</tr>
<tr>
<td>Janssen, I</td>
<td>868</td>
</tr>
<tr>
<td>Jean-Louis, G</td>
<td>690, 863</td>
</tr>
<tr>
<td>Jefferson, C</td>
<td>710, 711, 721</td>
</tr>
<tr>
<td>Jegley, S</td>
<td>349</td>
</tr>
<tr>
<td>Jelic, S</td>
<td>968</td>
</tr>
<tr>
<td>Jenni, O G</td>
<td>249</td>
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<tr>
<td>Jenny, N</td>
<td>544</td>
</tr>
<tr>
<td>Jensen, E</td>
<td>451</td>
</tr>
<tr>
<td>Jeong, D</td>
<td>647, 950, 953</td>
</tr>
<tr>
<td>Jeong, J</td>
<td>648</td>
</tr>
</tbody>
</table>

Jerin, M ........................................... 979
Jerome, D A ........................................ 577
Jha, S K ........................................... 1020
Jhaveri, K ........................................ 6
Jhaveri, K A ....................................... 33
Jia, F ............................................... 524
Jimenez-Anguiano, A ................................ 389
Jimenez-Genchi, A .................................. 909
Joehelson, P ...................................... 681, 682, 683, 684, 685
Johanson, C ........................................ 142
Johns, M W ......................................... 357, 359
Johnsen, S ......................................... 140
Johnson, B ......................................... 773
Johnson, D ......................................... 358, 416, 417, 428, 542, 962
Johnson, E O ...................................... 292, 295, 736
Johnson, K P ....................................... 204
Johnson, M ......................................... 132
Johnson, N L ....................................... 544
Johnson, S ......................................... 857, 870, 871
Johnston, L ......................................... 782
Jones, B E .......................................... 76, 85, 91
Jones, J H ......................................... 256
Jones-Parker, M .................................... 606, 982
Jooben, R ......................................... 276
Jordan, A S ........................................ 512, 554, 600, 611
Joseph, G .......................................... 863
Josephson, D ....................................... 837
Josephson, K R .................................... 328
Juhasz, A .......................................... 793
Julia, B ........................................... 140
Juliano, M ......................................... 269, 272, 538, 543, 545
Juliano, P .......................................... 451
Junk, L ............................................. 777
Jung, C M .......................................... 175
Jung, S ............................................. 547
Jungquist, C ....................................... 716, 734, 955

K
Kadi, F ............................................. 789
Kadotani, H ....................................... 499, 811
Kaebling, K L ...................................... 262
Kagrananov, V ...................................... 502
Kahn, A ............................................ 223, 238, 239
Kaida, K ........................................... 118
Kaiser, L R ......................................... 875
Kajimura, N ........................................ 178
Kaij, S ............................................. 742
Kalemba, C .......................................... 430
Kales, A ............................................ 752
Kaleth, A ........................................... 614
Kalimchuk, A ....................................... 63, 65
Kamimori, G H ...................................... 416, 417
Kampelman, J ........................................ 539
Kanayama, H ......................................... 698
Kanbayashi, T ...................................... 641, 698
Kandelerss, K ....................................... 192
Kaneko, Y .......................................... 641, 698
Kanemura, T ........................................ 59, 452
Kantor, S ........................................... 120
Kapas, L ............................................ 431, 448, 449
Kaplan, P ........................................... 270
Kapuniai, L E ..................................... 951
<table>
<thead>
<tr>
<th>Name</th>
<th>Page Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Krishnan, V</td>
<td>889</td>
</tr>
<tr>
<td>Kristjansson, K</td>
<td>824</td>
</tr>
<tr>
<td>Kristo, D A</td>
<td>941</td>
</tr>
<tr>
<td>Kronauer, R E</td>
<td>166, 212</td>
</tr>
<tr>
<td>Krouse, R S</td>
<td>858</td>
</tr>
<tr>
<td>Krueger, G P</td>
<td>1033</td>
</tr>
<tr>
<td>Krueger, J M</td>
<td>64, 70, 93, 98, 122, 123, 127, 1009, 1011</td>
</tr>
<tr>
<td>Kruger, M H</td>
<td>455, 573</td>
</tr>
<tr>
<td>Kryla, N R</td>
<td>321</td>
</tr>
<tr>
<td>Krystal, A</td>
<td>130, 684, 918</td>
</tr>
<tr>
<td>Krystal, A D</td>
<td>761</td>
</tr>
<tr>
<td>Krystal, A K</td>
<td>667</td>
</tr>
<tr>
<td>Krüger, K</td>
<td>704</td>
</tr>
<tr>
<td>Kubin, L</td>
<td>26, 28, 55, 102</td>
</tr>
<tr>
<td>Kubota, Y</td>
<td>564</td>
</tr>
<tr>
<td>Kuhens, P</td>
<td>291</td>
</tr>
<tr>
<td>Kuhn, B</td>
<td>865</td>
</tr>
<tr>
<td>Kuhn, B R</td>
<td>305</td>
</tr>
<tr>
<td>Kumar, A</td>
<td>526</td>
</tr>
<tr>
<td>Kumar, R</td>
<td>853</td>
</tr>
<tr>
<td>Kumar, S</td>
<td>79, 99</td>
</tr>
<tr>
<td>Kumar, Y</td>
<td>448</td>
</tr>
<tr>
<td>Kumru, H</td>
<td>775</td>
</tr>
<tr>
<td>Kuna, S T</td>
<td>606, 956, 982</td>
</tr>
<tr>
<td>Kao, T F</td>
<td>482, 674, 677, 692, 701</td>
</tr>
<tr>
<td>Kao, T</td>
<td>686</td>
</tr>
<tr>
<td>Kupfer, D J</td>
<td>691</td>
</tr>
<tr>
<td>Kurien, S A</td>
<td>305</td>
</tr>
<tr>
<td>Kushida, C A</td>
<td>109, 672, 781, 866</td>
</tr>
<tr>
<td>Kuttner, N G</td>
<td>877</td>
</tr>
<tr>
<td>Kwok, J T</td>
<td>583</td>
</tr>
<tr>
<td>Kwong, W J</td>
<td>803</td>
</tr>
<tr>
<td>Laatsch, C D</td>
<td>415</td>
</tr>
<tr>
<td>Labutta, R</td>
<td>834</td>
</tr>
<tr>
<td>Labyak, S</td>
<td>232</td>
</tr>
<tr>
<td>Lack, L</td>
<td>722</td>
</tr>
<tr>
<td>Lack, L C</td>
<td>116, 180, 720</td>
</tr>
<tr>
<td>Ladouceur, R</td>
<td>925</td>
</tr>
<tr>
<td>Lafrenz, P</td>
<td>894</td>
</tr>
<tr>
<td>Lah, J J</td>
<td>1023</td>
</tr>
<tr>
<td>Lahey, M</td>
<td>603</td>
</tr>
<tr>
<td>Lai, D</td>
<td>39</td>
</tr>
<tr>
<td>Lai, Y</td>
<td>69</td>
</tr>
<tr>
<td>LaJambe, C M</td>
<td>214</td>
</tr>
<tr>
<td>Lake, R C</td>
<td>616</td>
</tr>
<tr>
<td>Lakkis, C L</td>
<td>898</td>
</tr>
<tr>
<td>Lam, H A</td>
<td>642</td>
</tr>
<tr>
<td>Lam, O</td>
<td>240</td>
</tr>
<tr>
<td>Lamarche, L</td>
<td>153</td>
</tr>
<tr>
<td>Lamarche, L J</td>
<td>864</td>
</tr>
<tr>
<td>Lambert, C</td>
<td>337, 341, 349</td>
</tr>
<tr>
<td>Lambert, E</td>
<td>313</td>
</tr>
<tr>
<td>Lamers, G</td>
<td>636, 649, 910</td>
</tr>
<tr>
<td>Lamond, N</td>
<td>247</td>
</tr>
<tr>
<td>Lancel, M</td>
<td>696</td>
</tr>
<tr>
<td>Landis, A M</td>
<td>888</td>
</tr>
<tr>
<td>Landis, C A</td>
<td>232, 340, 758, 856</td>
</tr>
<tr>
<td>Landolt, H</td>
<td>1032</td>
</tr>
<tr>
<td>Landry, C</td>
<td>1047</td>
</tr>
<tr>
<td>Landry, M</td>
<td>769</td>
</tr>
<tr>
<td>Lanfranchi, P</td>
<td>746</td>
</tr>
<tr>
<td>Lanfranchi, P A</td>
<td>126</td>
</tr>
<tr>
<td>Langer, R D</td>
<td>439</td>
</tr>
<tr>
<td>Lankford, A</td>
<td>662</td>
</tr>
<tr>
<td>Lankford, J</td>
<td>685</td>
</tr>
<tr>
<td>Laposky, A</td>
<td>94</td>
</tr>
<tr>
<td>Laposky, A D</td>
<td>86, 88, 430</td>
</tr>
<tr>
<td>Lara-Carrasco, J</td>
<td>161</td>
</tr>
<tr>
<td>Latta, F</td>
<td>343</td>
</tr>
<tr>
<td>Lau, H</td>
<td>1039</td>
</tr>
<tr>
<td>Lauderdale, D</td>
<td>945, 946</td>
</tr>
<tr>
<td>Laura, C M</td>
<td>413</td>
</tr>
<tr>
<td>Lavalle, M</td>
<td>754</td>
</tr>
<tr>
<td>Lavertu, J</td>
<td>744, 750</td>
</tr>
<tr>
<td>Lavie, L</td>
<td>469, 535, 537, 572, 575</td>
</tr>
<tr>
<td>Lavie, P</td>
<td>194, 469, 535, 537, 572, 575</td>
</tr>
<tr>
<td>Lavigne, G</td>
<td>663</td>
</tr>
<tr>
<td>Lavigne, G J</td>
<td>768, 769, 894</td>
</tr>
<tr>
<td>Lawson, A</td>
<td>230</td>
</tr>
<tr>
<td>Le Jemtel, T H</td>
<td>968</td>
</tr>
<tr>
<td>LeBlanc, M</td>
<td>673, 689, 735, 925</td>
</tr>
<tr>
<td>LeBourgeois, M K</td>
<td>277, 1024</td>
</tr>
<tr>
<td>Lecendreux, M</td>
<td>285</td>
</tr>
<tr>
<td>Lee, C</td>
<td>701</td>
</tr>
<tr>
<td>Lee, C H</td>
<td>344</td>
</tr>
<tr>
<td>Lee, D Y</td>
<td>1045</td>
</tr>
<tr>
<td>Lee, H</td>
<td>156, 464, 952</td>
</tr>
<tr>
<td>Lee, J</td>
<td>675</td>
</tr>
<tr>
<td>Lee, J H</td>
<td>344, 1023, 1045</td>
</tr>
<tr>
<td>Lee, K A</td>
<td>222, 261, 296, 360, 1016, 1021</td>
</tr>
<tr>
<td>Lee, M</td>
<td>76</td>
</tr>
<tr>
<td>Lee, R</td>
<td>103</td>
</tr>
<tr>
<td>Lee, R S</td>
<td>104</td>
</tr>
<tr>
<td>Lee, S</td>
<td>648, 877, 1016</td>
</tr>
<tr>
<td>Lee, Y</td>
<td>647</td>
</tr>
<tr>
<td>Lee, e k</td>
<td>646</td>
</tr>
<tr>
<td>leech, j</td>
<td>949</td>
</tr>
<tr>
<td>Lefler, B J</td>
<td>204</td>
</tr>
<tr>
<td>Legangneux, E</td>
<td>729, 730, 731, 733</td>
</tr>
<tr>
<td>Leger, D</td>
<td>484</td>
</tr>
<tr>
<td>Leger, L</td>
<td>31</td>
</tr>
<tr>
<td>Leissner, L</td>
<td>792</td>
</tr>
<tr>
<td>Lemke, J H</td>
<td>979, 986</td>
</tr>
<tr>
<td>Lenhart, G</td>
<td>712</td>
</tr>
<tr>
<td>Lentini-Oliveira, D A</td>
<td>269, 272, 543, 545</td>
</tr>
<tr>
<td>Lentz, M J</td>
<td>232, 340, 758, 856</td>
</tr>
<tr>
<td>Leonard, M</td>
<td>726, 734, 844, 845</td>
</tr>
<tr>
<td>Leproult, R</td>
<td>343</td>
</tr>
<tr>
<td>Lerman, A</td>
<td>525</td>
</tr>
<tr>
<td>Lesage, S</td>
<td>815, 827, 828</td>
</tr>
<tr>
<td>Lesku, J A</td>
<td>46</td>
</tr>
<tr>
<td>Leslie, L K</td>
<td>243</td>
</tr>
<tr>
<td>Lester, K</td>
<td>739</td>
</tr>
<tr>
<td>Letonsaari, M</td>
<td>368, 374</td>
</tr>
<tr>
<td>Lettieri, C J</td>
<td>941</td>
</tr>
<tr>
<td>Levandoski, L J</td>
<td>963</td>
</tr>
<tr>
<td>Leveille, C</td>
<td>937</td>
</tr>
<tr>
<td>Levey, A I</td>
<td>1023</td>
</tr>
<tr>
<td>Levin, A L</td>
<td>378</td>
</tr>
<tr>
<td>Levin, R</td>
<td>155, 331, 332, 772</td>
</tr>
<tr>
<td>Lewin, D</td>
<td>255</td>
</tr>
<tr>
<td>Lewin, D S</td>
<td>301, 302, 1047</td>
</tr>
<tr>
<td>Name</td>
<td>Page Numbers</td>
</tr>
<tr>
<td>-----------------------</td>
<td>--------------------</td>
</tr>
<tr>
<td>Lewis, E</td>
<td>968</td>
</tr>
<tr>
<td>Lewy, A J</td>
<td>204</td>
</tr>
<tr>
<td>Li, J</td>
<td>524</td>
</tr>
<tr>
<td>Liao, W</td>
<td>340</td>
</tr>
<tr>
<td>Lichstein, K</td>
<td>739</td>
</tr>
<tr>
<td>Lieb, K</td>
<td>676</td>
</tr>
<tr>
<td>Lifschutz, P</td>
<td>542</td>
</tr>
<tr>
<td>Lim, L</td>
<td>787, 812</td>
</tr>
<tr>
<td>Lim, S</td>
<td>156</td>
</tr>
<tr>
<td>Lim, W</td>
<td>472, 507, 561</td>
</tr>
<tr>
<td>Lima, M D</td>
<td>351</td>
</tr>
<tr>
<td>Lima, S L</td>
<td>46</td>
</tr>
<tr>
<td>Limoges, E</td>
<td>937</td>
</tr>
<tr>
<td>Lin, H</td>
<td>533, 602, 752, 944</td>
</tr>
<tr>
<td>Lin, J</td>
<td>52, 238</td>
</tr>
<tr>
<td>Lin, L</td>
<td>11, 97, 843</td>
</tr>
<tr>
<td>Lin, S</td>
<td>1055</td>
</tr>
<tr>
<td>Lincoff, N</td>
<td>835</td>
</tr>
<tr>
<td>Lindsay, D R</td>
<td>1049</td>
</tr>
<tr>
<td>Lineberger, M D</td>
<td>943</td>
</tr>
<tr>
<td>Liskow, B I</td>
<td>616, 629</td>
</tr>
<tr>
<td>Lista, C</td>
<td>394</td>
</tr>
<tr>
<td>Litsch, S</td>
<td>761</td>
</tr>
<tr>
<td>Little, R</td>
<td>777</td>
</tr>
<tr>
<td>Littwack, S</td>
<td>336, 581</td>
</tr>
<tr>
<td>Liu, C</td>
<td>737</td>
</tr>
<tr>
<td>Liu, K</td>
<td>945, 946</td>
</tr>
<tr>
<td>Liu, L</td>
<td>322, 335, 345, 843, 844, 845, 857, 871</td>
</tr>
<tr>
<td>Liu, S</td>
<td>777</td>
</tr>
<tr>
<td>Liu, X</td>
<td>16, 18, 19, 20, 294, 297, 345</td>
</tr>
<tr>
<td>Lloyd, S R</td>
<td>954</td>
</tr>
<tr>
<td>Lo, H</td>
<td>708</td>
</tr>
<tr>
<td>Lo, Y</td>
<td>554</td>
</tr>
<tr>
<td>Lockley, S W</td>
<td>166</td>
</tr>
<tr>
<td>Loda, B</td>
<td>303</td>
</tr>
<tr>
<td>Loffer, R</td>
<td>840</td>
</tr>
<tr>
<td>Lofthouse, N</td>
<td>306</td>
</tr>
<tr>
<td>Lois, W</td>
<td>863</td>
</tr>
<tr>
<td>Lonart, G</td>
<td>20</td>
</tr>
<tr>
<td>Lopes, E A</td>
<td>770</td>
</tr>
<tr>
<td>Lopes, M C</td>
<td>304, 546</td>
</tr>
<tr>
<td>Lopez, C</td>
<td>901, 1041</td>
</tr>
<tr>
<td>Lopez, J</td>
<td>73</td>
</tr>
<tr>
<td>Lopez, L</td>
<td>517</td>
</tr>
<tr>
<td>Loredo, J</td>
<td>325, 1037</td>
</tr>
<tr>
<td>Loredo, J S</td>
<td>335, 472, 507, 560, 561</td>
</tr>
<tr>
<td>Lorenzen, T</td>
<td>558</td>
</tr>
<tr>
<td>Lorenzi-Filho, G</td>
<td>286</td>
</tr>
<tr>
<td>Lorr, D</td>
<td>966</td>
</tr>
<tr>
<td>Lortie-Lussier, M</td>
<td>153</td>
</tr>
<tr>
<td>Lortkipanidze, N D</td>
<td>376</td>
</tr>
<tr>
<td>Losee, M, W</td>
<td>206, 423</td>
</tr>
<tr>
<td>Lourenzi, V P</td>
<td>397</td>
</tr>
<tr>
<td>Loving, V</td>
<td>979</td>
</tr>
<tr>
<td>Lowe, A</td>
<td>169, 170</td>
</tr>
<tr>
<td>Lowe, A A</td>
<td>477, 504</td>
</tr>
<tr>
<td>Lowe, A S</td>
<td>818</td>
</tr>
<tr>
<td>Loyden, J</td>
<td>242</td>
</tr>
<tr>
<td>Lu, J</td>
<td>95, 434</td>
</tr>
<tr>
<td>Lu, J W</td>
<td>28</td>
</tr>
<tr>
<td>Luc, M</td>
<td>224</td>
</tr>
<tr>
<td>Lucas, E A</td>
<td>615</td>
</tr>
<tr>
<td>Luebke, A</td>
<td>13</td>
</tr>
<tr>
<td>Luiten, P</td>
<td>375</td>
</tr>
<tr>
<td>Lukas, S</td>
<td>451</td>
</tr>
<tr>
<td>Luke, C</td>
<td>201</td>
</tr>
<tr>
<td>Lumley, M A</td>
<td>697, 872</td>
</tr>
<tr>
<td>Lund, J</td>
<td>144</td>
</tr>
<tr>
<td>Lundahl, J</td>
<td>144, 715</td>
</tr>
<tr>
<td>Lundequarn, E</td>
<td>980, 983</td>
</tr>
<tr>
<td>Luo, A</td>
<td>106</td>
</tr>
<tr>
<td>Lushington, K</td>
<td>316</td>
</tr>
<tr>
<td>Lusignan, F</td>
<td>154, 914</td>
</tr>
<tr>
<td>Luxenberg, J S</td>
<td>164</td>
</tr>
<tr>
<td>Lyamin, O</td>
<td>43</td>
</tr>
<tr>
<td>Lydiard, R</td>
<td>685</td>
</tr>
<tr>
<td>Lydic, R</td>
<td>8, 36</td>
</tr>
<tr>
<td>Lyness, J M</td>
<td>907</td>
</tr>
<tr>
<td>Lyons, D M</td>
<td>418</td>
</tr>
<tr>
<td>Lyoo, I</td>
<td>647</td>
</tr>
<tr>
<td>Lousquey-Hermite-Ballacutelriaux, M</td>
<td>187</td>
</tr>
<tr>
<td>M</td>
<td></td>
</tr>
<tr>
<td>Ma, D</td>
<td>345</td>
</tr>
<tr>
<td>Macdonald, I</td>
<td>196</td>
</tr>
<tr>
<td>MacDonald, L</td>
<td>279</td>
</tr>
<tr>
<td>MacDonald, M M</td>
<td>491, 892</td>
</tr>
<tr>
<td>Mackedo, C R</td>
<td>269, 272, 543, 545, 770</td>
</tr>
<tr>
<td>Macey, P M</td>
<td>853</td>
</tr>
<tr>
<td>Machado, M A</td>
<td>538</td>
</tr>
<tr>
<td>Machado, M C</td>
<td>269, 272, 543, 545</td>
</tr>
<tr>
<td>Machamer, J</td>
<td>838</td>
</tr>
<tr>
<td>MacKenzie, T</td>
<td>907</td>
</tr>
<tr>
<td>Mackey, B A</td>
<td>890</td>
</tr>
<tr>
<td>Mackiewicz, M</td>
<td>1006</td>
</tr>
<tr>
<td>MacLean, A W</td>
<td>354, 450</td>
</tr>
<tr>
<td>Maeda, H</td>
<td>515</td>
</tr>
<tr>
<td>Maehlen, J</td>
<td>655</td>
</tr>
<tr>
<td>Magai, C</td>
<td>690, 863</td>
</tr>
<tr>
<td>Magalang, U J</td>
<td>971, 972</td>
</tr>
<tr>
<td>Magistra, A</td>
<td>283</td>
</tr>
<tr>
<td>Mahmoud, G</td>
<td>445</td>
</tr>
<tr>
<td>Mahowald, M</td>
<td>682</td>
</tr>
<tr>
<td>Mahowald, M W</td>
<td>773</td>
</tr>
<tr>
<td>Maidment, N</td>
<td>642</td>
</tr>
<tr>
<td>Mainville, L</td>
<td>91</td>
</tr>
<tr>
<td>Maislin, G</td>
<td>146, 508, 595, 738, 1033</td>
</tr>
<tr>
<td>Maisuradze, L M</td>
<td>376</td>
</tr>
<tr>
<td>Majde, J A</td>
<td>122, 123, 127, 1009</td>
</tr>
<tr>
<td>Makris, C M</td>
<td>939</td>
</tr>
<tr>
<td>Maldonado, C C</td>
<td>489</td>
</tr>
<tr>
<td>Malhotra, A</td>
<td>211, 215, 491, 512, 534, 554, 600, 611, 892</td>
</tr>
<tr>
<td>Malik, I</td>
<td>898</td>
</tr>
<tr>
<td>Malison, R T</td>
<td>927</td>
</tr>
<tr>
<td>Malliani, A</td>
<td>394, 500</td>
</tr>
<tr>
<td>Mallis, M M</td>
<td>173, 197, 413, 1038, 1050</td>
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<tr>
<td>Malow, B A</td>
<td>279, 313, 481, 626, 975, 978</td>
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<tr>
<td>Manber, R</td>
<td>482, 674, 677, 686, 692, 701, 906, 908, 911</td>
</tr>
<tr>
<td>Manconion, M</td>
<td>159, 976</td>
</tr>
<tr>
<td>manconion, m</td>
<td>822, 852</td>
</tr>
<tr>
<td>Mancuso, P</td>
<td>486, 879</td>
</tr>
<tr>
<td>Mander, B A</td>
<td>420, 421</td>
</tr>
<tr>
<td>Mandujano, M</td>
<td>246</td>
</tr>
<tr>
<td>Mann, G L</td>
<td>28</td>
</tr>
</tbody>
</table>
Mannino, D .................................................. 694
Manohar, P ................................................. 836
Manthena, P ............................................... 165
Mantzoros, C S ........................................... 213
Manzini, C ................................................ 769
Marchand, V ............................................... 433, 442
Marcom, P K ............................................... 678
Marcus, C L ................................................ 299
Margel, D .................................................. 497
Marioni, P .................................................. 226
Mark, S ..................................................... 467
Markowitz, T .............................................. 965
Marks, G A ................................................ 25, 74
Marler, M .................................................. 322, 325, 327, 335, 857
Marmar, C ................................................ 934
Marshall, B ............................................... 957
Martel, E ................................................... 158, 776
Marti, M ..................................................... 775
Martica, H ................................................ 324
Martin, J .................................................... 316
Martin, J L .................................................. 328
Martin-Okada, R ........................................ 911
Martinelli, C ............................................. 822
Martinez, J ................................................ 936
Martinez-Rodriguez, J ......................... 92
Martins, P J ............................................... 411
Marzano, C ............................................... 20, 121
Mascha, E ............................................... 1034
Mason, N H ............................................... 448
Mason, T .................................................. 270
Mason, T A ............................................... 839
Mason, W .................................................. 870
Massaro, A F ............................................. 211, 215
Massicotte-Marquez, J ......................... 318, 765
Massicotte-Merquez, J ......................... 465
Massie, C A ................................................ 609
Massimini, M ............................................ 121
Massimini, M ............................................ 15
Mast, B ..................................................... 258
Mastick, J .................................................. 164
Mastin, D F ............................................... 119
Mastronardi, M ......................................... 282
Masuko, A H ............................................ 234, 236
Masutani, H .............................................. 900
Mateika, J H .............................................. 112
Mathias, R ................................................ 815
Mathias, S ................................................ 696
Mathieu, A ................................................. 318, 465, 765
Matson, C C ............................................. 997
Mattle, S .................................................. 716, 734, 955
Matthews, K A ......................................... 350, 868
Matthewson, J .......................................... 494
Mattice, C D ............................................ 890
Matto, V .................................................. 65
Maxfield, N D ............................................ 370
Maxwell, J ............................................... 1024
Maxwell, J L ............................................. 188, 1051
May, J F ................................................... 930, 1018
Mayers, R ................................................ 492
Mazeika, G G ............................................ 959, 960
Mazza, S .................................................. 465
McBride, S ............................................... 402
McBride, S A ............................................. 401, 404
McCabe, M ............................................... 242
McCabe, V ............................................... 916, 917, 918
McClellan, L E ......................................... 7, 21, 35, 356, 410, 1003
McClelland, L E ....................................... 370
McCoy, J G ............................................... 21
McCoy, R W ............................................ 536, 584
McCrae, C ................................................ 739, 760
McCrae, C S ............................................. 352
McCubbin, J A ......................................... 370
McDaniel, W ........................................... 930
McDonough, J H ...................................... 252
McElroy, J ............................................... 558
McEvoy, D .............................................. 111
McGee, S ................................................ 693
McGoey, M .............................................. 618
McGillin, C ............................................. 1029
McGillie, E L ........................................... 380
McGillie, E L ........................................... 279, 313
McGrew, S .............................................. 21, 410
McKenna, J .............................................. 320
McKibben, C ........................................... 416, 417
McLellan, T .............................................. 743
McMahon, L ............................................. 133
McMillan, D ............................................. 758
McNab, B ............................................... 483
McNair, A L ............................................. 257, 284
McNamara, J P ........................................ 760
McNear, K K ............................................ 840
McPhail, L ................................................ 743
McQuaid, J .............................................. 919
McWilliam, R .......................................... 218
Means, M K ............................................. 490, 943
Medeiros, M ............................................. 308
Medley, E ................................................ 230
Mednick, S C .......................................... 1019
Meerlo, P ................................................ 375
Mehl, R C ............................................... 241, 256, 258, 298, 994
Mehra, R ................................................ 336, 453, 544
Mehta, J B ............................................... 576
Mehta, S .................................................. 291
Meier, M .................................................. 948
Meighan, P C .......................................... 435
Medjall, S ................................................ 197
Melissa, J ................................................. 935
Mellman, T .............................................. 932, 936
Mello, L E ............................................... 604
Mello, M T ............................................... 397, 419, 820
Mello, T .................................................. 125
Mello-Fujita, L ......................................... 582
Mello-Fujita, I ......................................... 590
Meloff, K ................................................ 780
Meltzer, C ............................................... 691
Meltzer, L J ............................................. 287, 963
Mendelson, W B ...................................... 131
Mengel, H ................................................ 144
Mento, G .................................................. 805
Meola, G .................................................. 763
Meraim, S ................................................ 563

SLEEP, Volume 28, Abstract Supplement, 2005
<table>
<thead>
<tr>
<th>Last Name</th>
<th>First Name</th>
<th>Page(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molfese, V J</td>
<td></td>
<td>260</td>
</tr>
<tr>
<td>Mohyuddin, T</td>
<td></td>
<td>552</td>
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<td>Mohan, K K</td>
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<td>837</td>
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<td></td>
<td>253, 527, 840</td>
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<tr>
<td>Modrak, J</td>
<td></td>
<td>229</td>
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<tr>
<td>Modirrousta, M</td>
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<td>253, 527, 840</td>
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<td>Mohler, M</td>
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<td>858</td>
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<td>Mohns, E J</td>
<td></td>
<td>27, 50</td>
</tr>
<tr>
<td>Mohyuddin, T</td>
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<td>552</td>
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<td>Mojica, J</td>
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<td>Moldofsky, H</td>
<td></td>
<td>185, 873, 874</td>
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<td>Molfese, V J</td>
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<td>260</td>
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<tr>
<td>Molinari, L</td>
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<td>249</td>
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<td>Moline, M</td>
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<td>291</td>
</tr>
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<td>Moller, H</td>
<td></td>
<td>924</td>
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<td>Molnar, E</td>
<td></td>
<td>120</td>
</tr>
<tr>
<td>Mongrain, V</td>
<td></td>
<td>167, 168</td>
</tr>
<tr>
<td>Mont, S</td>
<td></td>
<td>577</td>
</tr>
<tr>
<td>Montagna, P</td>
<td></td>
<td>657</td>
</tr>
<tr>
<td>Montano, N</td>
<td></td>
<td>394, 500</td>
</tr>
<tr>
<td>Montanye, M</td>
<td></td>
<td>518</td>
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<tr>
<td>Montemirto, E</td>
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<td>239</td>
</tr>
<tr>
<td>Monteverde, E</td>
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<td>909</td>
</tr>
<tr>
<td>Montgomery, G L</td>
<td></td>
<td>264</td>
</tr>
<tr>
<td>Montgomery-Downs, H E</td>
<td></td>
<td>231, 260</td>
</tr>
<tr>
<td>Montplaisir, J</td>
<td></td>
<td>126, 465, 746, 765, 766, 767, 771, 779, 785</td>
</tr>
<tr>
<td>Montplaisir, J Y</td>
<td></td>
<td>663, 768, 894</td>
</tr>
<tr>
<td>Montplaisir, J</td>
<td></td>
<td>318</td>
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<tr>
<td>Mood, D P</td>
<td></td>
<td>364</td>
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<tr>
<td>Moore, J</td>
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<td>263</td>
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<td>Moore, L P</td>
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<td>671</td>
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<td>Moore, M L</td>
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<td>880</td>
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<td>Moore, N</td>
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<td>395, 399</td>
</tr>
<tr>
<td>Moore, W R</td>
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<td>634</td>
</tr>
<tr>
<td>Moraes, W</td>
<td></td>
<td>125</td>
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<tr>
<td>Morarity, S</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Morarity, S R</td>
<td></td>
<td>89</td>
</tr>
<tr>
<td>Morales, F R</td>
<td></td>
<td>40, 58</td>
</tr>
<tr>
<td>Moran, C A</td>
<td></td>
<td>177, 234, 236</td>
</tr>
<tr>
<td>Moreau, V</td>
<td></td>
<td>293</td>
</tr>
<tr>
<td>Morgan, P T</td>
<td></td>
<td>927</td>
</tr>
<tr>
<td>Morgan, W J</td>
<td></td>
<td>262</td>
</tr>
<tr>
<td>Morgenthaler, T</td>
<td></td>
<td>525, 599, 899</td>
</tr>
<tr>
<td>Morgenthaler, T I</td>
<td></td>
<td>502</td>
</tr>
<tr>
<td>Morillo, R</td>
<td></td>
<td>882</td>
</tr>
<tr>
<td>Morin, A</td>
<td></td>
<td>1044, 1046</td>
</tr>
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<td>Morin, C M</td>
<td></td>
<td>293, 673, 687, 689, 700, 735, 747, 753, 754, 925</td>
</tr>
<tr>
<td>Moritz, M E</td>
<td></td>
<td>364</td>
</tr>
<tr>
<td>Moriwaki, H</td>
<td></td>
<td>556</td>
</tr>
<tr>
<td>Morlock, R J</td>
<td></td>
<td>706, 709, 748</td>
</tr>
<tr>
<td>Moroni, F</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>Morrison, A R</td>
<td></td>
<td>28, 928, 1020</td>
</tr>
<tr>
<td>Morrissey, A</td>
<td></td>
<td>539</td>
</tr>
<tr>
<td>Morrissey, A E</td>
<td></td>
<td>814</td>
</tr>
<tr>
<td>Morrissey, M J</td>
<td></td>
<td>67, 412</td>
</tr>
<tr>
<td>Moscovitch, A</td>
<td></td>
<td>426, 681, 682, 778</td>
</tr>
<tr>
<td>Mosek, A</td>
<td></td>
<td>854</td>
</tr>
<tr>
<td>Motivala, S J</td>
<td></td>
<td>129</td>
</tr>
<tr>
<td>Mottron, L</td>
<td></td>
<td>154, 905, 937</td>
</tr>
<tr>
<td>Mouren, M</td>
<td></td>
<td>285</td>
</tr>
<tr>
<td>Mozin, M</td>
<td></td>
<td>223</td>
</tr>
<tr>
<td>Mu, Q</td>
<td></td>
<td>361</td>
</tr>
<tr>
<td>Mucha, L</td>
<td></td>
<td>712</td>
</tr>
<tr>
<td>Muchalski, T</td>
<td></td>
<td>813</td>
</tr>
<tr>
<td>Mueller, A</td>
<td></td>
<td>631</td>
</tr>
<tr>
<td>Mueller, J</td>
<td></td>
<td>817</td>
</tr>
<tr>
<td>Muhlthaler, M</td>
<td></td>
<td>85</td>
</tr>
<tr>
<td>Mukhametov, L</td>
<td></td>
<td>43</td>
</tr>
<tr>
<td>Mukherjee, S</td>
<td></td>
<td>93</td>
</tr>
<tr>
<td>Muller, K</td>
<td></td>
<td>374</td>
</tr>
<tr>
<td>Mullington, J</td>
<td></td>
<td>207</td>
</tr>
<tr>
<td>Mullington, J M</td>
<td></td>
<td>427</td>
</tr>
<tr>
<td>Multisine, G</td>
<td></td>
<td>508</td>
</tr>
<tr>
<td>Munch, M</td>
<td></td>
<td>199</td>
</tr>
<tr>
<td>Name</td>
<td>Pages</td>
<td></td>
</tr>
<tr>
<td>---------------------------</td>
<td>----------------------------</td>
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</tr>
<tr>
<td>Nishizawa, M</td>
<td>559</td>
<td></td>
</tr>
<tr>
<td>Nissen, C</td>
<td>145</td>
<td></td>
</tr>
<tr>
<td>Niyogi, S</td>
<td>143</td>
<td></td>
</tr>
<tr>
<td>Niyar, V</td>
<td>877</td>
<td></td>
</tr>
<tr>
<td>Nkwuo, J</td>
<td>568</td>
<td></td>
</tr>
<tr>
<td>Nkwuo, J E</td>
<td>875</td>
<td></td>
</tr>
<tr>
<td>Noda, A</td>
<td>592</td>
<td></td>
</tr>
<tr>
<td>Nofzinger, E A</td>
<td>691</td>
<td></td>
</tr>
<tr>
<td>Nolan, K</td>
<td>109</td>
<td></td>
</tr>
<tr>
<td>Nomura, T</td>
<td>847</td>
<td></td>
</tr>
<tr>
<td>Nordhus, I H</td>
<td>792</td>
<td></td>
</tr>
<tr>
<td>Norman, R</td>
<td>942</td>
<td></td>
</tr>
<tr>
<td>Nosetti, L M</td>
<td>303</td>
<td></td>
</tr>
<tr>
<td>Novak, M</td>
<td>195</td>
<td></td>
</tr>
<tr>
<td>Nowakowski, S</td>
<td>935</td>
<td></td>
</tr>
<tr>
<td>Nuhic, Z</td>
<td>139</td>
<td></td>
</tr>
<tr>
<td>Nunuez-Ortiz, R</td>
<td>278</td>
<td></td>
</tr>
<tr>
<td>O'Brien, L</td>
<td>309</td>
<td></td>
</tr>
<tr>
<td>O'Brien, L M</td>
<td>241, 256, 258, 266, 268, 298</td>
<td></td>
</tr>
<tr>
<td>O'Connell, W P</td>
<td>890</td>
<td></td>
</tr>
<tr>
<td>O'Conner, G T</td>
<td>461</td>
<td></td>
</tr>
<tr>
<td>O'Conner, R</td>
<td>379</td>
<td></td>
</tr>
<tr>
<td>O'Hara, B F</td>
<td>1012, 1013</td>
<td></td>
</tr>
<tr>
<td>O'Hara, R M</td>
<td>321</td>
<td></td>
</tr>
<tr>
<td>Oldani, A</td>
<td>922</td>
<td></td>
</tr>
<tr>
<td>Olesen, E</td>
<td>853</td>
<td></td>
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<tr>
<td>Olesen, M K</td>
<td>943</td>
<td></td>
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<tr>
<td>Olsen, E</td>
<td>601</td>
<td></td>
</tr>
<tr>
<td>Olsen, E J</td>
<td>899</td>
<td></td>
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<tr>
<td>Omran, Q</td>
<td>548</td>
<td></td>
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<tr>
<td>Onat, H D</td>
<td>968</td>
<td></td>
</tr>
<tr>
<td>Onder, G</td>
<td>842</td>
<td></td>
</tr>
<tr>
<td>Ong, J C</td>
<td>674, 686</td>
<td></td>
</tr>
<tr>
<td>Oniani, N T</td>
<td>376</td>
<td></td>
</tr>
<tr>
<td>Oniani, T N</td>
<td>376</td>
<td></td>
</tr>
<tr>
<td>Oosterloo, M</td>
<td>910</td>
<td></td>
</tr>
<tr>
<td>Opp, M R</td>
<td>2, 22, 30, 37</td>
<td></td>
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<tr>
<td>Orem, J M</td>
<td>115</td>
<td></td>
</tr>
<tr>
<td>Orff, H J</td>
<td>387, 438, 440</td>
<td></td>
</tr>
<tr>
<td>Orglindull, S</td>
<td>704</td>
<td></td>
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<tr>
<td>Orjci, C</td>
<td>939</td>
<td></td>
</tr>
<tr>
<td>Orlova, C</td>
<td>213</td>
<td></td>
</tr>
<tr>
<td>Orr, L</td>
<td>718</td>
<td></td>
</tr>
<tr>
<td>Orr, W C</td>
<td>861, 895, 897</td>
<td></td>
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<tr>
<td>O'Sullivan, P</td>
<td>337</td>
<td></td>
</tr>
<tr>
<td>Name</td>
<td>Page Numbers</td>
<td></td>
</tr>
<tr>
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<tr>
<td>Otsuka, R</td>
<td>477</td>
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<td>Otsuka, Y</td>
<td>118</td>
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<tr>
<td>Otte, A</td>
<td>832</td>
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<td>Ouslander, J G</td>
<td>475</td>
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<td>Overeem, S</td>
<td>636, 649, 910</td>
<td></td>
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<tr>
<td>Owen, R J</td>
<td>372, 478</td>
<td></td>
</tr>
<tr>
<td>Owens, J A</td>
<td>233</td>
<td></td>
</tr>
<tr>
<td>Owens, J F</td>
<td>350</td>
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<tr>
<td>Oyane, N M</td>
<td>913</td>
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<tr>
<td>Oyung, R L</td>
<td>173, 413</td>
<td></td>
</tr>
<tr>
<td>Ozaki, N</td>
<td>178</td>
<td></td>
</tr>
<tr>
<td>Ozawa, T</td>
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<td>Richardson, G S</td>
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</tbody>
</table>
Richardson, J W .............................................. 634
Richardson, L P ............................................. 232
Richelson, E .................................................. 12
Richert, A C .................................................. 149
Richter, L ....................................................... 676
Riemann, D .................................................... 145, 676, 796
Rifai, N ........................................................ 207
Rifkin, D ........................................................ 835
Rifkin, D I ....................................................... 476
Riggins, M A .................................................. 938
Riley, J ........................................................ 12
Ringler, J ........................................................ 571, 807
Rintelmann, J .................................................. 263
Ris, M ............................................................ 242
Riskalla, M M .................................................. 265
Ritchie, S ........................................................ 802
Rizzi, D .......................................................... 283
Rizzo, W ........................................................ 1006
Roach, J ........................................................ 454, 917
Robbins, J ....................................................... 463
Robillard, A .................................................... 767
Robillard, R .................................................... 148, 342
Robinson, E ..................................................... 487
Robinson, E L .................................................. 198
Rocca, M A ..................................................... 852
Roche, F ........................................................ 797
Rodgers, G ...................................................... 994
Rodgers-Rawden, A ......................................... 716
Rodriguez, A J ................................................ 829
Rodway, G W .................................................. 627
Roehrs, J D ..................................................... 630
Roehrs, T ........................................................ 660, 710
Roehrs, T A ..................................................... 142, 319, 326, 377, 697, 725, 742, 872
Roffwarg, H P ................................................ 73
Rogers, A E ...................................................... 875
Rogers, N L ...................................................... 143, 146
Rogowski, R .................................................... 150
Roizenblatt, S ................................................ 304, 582, 590
Rojas, M ........................................................ 78, 81
Roman, V ......................................................... 375
Romppe, P H ................................................... 768, 769, 894
Romppe, S ....................................................... 465, 663, 767
Ronda, J M ....................................................... 365
Ronksley, P ...................................................... 509
Rosa, A .......................................................... 304, 582
Rosa, A C ....................................................... 887
Rosa, R .......................................................... 885
Rosekind, M ................................................... 391, 958
Rosen, C L ....................................................... 233
Rosen, I M ....................................................... 403
Rosenberg, C E ............................................... 518, 520, 542
Rosenberg, P A ............................................... 63
Rosenberg, R ................................................... 454, 727
Rosenfeld, K ................................................... 452
Rosenfeld, A .................................................... 1026
Rosenfeld, K .................................................... 858
Rosenthal, L .................................................. 528, 532, 628
Ross, R J ......................................................... 28, 928, 1020
Rotenberg, J .................................................... 806
Roth, E .......................................................... 186
Roth II, T C ..................................................... 46
Rothermel, J J .................................................... 758
Roux, D ........................................................ 1024
Row, B W ....................................................... 24, 80, 83
Rowe, K M ...................................................... 985
Rowe, M ........................................................ 230
Rowe, M A ...................................................... 352, 760
Rowe, V D ....................................................... 616, 629
Rowell, P P ..................................................... 80
Rowland, L ..................................................... 358
Rowley, J ....................................................... 474
Rowley, J A ..................................................... 548
Royant-Parola, S ............................................. 878
Rubens, R ..................................................... 705, 916, 918
Rubin, S ......................................................... 348
Rueda, A ......................................................... 125
Ruiz, M ........................................................ 246
Rumble, M .................................................... 678
Rundo, F ......................................................... 108
Rupp, T ........................................................ 1025
Russell, A J .................................................... 743
Russell, J ......................................................... 598
Russio, M ....................................................... 358
Ruoso, M B ..................................................... 422, 962
Ruyak, P S ..................................................... 503, 506, 574
Ruzicka, D L ................................................... 550, 555
Ryan, C ........................................................ 477
Rybarczyk, B ................................................... 670
Ryckebusch, H ................................................ 878
Rye, D .......................................................... 802
Rye, D B ......................................................... 824, 849, 851
Ryter, S ........................................................ 627
Sachdeo, R ..................................................... 780
Sachs, O ........................................................ 25
Sadeh, A ......................................................... 250
Sadek, M ........................................................ 38
Saeian, K ......................................................... 799
Sahota, P K ...................................................... 471, 557
Sainati, S ......................................................... 479, 480, 679, 680
Saip, S .......................................................... 842
Sakai, K ......................................................... 559, 564
Sakurai, T ....................................................... 3, 56, 71, 97, 640, 653, 654
Salamat, J S ................................................... 387, 438, 440, 964, 1041, 1052
Salamone, C ................................................... 716, 726
Salehi, A ........................................................ 655
Sales, L V ........................................................ 569
Sallinen, M ..................................................... 368, 374
Salvatore, S .................................................... 303
Sammel, M D .................................................. 944
Sampogna, S ................................................... 58
Sanchez, C ..................................................... 246
Sanchez-Alavez, M ......................................... 49, 103, 104
Sanders, M ..................................................... 329, 463, 606, 982
Sanders, M A .................................................. 350
Sanders, M H .................................................. 627
Sandra, S ....................................................... 488
Sanford, L ....................................................... 20
<table>
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**Notes:**

- Taibl, D: 896
- Taillard, J: 395, 399
- Taishi, P: 1009, 1011
- Takahashi, K: 178, 499
- Takahashi, M: 118
- Takahashi, Y: 556
- Takano, A: 178
- Takaya, R: 280
- Takegami, M: 811
- Takehara, T: 698
- Take, Y: 473
- Takeuchi, T: 158, 161, 776
- Tan, M: 706, 709
- Tanaka, S: 655
- Tancer, M: 142
- Tang, J P: 281
- Tang, X: 16, 17, 18, 19
- Tao, R: 35
- Tapert, S: 901
- Tartar, J L: 21, 410
- Tartarini, W: 451
- Tasali, E: 343, 441
- Tauber, D: 271, 274
- Tauman, R: 241, 266, 268
- Tavares, S M: 885
- Taw, M: 861
- Taylor, A G: 896
- Taylor, D J: 933
- Tchmoutina, E: 169, 170
- Tee, B: 5
- Teixeira, V G: 885
- Tekell, J L: 114
- Tekwani, S: 109
- Tembl, A: 612
- Temkin, N R: 838
- Temple, J: 933
- Teodorescu, M: 486, 879, 881, 996
- Teodorescu, M C: 996
- Teran-Perez, G: 246, 278
- Terstespanian, M: 276
- Terturen, J: 788
- Terziano, M G: 108, 468, 695
- Tese, R: 282, 283
- Thacker, P V: 447
- Thakkar, M: 1003
- Thakkar, M M: 35
- Thannickal, T C: 651
- Thayer, J F: 129
- Theres, H: 631
- Thiele, K: 450
- Thieriejan, R: 630
- Thomas, K: 1037
- Thomas, M: 358
- Thomas, R: 578
- Thomas, R J: 444, 468
- Thomasanz, R: 1012
- Thomsen, W: 5
- Thorne, D: 358
- Thorne, D R: 428
- Thornton, A T: 987
- Thornton, A C: 843
- Tierney, C G: 760
<table>
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<tr>
<th>Name</th>
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<tr>
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<td>64, 70</td>
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**SLEEP, Volume 28, Abstract Supplement, 2005**

**AXXXIV**
**0001**

**Interleukin-1 (IL-1) Mediates Parkinsonism-Induced Sleep Alterations**

*Chang F, Yi P, Tsai C, Chen Y*

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**Introduction:** Recently the pathogenesis of Parkinson’s disease (PD) has been focused on the microglia activation and the increased secretion of cytokines. A body of clinical evidence suggests that sleep is altered in PD patients, however there is a lack of basic cellular mechanisms. This study is designed to elucidate the effect of IL-1 in the animal PD model.

**Methods:** Male Sprague-Dawley rats were surgically implanted with EEG recording electrodes and intracerebroventricular (ICV) cannula. Rats were allowed a minimum of one-week recovery period, and kept on a 12:12h Light:Dark cycle at 23 ± 1 °C. Locomotion was recorded by infrared motion detector. After recovery, 24-h baseline recording and pyrogen-free saline (PFS)-treated recording were obtained as control. Subcutaneous osmotic minipump filled with rotenone, which delivers 3 mg/kg/day consistently in the consequent 14 days, was then implanted to induce parkinsonism. Sleep was recorded from the 14th day after rotenone-treatment. Two doses of IL-1 receptor antagonist (IL-1ra; 100 and 200 ng) were administered in the subsequent days. The success of parkinsonism model was confirmed by behavioral test, locomotion and immunohistochemistry.

**Results:** Slow wave sleep (SWS) increased from 20.0 ± 1.6 % obtained after control to 26.7 ± 1.7 % after 14-day rotenone treatment during the dark period, but decreased from 44.3 ± 2.0 % to 35.4 ± 1.8 % during the light period. Rapid eye movement sleep (REMS) also increased during the dark period after rotenone treatment, from 3.8 ± 0.7 % to 7.9 ± 1.0 %; but REMS is not significantly altered in the light period. IL-1ra dose-dependently blocked rotenone-induced sleep alterations in SWS and REMS during the dark period, but not in the light period. IL-1ra did not change rotenone-induced decrease in locomotion. Neither rotenone nor IL-1ra alters slow wave activity during SWS.

**Conclusion:** These results suggest that IL-1 mediates parkinsonism-induced sleep alterations.

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**0002**

**Interleukin-1 Enhances GABAergic Inhibitory-Post-Synaptic Potentials In Dorsal Raphe Serotonergic Neurons**

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**Introduction:** Recent in vitro data obtained from guinea pig slice preparations suggest that interleukin-1 (IL-1) may promote NREM sleep by inhibiting the spontaneous firing rates of wake-active serotonergic neurons in the dorsal raphe nucleus (DRN). IL-1 also increases GABA receptor function. DRN neurons are under an inhibitory GABAergic control. This study aimed a) to determine if IL-1 inhibits firing rates of DRN serotonergic neurons in a different animal species (rat) and b) to test the hypothesis that IL-1 inhibits DRN serotonin neurons by potentiating GABAergic inhibitory effects.

**Methods:** In vitro intracellular recordings were performed to assess the responses of physiologically and pharmacologically identified DRN serotonergic neurons to rat recombinant IL-1β. Coronal slices containing DRN were obtained from male Sprague-Dawley rats. The impact of IL-1β on spontaneous firing rates and on evoked postsynaptic potentials (evPSPs) was determined. evPSPs were induced by stimulation with a bipolar electrode placed on the surface of the slice ventro lateral to DRN. **Results:** IL-1β administration (25 ng/ml) decreased spontaneous firing rates of DRN serotonergic neurons. The electrical stimulation induced depolarizing evPSPs in most DRN serotonergic neurons. The application of glutamatergic and GABAergic antagonists unmasked two different PSP components: a GABAergic inhibitory evPSP (evIPSP) and a glutamatergic excitatory evPSP (evEPSP) respectively. IL-1β increased GABAergic evIPSP amplitudes by 30.3 ± 3.8 % (n = 6) without affecting glutamatergic evEPSPs.

**Conclusion:** These results indicate that the IL-1 inhibitory effect on spontaneous firing rate of DRN serotonergic neurons can be observed in rat slice preparations. Furthermore, these data support the hypothesis that the inhibitory effects of IL-1 on DRN serotonergic neurons may be mediated by an IL-1-induced potentiation of GABAergic transmission on these neurons.

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**0003**

**Hypocretins/Orexins Are Involved In Enhanced Locomotor Activity Of Mice In Novel Environment**

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**Introduction:** Hypocretins/orexins are neuropeptides produced by neurons located in lateral hypothalamus. These neurons project to a wide range of brain areas, permitting multiple physiological functions. We used orexin/ataxin-3 transgenic (TG) narcoleptic mice, a postnatal hypocretin cell death model, to study the function of these peptides in novel environment adaptation.

**Methods:** TG colony (N8 backcrossed to C57BL/6) and C57BL/6 mice were maintained under a 12h:12h light/dark cycle. In experiment 1, 8 TG and 8 wild type (WT) littersmates (male, 5-6 month old) were housed in Plexiglas chambers with continuous monitoring of locomotor activity, drinking and feeding for 7 days. In experiment 2, 16 C57BL/6 mice (male, 3 months old) were injected intraperitoneally with SB-334867 (a hypocretin receptor-1 specific antagonist) or vehicle at zeitgeber time 12h (ZT12, light-off) and monitored in the chambers.

**Results:** Experiment 1. WT mice showed significantly higher locomotor activity when introduced into the recording chambers. Activity during the first 12-hours (dark period) was 1.6 times higher than that measured during the second dark period. Feeding and drinking were slightly but not significantly increased. TG mice did not show significant enhancement in these parameters. During the following days, the overall levels of activity, feeding and drinking remained stable, and were comparable in both groups. Experiment 2. Locomotor activities in vehicle-injected animals were the highest at the beginning of the night and decreased continuously until ZT18. Mice treated with SB-334867 (1-10 mg/kg) showed reduced activity enhancement for the first two hours. However, the activity level remained elevated until ZT18, and was significantly higher than controls at ZT15-ZT20.

**Conclusion:** These results, along with our previous findings that prepro-hypocretin knockout mice displayed an attenuation in novelty-seeking behavior (Yoshida et al, APSS 2004), suggest that endogenous hypocre-
Category A—Basic Neuroscience

tins, possibly acting through the hypocretin receptor-1, may contribute to enhanced locomotor activity during novel environment adaptation.

This work was supported by the Howard Hughes Medical Institute and the National Institutes of Health (NS23324).

0004

A Spectral Power Analysis Of The Sleep Inertia Period
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Introduction: Although several studies have investigated the sleep offset period by means of vigilance and performance measures, the EEG spectral changes underlying sleep inertia have been largely ignored. The aim of this study was to provide the first description of the changes by evaluating the cortical EEG topography upon awakening from NREM and REM sleep. We hypothesized that different frequency bands and/or cortical areas along the antero-posterior axis are differentially involved in the sleep inertia phenomenon.

Methods: Twenty-five female students (20-26 years) participated in the study for two nights. During the 2nd night, the EEG was recorded twice: just after lights-off and immediately after final awakening (after 7-8 hours of sleep). Each EEG recording was carried out while subjects were in bed in the dark, and lasted 10 minutes (5 min with closed eyes -CE-, 5 min with open eyes -OE-). Thirteen subjects were recorded after REM awakenings, while twelve subjects after stage 2 awakenings. EEG from Fz-A1, Cz-A1, Pz-A1, Oz-A1, EOG and submental EMG were digitized at 128 Hz. After an off-line artifact rejection based on a 4-sec epochs visual inspection, the EEG signals were analyzed by the Fast Fourier Transform (FFT) algorithm. Power values were calculated across a 1-25 Hz frequency range in a 1-Hz resolution.

Results: As compared to pre-sleep wakefulness, the sleep inertia period is characterized by an increase of power in the alpha band (8-10 Hz), and by a decrease of power in the beta frequency range (19-25 Hz). As regards EEG topography, the post-awakening period shows higher EEG power in the delta, theta and alpha range (1-11 Hz) on the occipital derivation, as well as a decrease of power in the beta range (18-25 Hz) on the same scalp location. Although the sleep inertia effects are similar in the CE and OE conditions, they encompass a wider frequency range in the former. Finally, NREM awakenings show a larger decrease in beta power (23-25 Hz) on the occipital derivation, as compared to REM awakenings.

Conclusion: The increase of alpha activity and the decrease of beta activity upon awakening, compared to the pre-sleep wakefulness, seems to be the EEG substrate of the behaviorally identified sleep inertia. Independent from the sleep inertia issue, regional changes suggest an asynchronous development of sleep offset, characterized by a postero-anterior gradient that seems complementary to the antero-posterior gradient of the sleep onset period.

0005

The Selective Serotonin 5-HT2a Inverse Agonist APD125 Promotes Sleep Onset And Consolidation In Male Wistar Rats During The Normal Active Phase
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Introduction: We have prepared a novel series of selective 5-HT2a inverse agonists that promote sleep consolidation and increase NREMS delta power in rats during the inactive phase. Here we describe a potent development lead from this series, APD125, tested during the active phase in rats.

Methods: Male Wistar rats (n=8; ~300 g) were instrumented for standard polygraphic recordings. In a repeated measures design, each rat received seven oral doses (6 hrs after lights off) including a vehicle ‘acclimation’ dose first, followed by 4 concentrations of APD125 (0.5, 1.5, 5 and 15 mg/kg), zolpidem (5mg/kg) and vehicle given in randomized order. Polygraphic recordings were scored visually in 10s epochs for Waking, REMS and NREMS. Time in each state per half-hour was assessed, and sleep bout length and number were calculated for each state in hourly bins as well as delta power (0.5-3.5 Hz).

Results: APD125 showed a significant dose-dependent 1) increase in NREMS time, 2) increase in NREMS bout length, 3) decrease in NREMS bout number, 4) decrease in waking bout number, and 5) increase in delta power, compared to control. Zolpidem had similar effects on NREMS parameters, but unlike APD125, significantly decreased REM bout length and number compared to control.

Conclusion: These results suggest that the selective 5-HT2a inverse agonist APD125 1) promotes sleep onset, indicated by the increase in NREMS time, 2) promotes sleep consolidation, indicated by the decrease in NREMS bout number coupled with the increase in bout length, and 3) promotes ‘deeper’ sleep indicated by increases in delta power. In contrast to zolpidem, a prototypic GABAa agonist, these favorable effects on sleep architecture were obtained without adversely impacting REM sleep. These findings highlight the therapeutic potential of APD125 in the treatment of both sleep onset and sleep maintenance insomnias.

0006

Reciprocal Modulation Of Adenosine A1 And A2a Receptors In Striatum Of NF-kB P50 Knockout Mice
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Introduction: Activation of adenosine receptors (ARs) A1 and A2A trigger opposing intracellular signaling pathways and differentially influence neurotransmission in striatum, suggesting inhibitory interactions. Because ARs expressions are modulated by the transcription factor NF-kB, NF-kB may mediate distinctive regulation on AR subtypes functions in striatum.

Methods: B6129PF2/J (F2) and B6.129 NF-kB p50 subunit knockout (KO) mice were treated for 96 hours with caffeine (ARs antagonist, 0.3 gram/L in drinking water) or vehicle. Assays with sampled striata included ARs specific bindings with 3H DPCPX for A1AR and 125I ZM 241385 for A2AR, gel electrophoresis and x-ray imaging of immunoprecipitation-purified 125I labeled ARs, western blot of cytosolic G protein Gsa subunit, and quantitative PCR.

Results: For F2 and KO mice, A1AR bindings levels (fm/gram protein, mean ± SD) were 322.6 ± 19.4 vs. 129.7 ± 64.3 for control mice (n = 6; p<0.01), and 217.0 ± 24.0 ± 129.7 versus 71.8 ± 34.3 for caffeine treated mice (n = 6; p<0.01); A2AAR bindings were 53.7 ± 22.2 vs. 135.1 ± 75.2 (n = 8; p < 0.05), and 182.5 ± 74.6 vs. 229.4 ± 71.6 (n = 8; p < 0.05), respectively. Radioactivity quantitation of radiolabelled purified A1AR and A2AAR bands (F2 vs. KO) revealed 496 vs. 1980 cpm, and 1278 vs. 794 cpm, respectively. Western blot band density of KO Gsa short chain was 84.5% higher than F2s. ARs mRNA expression did not differ between strains.

Conclusion: In mouse striatum, NF-kB functional defect (p50 subunit deficiency) promotes A2AAR binding but reduces A1AR binding. Caffeine treatments tend to augment these effects. We speculate that p50 absence reduces tonic suppression of A2AAR by A1AR and thereby promotes A2AAR coupling to Gs protein, resulting in receptor sensitization. The dissociation between ARs mRNA and binding suggests a novel mechanism of...
NF-kB regulation, such as direct modulatory effects on AR turnover.

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0007
Age Related Changes In Basal Forebrain Cholinergic Neurons: A Morphological And EEG Power Spectral Study
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Introduction: The cholinergic neurons of basal forebrain (CBF), comprising of SI, MCPO and HDB, are implicated in promoting cortical activation and state-dependent gamma and delta activity. The process of aging has been associated with hypofunction due to gradual loss of cholinergic neurons. To examine the effects of aging-associated changes in cholinergic morphology and cortical activation in CBF during sleep-wake cycle, EEG and immunohistochemistry was compared between young (2-3 months) and old (22-24 months) F344/NB rats.

Methods: Chronic indwelling electrodes for EOG, EEG and EMG were stereotaxically implanted. After total recovery, the rats (young and old) were acclimatized with the recording cables for 3 days. On day four, 24h of base line recording of sleep-wakefulness was carried out followed by 6h of sleep deprivation and 18h of recovery sleep on day five. Five parallel data was split into 10s epochs and the durations of wake, NREM and REM sleep were compared between young and old. EEG power spectral changes in delta activity (0.5 - 4.0 Hz) and gamma activity (30.5 - 58.0 Hz) were also compared. Furthermore, to examine the morphological changes in the cortically projecting CBF, 1.08µg (3µl) of 192-IgG conjugated with Cy3 was microinjected bilaterally into the lateral ventricles at the rate of 0.5µl/min for retrograde labeling of cortically projecting CBF neurons.

Results: Our preliminary results showed that old rats spent more time waking when compared to young animals. However, in old rats the gamma activity during waking showed considerable decrease. In addition, the delta activity in NREM sleep also showed considerable reduction, even in recovery sleep when the sleep propensity is enhanced following 6h of SD. Initial immunohistochemical examination of the CBF neurons in old rats showed smaller somata with irregular outlines as compared to healthy looking neurons in young rats. Further analysis of these neurons to study the number and volume are in progress.

Conclusion: These preliminary results further suggest that changes in the cholinergic neurons may be responsible for the reduction in cortical gamma and delta activity in aging rats.

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0008
Morphine Sulfate Dialyzed Into The Pontine Reticular Nucleus, Oral Part (PnO) Of Unanesthetized Rat Decreases PnO Levels Of GABA
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Introduction: Opioids are the most commonly prescribed drugs for treating pain, and one unwanted side effect is disruption of the sleep-wake cycle. Systemic morphine obtunds wakefulness, and morphine administered systemically or into the pontine reticular formation (PRF) inhibits REM sleep. The mechanisms by which morphine alters arousal are unknown, but may include modulation of PRF GABA, GABAergic transmission in the PRF is suggested to promote wakefulness based on the finding that PRF microinjection of a GABA_A receptor agonist increases wakefulness and suppresses sleep (J Neurophysiol 82:2015, 1999). In addition, PRF administration of a GABA_A antagonist decreases wakefulness, increases REM sleep (ibid), and increases PRF acetylcholine release (J Neurophysiol 92:2198, 2004). This study is the first to test the hypothesis that dialysis administration of morphine to rat PnO alters PnO GABA levels. The PnO is the rostral part of rat PRF.

Methods: Adult male Sprague-Dawley rats are implanted with guide tubes aimed unilaterally for the PnO. Following 7-14 days of recovery and conditioning, dialysis probes are inserted 17 hr prior to collection of brain samples and perfused continuously (2 µl/min) with Ringer’s. Samples (n=6/dialysis condition) are collected every 7 min during sequential perfusion of the probe with Ringer’s (vehicle control), morphine (100 µM), and Ringer’s. GABA is quantified by HPLC with electrochemical detection. Data are evaluated by one-way ANOVA and Tukey-Kramer multiple comparisons test.

Results: Morphine significantly decreased PnO GABA levels (F(2,47)=3.982; p=0.025) by 26%. MeantSD GABA levels (pmol/10 µl) were 0.057±0.018 during dialysis with Ringer’s and 0.042±0.016 during dialysis administration of morphine. GABA returned to control levels during dialysis with Ringer’s following morphine (0.055±0.015). Histology confirmed dialysis probe placement in the PnO.

Conclusion: The finding that morphine significantly reduced GABA levels in rat PnO suggests that opioids may alter levels of arousal, in part, by modulating PnO GABAergic transmission.

This research was supported by National Institute of Health grants HL57120, MH45361, HL40881, HL65272, and the Department of Anesthesiology.

0009
Acute Effects Of The 8-OHDPAT (5-HT1A Agonist), The SB 224289 (5-HT1B Antagonist) And The Doi (5-HT2A/2C Agonist) On The Genioglossus Muscular Tone In Rat
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Introduction: The XIIth cranial nerve motoneurons under serotonergic modulation constitute a potential strategic target for pharmacological therapy in Obstructive Sleep Apnea Syndrome (OSAS). From our previous study, no significant increase of the genioglossus electromyogram (GG EMG) was reported after chronic injections of the 8-OHDPAT (5-HT1A agonist), SB224289 (5-HT1B antagonist) and DOI (5-HT 2A/2C agonist)(Besnard,APSS,2004). The objective was to evaluate the time and dose-related effects of central and systemic injections of the same serotonergic drugs on the GG activity in rat.

Methods: The GG EMG was recorded in 35 anaesthetised rats. The tonic activity and phasic (amplitude,surface) respiratory activity were analysed after infra-cerebroventricular (ICVi)(n=20) and intra-peritoneal injections (IPi)(n=15) of 8-OHDPAT, DOI and SB224289 and compared to NaCl injection.

Results: The GG phasic activity was significantly increased after acute ICVi for each drug and maximal with the 8-OHDPAT. The DOI significantly increased the GG tonic activity after both ICVi and IPi. A dose-dependant effect was observed on both tonic and phasic GG EMG respectively with the DOI and the 8-OHDPAT. However the time-related effect remained inferior to 30 minutes with the 8-OHDPAT (ICVi) and is maintained over 50 minutes DOI (ICVi and IPi) whatever the dose used.

Conclusion: The short time-related effects on the GG EMG activity after acute injections explain why no significant increase was reported on chronic experiments. To stimulate the upper airway tone (GG muscle) throughout the sleep period, we suggest the serotonergic drugs might be continuously delivered via a pump or a patch throughout the sleep period.
0010
Ketamine Blocks Respiratory Dysrhythmia And EMG Power Induced By Glutamate Injection Into Pedunculopontine Tegmental Nucleus (PPT) Of Anesthetized Rat
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Introduction: We recently demonstrated modulation of respiratory pattern by glutamate injection into PPT. The aim of this study was to determine whether this effect can be antagonized by a non-competitive NMDA channel blocker ketamine.

Methods: In 4 Sprague-Dawley rats anesthetized with ketamine/xylazine (80/5 mg/kg i.p.), and 4 rats with nembutal (50 mg/kg i.p.) we recorded cortical EEG, genioglossal EMG, and respiratory movements. Three-barrel micropipettes were filled with glutamate (10 mM), ketamine HCl (0.2M) and oil red-O dye. Microinjection of glutamate produced immediate apnea followed by tachypnea. After recovery of the breathing pattern, ketamine was microinjected followed by a glutamate microinjection. Responses were quantified as: total duration of apnea, coefficient of variation for breath duration (CVTT), and total powers for EEG and EMG over 30 s intervals during baseline, and immediately preceding and following each microinjection.

Results: Glutamate injection into PPT induced immediate apnea and increased CVTT 30s after the injection (F > 5.69; p < 0.03), CVTT of baseline and all preinjection intervals were equivalent in N rats and K rats (p > 0.20), as well as glutamate induced apnea duration (p = 0.64) and increased CVTT (p > 0.24). In addition to respiratory changes, glutamate injection also increased total EMG power (t = -3.29; p = 0.05), but did not change the total EEG power (F < 0.58; p > 0.86). Ketamine injected at the same site did not induce apnea, change in respiratory timing variability (F > 0.70; p > 0.19) or genioglossal EMG tone (F = 0.42; p = 0.67), but blocked glutamate induced apnea, increase of CVTT (F > 0.85; p > 0.08), and increase of genioglossal EMG tone (F = 0.002; p = 1).

Conclusion: NMDA receptor mechanisms of PPT are important for glutamate inducing respiratory dysrhythmia and regulation of genioglossal muscle tone.

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0011
Adenosine Levels In The Basal Forebrain Do Not Increase With Waking In Rats With LH Lesions
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Introduction: The lateral hypothalamus (LH) has been implicated in wakefulness. One possibility is that it induces wakefulness by driving the basal forebrain (BF) wake-active neurons (Gerashchenko and Shiromani, 2004). The activity of the BF wake-active neurons is hypothesized to release the sleep-inducing factor adenosine (AD) which begins to accumulate as wakefulness progresses. The AD is then hypothesized to inhibit the wake-active neurons (Strecker et al., 2000) and their silence allows the VLPO and median preoptic GABAergic sleep-active neurons to fire and sleep ensues. Here we measure AD levels in the BF and test the LH-BF circuit in Sprague-Dawley rats with lesions of the LH induced by hypocretin-2-saporin.

Methods: 64 days after lesions the rats were implanted with sleep-recording electrodes and a guide cannula into the basal forebrain. Two weeks later, the rats were kept awake (gentle handling) for six hours (ZT 3-9) and microdialysis samples (5ul) were collected hourly for 9 hours (24h after probe stabilization). AD levels were assessed using HPLC (see (Murillo-Rodriguez et al., 2004) for details).

Results: Hypocretin-saporin ablated 95% of the hypocretin neurons with a resultant decline in CSF levels (~75% versus control). AD levels increased with 6h waking in saline control rats (n=9), consistent with previous studies in cats (Strecker et al., 2000) and rats (Murillo-Rodriguez et al., 2004). However, in rats with LH lesions (n=5) such an increase with waking did not occur. The homeostatic response to sleep loss was measured by conducting a rodent version of an MSLT where the rats were kept awake for 20min and then allowed 20min to sleep. This protocol was started at ZT2 and continued until lights turned off. The lesioned rats were found to have more sleep during the 20min sleep periods indicating a higher sleep drive in these rats.


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0012
Effect Of An Extracranially Administered Neurotensin Analog On Wakefulness
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Introduction: Neurotensin (NT) is a 13 amino acid peptide found in brain and gut, and may play a role in modulating circadian pacemaker function. Reductions in NT and other suprachiasmatic nucleus peptides may contribute to vascular morbidity risk, particularly morning clustering of cardiovascular events. NT injected intraventricularly has an awakening effect. When injected into basal forebrain, NT produces dose-dependent decreases in slow wave sleep, while increasing wake and paradoxical sleep. NT, because it is rapidly degraded by peptidases, cannot be given extracranially. Our group has developed a series of peptidase-resistant NT analogs that penetrate into brain when given extracranially. Following intraperitoneal injection of one of these analogs, animals exhibit inactivity and ptosis for several minutes. These findings may be explained by transiently decreased muscle tone, but have also been attributed to possible sedation. Therefore we sought to clarify the mechanism behind these observations.

Methods: We implanted two rats with electrodes in the right amygdala. Both animals were injected intraperitoneally with a brain-penetrating neurotensin analog called NT69L at a dose of 2 mg/kg. Testing was done during the light cycle. Animals were observed for the typical behavioral effects of NT69L while simultaneously monitored electroencephalographically pre- and post injection.

Results: As expected, the rats appeared sedated based on ptosis and activity for approximately 30 minutes. EEG frequency and amplitude did not change significantly following injection of NT69L. During the period of apparent sedation, the animals did not exhibit slow waves, spindles or other EEG markers of sleep.

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Conclusion: These results confirm our impression that behavioral effects of a neurotensin analog in animal models of psychosis and addiction are not due to sedation. Further study is needed as to whether the effects of a neurotensin analog on sleep and wakefulness measures may be clinically useful.

0013
Exploratory Behavior, Gene Expression, And EEG Slow-Waves: How Waking Activities Affects Sleep Homeostasis
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Introduction: It is not known why sleep slow-wave activity (SWA) increases with time spent awake. According to a recent hypothesis (Tononi and Cirelli, 2003) the increase in SWA occurs because during wakefulness cortical circuits undergo synaptic potentiation. The hypothesis predicts that waking associated with more exploratory behavior should increase molecular markers of synaptic potentiation and be followed by increased SWA. Here we sought to modulate waking exploratory behavior by changing lighting conditions.

Methods: Male WKY rats implanted with EEG electrodes were recorded under 4 conditions: LD baseline (12:12, lights on at 10am); DD baseline (lights stay off at 10am); LD sleep deprivation (SD, 6 hours starting at 10am); DD-SD (also at 10am). Sleep stages were scored visually and power spectra calculated for 4-s epochs. Behavior was scored for 3-s epochs based on real-time video recordings. mRNA levels of plasticity-related genes Arc, NGFI-A and Homer were measured in the cerebral cortex using qPCR after 8-hour sleep, SD-LD, and SD-DD.

Results: Sleep duration and continuity during baseline did not differ between LD and DD. SD was equally effective in LD and DD, and produced a similar increase in sleep duration. However, rats exhibited more exploratory behavior during SD-DD than SD-LD (68.6±1.3 vs 58.5±2.2, % of recording time, p<0.05, n=4). Cortical levels of all transcripts increased more in SD-DD than in SD-LD (% increase relative to 8-hour sleep; Arc, 1278.0±109.3 vs 901.9±97.1; NGFI-A, 196.5±24.8 vs 111.3±11.5; Homer, 237.3±53.4 vs 55.0±11.0, n=5 rats/group). Also, the initial SWA response was larger after SD-DD than after SD-LD (209.6±10.1 vs 174.1±10.4, first 1-h interval after SD, % of baseline, p<0.01, n=8). Finally, exploratory behavior during SD was positively correlated with SWA increase after SD (r=0.86, p<0.05).

Conclusion: Wakefulness with more exploratory behavior is associated with more pronounced upregulation of genetic markers of synaptic potentiation and larger SWA increases during subsequent sleep.

SSMBS and NIMH

0014
Modeling Synaptic Homeostasis In Wakefulness And Sleep
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Introduction: We have hypothesized that plastic changes during wakefulness result in a net increase in synaptic weight in cortical circuits; that increased synaptic strength is reflected in increased slow wave activity (SWA) during sleep; that slow waves themselves produce synaptic downscaling (a proportional decrease in synaptic strength); and that this process guarantees the homeostasis of synaptic weight and improves performance (Tononi and Cirelli, 2003). Here we use a computer model to validate this hypothesis.

Methods: We have employed a simplified version of a large-scale thalamocortical model that can transition between a waking and a sleep state (Hill and Tononi, 2004). Learning during waking was implemented by a Hebbian mechanism gated by neuromodulatory feedback. In the sleep mode, model neurons exhibited slow oscillations mediated by intrinsic currents and synchronized by corticocortical interactions. Slow oscillations triggered synaptic downscaling according to two mechanisms: 1. presynaptic firing followed by post-synaptic hyperpolarization, or 2. presynaptic depolarization followed by post-synaptic hyperpolarization.

Results: In the waking mode, the model learned to adapt to a visuomotor shift (as in a human visuomotor learning task, Ghilardi et al., 2000; Huber et al., 2004). Learning resulted in potentiation of a large subset of synapses mediating the visuomotor shift. In the sleep mode, the intracellular slow oscillation exhibited increased amplitude and synchronization, reflected in an increased local field potential (SWA). The slow oscillations downscaled all synapses uniformly at an exponential rate, resulting in reduced SWA. Downscaling was self-limiting, stopping when the amplitude of the intracellular slow oscillation reached a low level. The results of downscaling were similar irrespective of the downscaling method used. Due to an increased signal-to-noise ratio, performance increased further after downscaling.

Conclusion: The model demonstrates how synaptic downscaling mediates the slow sleep oscillation can maintain synaptic homeostasis after learning while improving performance.

SSMBS, NINDS and NIMH
Influence Of Tetrodotoxin (TTX) Inactivation Of The Central Nucleus Of The Amygdala (CNA) On Sleep And Arousal

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Introduction: Lesion studies have implicated the amygdala in regulating sleep and arousal. However, there is minimal information on the effects of lesions specific to CNA, a region linked to the control of rapid eye movement sleep (REM) and arousal. We produced temporary lesions of CNA with TTX, a sodium channel blocker that inactivates neurons and tracts and thought to produce outcomes similar to those of electrolytic lesions, and examined their effects on sleep and behavior in an open field (OF), a putatively arousing environment.

Methods: Wistar rats (n=9) were implanted with electrodes for recording cortical EEG and with guide cannulae aimed into CNA. Sleep was recorded to ascertain baseline levels, and for 22 h (10 h light, 12 h dark) following microinjections of TTX (5.0 ng/0.2 µl given unilaterally (TTXUH) or bilaterally (TTXBH), and 2.5 ng/0.1 µl given bilaterally (TTXBL)) or saline (SAL) on separate days. Activity during 1 h in an OF was recorded after microinjections of TTXBH or SAL.

Results: Compared to SAL, all TTX microinjections significantly shortened REM latency, but did not alter total NREM during either light or dark periods. During the light period, TTXBH significantly reduced total REM and REM episode number, and TTXBL decreased REM episode number. All TTX microinjections increased slow wave activity (0.5-4 Hz, SWA) in cortical EEG during wakefulness, NREM and REM. Activity in OF was decreased after TTXBH compared to SAL.

Conclusion: Functional lesions of CNA decreased REM and reduced arousal as indicated by shortened NREM latency and decreased activity in an arousing environment. These findings suggest that the amygdala plays a broad role in modulating spontaneous sleep and wakefulness, and in modulating responsiveness in arousing situations.

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Rat Strain Differences In Freezing And Sleep Alterations Associated With Contextual Fear

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Introduction: The level of stress-induced behavioral anxiety exhibited in wakefulness is related to subsequent reductions in REM in many rat and mouse strains. However, we recently found that Fischer 344 rats (F344), a strain with high behavioral anxiety, displayed greater increases in REM after exposure to mild stressors (e.g., open field) compared to other strains (e.g., Lewis [LEW] and Wistar [WST]). In this study, we examined behavioral anxiety (indicated by freezing) and sleep in these strains in context fear, a paradigm with putatively greater stress that produces significant reductions in REM in rats and mice.

Methods: 7-8 rats of each strain were studied. Sleep was recorded during baseline and for 20 h (8 h light, 12 h in dark period) after 30 min in a novel enclosure (control), after two 30 min training sessions (ST1 and ST2) with 15 footshocks (0.5 s, 0.2 mA) and after 30 min in the fearful context (FC) alone. Percentage time freezing (FT%) during ST and FC was calculated.

Results: During ST2 and FC, F344 and LEW displayed significantly greater FT% than did WST. Light period REM after ST1, ST2 and FC was reduced in LEW and WST compared to baseline and control, whereas F344 showed no significant changes. Dark period REM in F344 and WST was increased compared to baseline, but not in LEW. WST had decreased light period NREM after ST2 and FC, and LEW and WST displayed increased dark period NREM after ST1, ST2 and FC relative to baseline.

Conclusion: F344 exhibited equivalent anxiety to LEW and greater anxiety than WST, yet showed less reduction in REM after ST and FC. This difference compared to many rat and mouse strains may be related to the high expression of prolactin in response to stress in F344.

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Influence Of Avoidance Training (AT) And AT Cues On Sleep In C57BL/6J (B6) And BALB/cJ (C) Mice

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Introduction: AT is a sodium channel blocker that temporarily inactivates neurons and tracts in a manner thought functionally similar to the damage produced by electrolytic lesions. TTX inactivation of CNA significantly reduces REM, shortens sleep latency and increases EEG delta power in rats during the light period. TTX inactivation of CNA also reduces activity in the open field. These findings suggest that the amygdala modulates arousal in a variety of situations. To further test this hypothesis, we examined the effects of TTX inactivation of CNA on sleep and activity during the dark period when rats show higher spontaneous arousal and less sleep.

Methods: EEG and activity were recorded via telemetry in Wistar rats (n=8). Bilateral microinjections of TTX (L: 2.5 ng/0.1 µl; H: 5.0 ng/0.2 µl) or SAL (saline, 0.2 µl) were administered before lights off followed by recording throughout the 12 h dark period. Microinjections were given at 5-day intervals and were counterbalanced across condition.

Results: TTX significantly shortened sleep latency (SAL: 42.9±12.1; L: 15.9±3.6, p < 0.01; H: 22.3±15.6, p < 0.05), increased NREM (SAL: 189.4±14.0; L: 222.5±16.7, p < 0.006; H: 222.9±10.3, p < 0.03), decreased REM (SAL: 33.8±2.3; L: 20.1±2.6, p < 0.01; H: 22.6±2.3, p < 0.04) and decreased activity (SAL: 1403±109; L: 1072±967, p < 0.02; H: 1084±1211, p < 0.04). Compared to SAL, TTX increased NREM episode duration (L: p < 0.001; H: p < 0.007) and decreased REM episode duration (L: p < 0.02; H: p < 0.05) and number of episodes (L: p < 0.05; H: p < 0.04).

Conclusion: TTX inactivation of CNA before lights off decreased REM and reduced arousal, as indicated by decreased activity and increased NREM. Understanding the ways in which the amygdala modulates arousal may provide insight into the mechanisms underlying altered sleep in mood and anxiety disorders.

Supported by NIH grant MH64827

Influence Of Avoidance Training (AT) And AT Cues On Sleep In C57BL/6J (B6) And BALB/cJ (C) Mice

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Introduction: A number of investigators have demonstrated that shuttle-box AT is followed by an increase in REM in rats. To our knowledge, this increase has not been demonstrated in mice, and no one has examined the effects of AT cues on sleep. In this study, we examined sleep after AT and AT cues in two mouse strains that differ in behavioral anxiety (C > B6).

Methods: Mice were implanted for recording sleep via telemetry and allowed to recover. The mice then received AT in a shuttlebox (15 tone-
GABA release from amygdalar (FC: 4.93±1.29; NC: 0.67±0.43, 0.001) and 4 h after presentation. To assess GABA release, slices were labeled with [14C]GABA and 14C-GABA release did not significantly differ between FC and NC at 4 h after presentation. Basal 14C-GABA release did not differ between groups in any brain region at either time (p>0.05).

Conclusion: Enhanced evoked 14C-GABA release from slices suggests that FC changed the responsiveness of GABAergic neurons. The time course of altered evoked release was similar to that characterizing sleep alterations produced by FC, suggesting a role for GABA in these regions in regulating arousal in conditioned fear.

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0021
Hippocampal-Dependent Memory In A Rat Model Of Obstructive Sleep Apnea
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Introduction: Obstructive sleep apnea (OSA) is primarily characterized by intermittent hypoxia (IH) and sleep fragmentation (interruption; SI). Chronic IH has been reported to induce apoptosis in the CA1 region of the hippocampus and impair water maze (WM) performance in rats. The effects of SI on hippocampal function have not been fully tested. Total sleep deprivation and REM deprivation can impair WM performance in rodents. We have recently shown that SI can impair hippocampal LTP. The present study seeks to compare the effects of acute exposures of IH and SI on WM performance in rats.

Methods: Treadmills were used to induce locomotor activity for 30s every 2 min throughout a 24h period, thereby fragmenting sleep. Exercise control animals were on a schedule that allowed consolidated sleep yet controlled for exercise; cage controls lived on a non-moving treadmill. Separate groups of rats were exposed to IH by cycling environmental oxygen levels between 6% and 19%. Control animals had room air cycled through their cages. Immediately after 1d exposure to IH, or SI, rats were trained to find a submerged platform in the WM task for 8 trials. This massed trials acquisition protocol for the WM allowed us to fully train the rats to find the platform in ~20min, followed by a 24h undisrupted recovery period, and finally the assessment of the rats’ retention of the platform location using a probe trial.

Results: Rats exposed to SI showed no differences in acquisition performance but were impaired in the 24h retention of the platform location compared to both exercise controls and cage controls (F2,30=10.05, p<.001; Tukey’s p=.005 and p=.001 respectively). Rats exposed to IH showed no differences in either acquisition or 24h retention performance.

Conclusion: 24h of SI prior to learning a spatial learning task did not alter acquisition of the task, but did impair the memory of the task upon re-test 24 hours later, suggesting that the memory of the platform location was abnormal. The behavioral effects of SI are consistent with those seen with total sleep deprivation (Guan et al., 2001; Gozal et al., 2003), we attribute the established findings (Gozal et al., 2001; Gozal et al., 2003), we attribute the present lack of an IH effect on WM performance to our use of a less sensitive massed trials protocol during the acquisition training. With this WM protocol, we conclude that a single day of SI has a greater effect on spatial memory than does 1d of IH.

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0022
Central Inhibition Of Caspase - 1 Blocks NREM Sleep Enhancement Induced By Peripheral Lipopolysaccharide Administration
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Introduction: Interleukin-1 (IL-1) may mediate NREM sleep enhancement induced by the bacterial antigen lipopolysaccharide (LPS). Mature and biologically active IL-1 is cleaved from an inactive prohormone precursor by a pro tease termed caspase-1. This study tested the hypothesis that antagonizing caspase-1 in brain would block NREM sleep enhancement induced by peripheral LPS administration. To this purpose, freely behaving rats were pretreated intracerebroventricularly (ICV) with either the caspase-1 inhibitor YVAD (Ac-Tyr-Val-Ala-Asp chloromethyl ketone; 300 ng) or its vehicle and then administered LPS (250 μg/kg) or its vehicle intraperitoneally (IP).

Methods: Male Sprague-Dawley rats (n = 15), maintained on a 12:12 h light-dark cycle, were instrumented for standard polygraphic determination of sleep-wake activity. YVAD was dissolved in pyrogen-free saline (PFS) and administered 45 min before dark onset. LPS was dissolved in PFS and administered 15 min before dark onset. Animals were subjected to the following treatments: 1) vehicle (VEH) ICV + VEH IP, 2) YVAD ICV + VEH IP, 3) VEH ICV + LPS IP, 4) YVAD ICV + LPS IP. Experimental treatments were randomly scheduled and were made at least 4 days apart.

Results: The amount of time spent in NREM sleep during the 12-h postinjection dark period was 24.5 ± 0.9% (mean ± sem of recording time) during control conditions (VEH ICV + VEH IP) and 23.7 ± 1.4% when animals received YVAD ICV + VEH IP. NREM sleep increased to 35.11 ± 2.0% after VEH ICV + LPS IP. When animals received YVAD ICV + VEH IP, NREM sleep increased to 45.8 ± 2.5% after YVAD ICV + LPS IP. NREM sleep increased to 45.8 ± 2.5% after YVAD ICV + LPS IP.

Conclusion: These results indicate that interfering in brain with the cleavage of mature IL-1 from its inactive precursor completely abolishes NREM sleep enhancement induced by the peripheral administration of the gram negative bacterial cell wall component LPS. These data suggest interfering with posttranslational processing of cytokines may be of functional relevance for targeting systems in brain that are responsible for alterations in sleep during immune challenge.

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0023
Circadian Motor Behavior Of The Rat After Chronic Treatment With A Selective D3 Or A D2/D3 Antagonist
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Introduction: Although the pathophysiology of RLS still is unclear, the efficacy of levodopa and dopamine D2/D3-receptor agonists (e.g. ropinirole) on the sensory and motor symptoms of RLS implicate the dopaminergic system. The development of an animal model for RLS will aid understanding of the pathophysiological mechanisms of this disorder. We investigated whether symptoms frequently seen in RLS can be observed in rodents, following the administration of a selective dopamine D3 or mixed D2/D3 receptor antagonist.

Methods: Male Wistar rats were randomized to receive daily oral treatment with the selective dopamine D3 receptor-antagonist SB277011-A (SB-27: 3 mg/kg) (n=9), the dopamine D2/D3 receptor-antagonist sulpiride (SUL: 200 mg/kg) (n=9) or placebo (n=9) for 5 weeks. Animals were subjected to a 12:12-hour light-dark (L/D) cycle. Polysomnography and motor activity assessments were performed at baseline and at the end of the treatment phase.

Results: Animals treated with SB27 showed an increase in sleep latency (baseline: 15±6 min; SB27: 34±5 min, p=0.01; placebo: 28±4 min, n.s.; VEH: 24±4 min, n.s.). The SB27 and placebo groups showed more sleep fragmentation compared with baseline than the SUL group, with increased non-REM episode counts (baseline: 14±4; SB27: 17±8, p=0.02; placebo 16±5; p=0.12; SUL: 14±6; p=0.90) and decreased non-REM episode duration (baseline: 25±15 s; SB27: 17±11 s, p<0.01; placebo: 19±12 s, p=0.02; SUL: 22±27 s, p=0.39). In the first 4 hours after treatment, non-REM was reduced in the SB27 group (46±4%) compared with baseline (73±3%; p=0.01), but not in the other groups. The total distance travelled during the 12-hour dark phase (baseline: 954±170 m; SB27: 1728±446 m; p=0.06; SUL: 1149±383 m; p=0.61) and entire 12:12-hour L/D assessment period (baseline: 1380±185 m; SB27: 2222±453 m, p=0.05; SUL: 1715±399 m; p=0.42) was significantly increased in the SB27 group compared with baseline. No significant differences between groups were observed during the light phase.

Conclusion: Selective dopamine D3-receptor antagonism, in contrast to combined D2/D3-antagonism, lead to increased locomotor activity, a possible correlate to an urge to move, and to sleep disturbance. Although these symptoms mirror those seen in human RLS, further studies are required to validate the role of periodic limb movements during sleep in this pharmacologically induced model.

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0024
Susceptibility To Intermittent Hypoxia (IH) Induced Spatial Learning Deficits Is Not Dependent On The Circadian Phase Of Exposure
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Introduction: Exposure to IH, such as occurs in sleep disordered breathing (SDB), is associated with neurobehavioral impairments in the rodent. However, previous studies have focused on exposure to IH during the light phase of the rodent circadian cycle in order to replicate the type of hypoxia encountered in patients with SDB. The present study was designed to compare the effects of exposure to IH during the active dark cycles and the resting light cycles of the rat.

Methods: 36 male Sprague-Dawley rats were exposed to Room Air (RA, n=12) or 14 days of IH exposure (oscillating between 21% and 10% O2 every 90 seconds) either during the light phase (IH-Light) or during the dark phase (IH-Dark). Behavioral testing consisted of a standard place-training reference memory task in the water maze, in which rats were trained to locate a hidden, submerged platform using only distal, spatial cues.

Results: ANOVA revealed that IH-Light and IH-Dark rats were impaired with respect to control animals on task acquisition and retention, as both IH-Light and IH-Dark rats required significantly longer times (latency) and distances (pathlength) to locate the hidden platform. Furthermore, IH-exposed rats showed poorer performance on a probe trial administered at the end of training to assess spatial bias. Post-hoc analyses revealed that the IH-Light and IH-Dark groups were equally impaired. No significant differences were found between groups in regards to swim speeds or on a cued task, indicat-
ing that group differences were not due to sensorimotor impairments.  

**Conclusion:** Exposures to IH during either the light or dark phases of the rat circadian cycle produce similar levels of neurobehavioral impairment, suggesting that IH exposure exerts similar effects on brain function irrespective of the time of day that it occurs.

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0025

**REM Sleep Induction By Antagonism Of GABAa Receptors In The Pontine Reticular Formation Of The Rat Is Blocked By Atropine**

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**Introduction:** Antagonism of GABAa receptors in the nucleus pontis oralis (PnO) results in a long-lasting increase in REM sleep in the rat and a short-lasting, triggering of REM sleep in the cat. The long-lasting effect in rat may result from secondary influences on other neurotransmitter systems known to have long-lasting effects. Here, we test the hypothesis that inhibiting GABA transmission in PnO increases REM sleep through increases in acetylcholine release.

**Methods:** Under anesthesia, Long-Evans Hooded rats were surgically prepared for chronic sleep recording and additionally implanted with guide cannulae aimed at sites in the PnO. After recovery, animals received multiple injections at each site with 60 nl of drug solution within one-half hour before lights-out. Bicuculline methiodide (bic, 1 mM), gabazine (GZ, SR95531, 0.01 and 0.1 mM), carbachol (0.1 and 1 mM), atropine (4 mM) and saline-vehicle injections were administered unilaterally. Following each injection, 24-hour electrographic recordings were obtained.

**Results:** Compared to mean control values, both GABAa receptor antagonists, bic and GZ, produced long-lasting (>8 hr) increases in REM sleep. GZ had a greater potency, which is consistent with its higher affinity for the GABAa receptor. At sites in which the cholinergic agonist, carbachol, and GZ were both effective, pre-injection of the muscarinic antagonist, atropine, completely blocked the REM sleep increase of GZ. Atropine alone did not decrease REM sleep amounts.

**Conclusion:** GABAa receptor mechanisms operate in the pontine reticular formation in the control of REM sleep. In the rat, blockade of GABAa receptors augments REM sleep through action on the cholinergic system. A different mechanism appears to operate in the cat where it has recently been reported that scopolamine does not affect REM sleep induction by bic. This difference may underlie the species-disparity in the duration of effects on REM sleep by inhibition of GABAa transmission.

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0026

**Dorsomedial Pontine Injections Of Bicuculline And Carbachol Elicit Similar REM Sleep-Like Effects In Urethane-Anesthetized Rats**

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**Introduction:** In urethane-anesthetized rats, microinjections of the cholinergic agonist, carbachol, into a discrete region of the dorsomedial pons elicit REM sleep-like episodes that comprise cortical and hippocampal activation, silencing of pontine noradrenergic neurons and a profound suppression of hypoglossal (XII) nerve activity. Similar REM sleep-like effects can be produced by pontine carbachol in chronically instrumented-intact, decerebrate or anesthetized cats. However, carbachol is relatively ineffective in behaving rats; it does not elicit immediate effects, and often increases wakefulness, rather than REM sleep. In contrast, the GABAa receptor antagonist, bicuculline (BIC), effectively triggers REM sleep-like state in both behaving rats and cats. Our goal was to determine whether BIC and carbachol elicit similar REM sleep-like effects in urethane-anesthetized rats and whether they act at overlapping pontine sites.

**Methods:** In 6 urethane-anesthetized, paralyzed, vagotomized and artificially ventilated rats, we recorded the cortical EEG, hippocampal and XII nerve activity, and injected carbachol (10 nl, 10 mM) and subsequently BIC (10 nl, 0.5 mM) at 9 dorsomedial pontine sites.

**Results:** Twenty one REM sleep-related responses were obtained. At most sites (6/9), carbachol and BIC could repeatedly elicit REM sleep-like episodes of similar durations (190 s ± 20(SE) vs. 220 s ± 30), magnitudes of suppression of XII nerve activity (to 20 % ± 4 vs. 23 % ± 4 of control), and patterns of cortical and hippocampal changes. The latencies were shorter for carbachol than for BIC (34 s ± 7 vs. 270 s ± 80, n=6, p<0.05), with a proportionate relationship between the two drugs for injections made at antero-posterior levels -8.3 ÷ -8.7 from Bregma (Paxinos & Watson, 1986).

**Conclusion:** Both carbachol and BIC can trigger REM sleep-like effects in urethane-anesthetized rats from at least partially overlapping pontine sites. Both drugs can act repeatedly, thus allowing for acute studies of the underlying cellular behaviors. The results demonstrate a similarity between pontine mechanisms of REM sleep in rats and cats.

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0027

**The Ventrolateral Preoptic Area And Basal Forebrain Play Opposing Roles In The Descending Modulation Of Sleep-Wake Cyclicity In Infant Rats**

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**Introduction:** Infant rats cycle rapidly between periods of sleep and wakefulness. At two days of age (P2), sleep cycles are characterized by short periods of sleep followed by equal short periods of wakefulness. By P8, however, sleep periods have lengthened disproportionately in relation to wake periods. Recent findings from our laboratory indicate that brain transections caudal, but not rostral, to the preoptic hypothalamus in P8 rats result in rapid sleep-wake cycles that are similar to those typical of P2 rats. The two primary sleep-related areas within the region spared by these transections are the sleep-promoting ventrolateral preoptic area (VLPO) and the primarily wake-promoting basal forebrain (BF). The purpose of the present study was to investigate both the individual and the combined contributions of these two areas to sleep-wake cyclicity.

**Methods:** Bilateral electrolytic lesions of the VLPO or the BF were made in P8-10 rats, as well as combined lesions of both structures (VLPO+BF). To examine the possible contributions of these areas at P2, transections caudal to the preoptic hypothalamus were made and sleep-wake cyclicity was examined. In addition, single-unit neuronal activity was recorded from the preoptic area of spontaneously sleeping rats at P8-10.

**Results:** At P8, selective lesions of the VLPO or BF have differential effects on sleep and wake bout durations, while combined lesions of the VLPO and BF result in rapid cycling similar to that of normal P2 rats as well as P8 rats with transected forebrains. At P2, transections reduce the duration of sleep bouts, suggesting that even at this early point in ontogeny forebrain structures are modulating sleep-wake cyclicity. Preliminary results also indicate that neurons within the neonatal preoptic area exhibit state-dependent discharge patterns.

**Conclusion:** The VLPO and BF appear to have opposing descending modulatory effects on sleep-wake cyclicity during the first postnatal week.

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Periformal Hypothalamic Microinjections Of Antisense Oligodeoxynucleotides Against B3 Subunit Of GABA A Receptor Reduce REM Sleep

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Introduction: We previously reported that microperfusion of the periformal region of the posterior hypothalamus (PF) with the GABA A receptor antagonist, bicuculline, suppresses REM sleep. We also found that the expression of selected GABA A receptor subunits varies in PF with both circadian time and sleep need, suggesting that transcriptional changes involving these receptors play a role in the circadian and/or homeostatic regulation of sleep. The GABA A receptors are pentamers whose properties are determined by their subunit composition. To further investigate the role of transcriptional changes involving PF GABA A receptors in sleep regulation, we used antisense against the β3 subunit. This subunit plays an important role in the assembly and intracellular transport of GABA A receptors; its expression is altered by sleep deprivation, and its mutations in humans are associated with insomnia.

Methods: Five adult, male Sprague-Dawley rats were instrumented for chronic recording of the cortical EEG, hippocampal activity and nuchal EMG, and had a microinjection cannula implanted in PF. Following adaptation to the recording conditions, at ~9:00 am, the rats received 0.5 µl microinjections of anti-β3 subunit, 18-base oligodeoxynucleotide (oligo) (2 mM), or scrambled (SC) oligo (2 mM), or artificial cerebrospinal fluid (csf). The treatments were separated by at least 7 days, with sleep-wake behavior then monitored for 8-9 hrs.

Results: Between 1:00 and 5:00 pm, treatment-related changes in the percentage of slow-wave sleep (SWS) were insignificant; across all subjects and conditions, SWS averaged 48.3% ±1.9 (SE), n=15. In contrast, the percentage of REM sleep was significantly reduced following the β3 antisense oligo injections (10.6% ±1.5) compared to csf (18.9% ±1.9; n=5, p<0.04). This was mainly due to a decrease in the frequency of REM sleep episodes, from 7.3 hr-1 ±0.3 to 5.0 hr-1 ±0.8 (p<0.03). After SC oligo, REM sleep percentage was only slightly reduced, to 15.1% ±1.8.

Conclusion: These data suggest that transcriptional activity in PF that involves the role of transcriptional changes involving PF GABA A receptors in the regulation of sleep. The GABAA receptors are pentamers whose properties are determined by their subunit composition.

Neuropeptide S Projects To Arousal Nuclei

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Introduction: Neuropeptide S (NPS) promotes waking when administered icv. Recent data show that NPS can actively enhance wakefulness even when the physiological demand of sleep is high. Here we have investigated the output of NPS-containing neurons by immunocytochemistry to NPS and by c-fos immunostaining after icv NPS injection.

Methods: Sprague-Dawley rats (n=3) were perfused with 4% paraformaldehyde at 11 am (5 h after light onset) and processed for immunocytochemistry. A group of 3 rats was implanted an icv cannula and with a single injection of NPS (0.1 nmol) was administered. Animals were perfused 45 min after injection and processed for c-fos immunoreactivity (Ab5 Calbiochem, 1:10,000). Double c-fos hypocretin immunoreactivity was also conducted in a group of sections (n=3) using 2123 antibody (1:500). Statistical analysis was carried out using ANOVA.

Results: NPS-containing fibers were observed in the tuberomammillary nucleus, the ventrolateral preoptic area, medial and lateral thalami and in several hypothalamic areas. C-fos immunoreactivity after 0.1 nmol infusion of NPS was confirmed in these areas, as well as the cerebral cortex, amygdala and different brainstem nuclei. This distribution matches that of the NPS receptor. Since hypocretin neurons are important regulators of the stability of the states of vigilance, we determined whether NPS activates hypocretin neurons using double label immunocytochemistry. Thirty percent of hypocretin positive neurons were double labeled with c-fos after NPS injection.

Conclusion: These results indicate that NPS projects to key arousal centers including the hypocretinergic system.

Interleukin-1 (IL-1)-Induced Changes In Sleep And Body Temperature Of IL-6-Deficient Mice

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Introduction: Synthesis and release of proinflammatory cytokines, such as IL-1 and IL-6, increases during immune challenge. IL-1 and IL-6 mediate changes in body temperature during immune challenge, and both cytokines increase NREM sleep. IL-1 and IL-6 may therefore mediate changes in sleep-wake behavior during immune challenge.

Methods: To further elucidate the role of IL-6 as a mediator of immune-induced alterations in body temperature and sleep, we used IL-6 knockout (KO) mice (n=6) and C57BL/6j (B6, Jackson Labs, Bar Harbor, ME) control mice (n=7). Transmitters used to record core body temperature and EEG were surgically implanted under isoflurane anesthesia into the peritenuine and guide cannulae were directed into a lateral ventricle. Mice were held under a 12:12 hour light:dark cycle at a constant temperature of 29°C. Mice were injected ICV with either vehicle (pyrogen-free saline) or 2.5, 5, 10 or 50 ng of murine recombinant IL-1. All injections were given 20 minutes before dark onset. Recordings began at dark onset and continued for 24 hours.

Results: The highest dose of IL-1 (50 ng) increased NREM sleep of IL-6 KO mice by 41.7% relative to control values, whereas NREM sleep of B6 mice increased by 48.5%. IL-6 KO mice did not fever in response to any dose of IL-1, whereas B6 mice developed a fever after the 10 and 50 ng doses (peak magnitudes: 1.45 +/- 0.80 °C; 1.75 +/- 0.91 °C, respectively).

Conclusion: These data corroborate previous studies indicating that IL-6 is necessary for cytokine-induced fever. However, in this study we demonstrated that IL-1-induced enhancement of NREM sleep does not require IL-6.

Temperature Of IL-6-Deficient Mice

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Introduction: Synthesis and release of proinflammatory cytokines, such as IL-1 and IL-6, increases during immune challenge. IL-1 and IL-6 mediate changes in body temperature during immune challenge, and both cytokines increase NREM sleep. IL-1 and IL-6 may therefore mediate changes in sleep-wake behavior during immune challenge.

Methods: To further elucidate the role of IL-6 as a mediator of immune-induced alterations in body temperature and sleep, we used IL-6 knockout (KO) mice (n=6) and C57BL/6j (B6, Jackson Labs, Bar Harbor, ME) control mice (n=7). Transmitters used to record core body temperature and EEG were surgically implanted under isoflurane anesthesia into the peritenuine and guide cannulae were directed into a lateral ventricle. Mice were held under a 12:12 hour light:dark cycle at a constant temperature of 29°C. Mice were injected ICV with either vehicle (pyrogen-free saline) or 2.5, 5, 10 or 50 ng of murine recombinant IL-1. All injections were given 20 minutes before dark onset. Recordings began at dark onset and continued for 24 hours.

Results: The highest dose of IL-1 (50 ng) increased NREM sleep of IL-6 KO mice by 41.7% relative to control values, whereas NREM sleep of B6 mice increased by 48.5%. IL-6 KO mice did not fever in response to any dose of IL-1, whereas B6 mice developed a fever after the 10 and 50 ng doses (peak magnitudes: 1.45 +/- 0.80 °C; 1.75 +/- 0.91 °C, respectively).

Conclusion: These data corroborate previous studies indicating that IL-6 is necessary for cytokine-induced fever. However, in this study we demonstrated that IL-1-induced enhancement of NREM sleep does not require IL-6.
0031 Characterization Of The MCH Neurons Activated After REM Sleep Rebound
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Introduction: The tuberal hypothalamus is usually seen as responsible
for the promotion of wakefulness via two neuronal populations, the
hypocretins (orexins) and histaminergic neurons. Recently, Verret et al.
(2003) showed that it contains a third neuronal population involved in
the regulation of vigilance states, namely the melanin concentrating hormone
(MCH) neurons. These neurons are intermingled but distinct from the
hypocretin cells and play an opposite role. Indeed, hypocretins promote
waking while MCH induces an increase in REM sleep (Verret et al.,
2003). Approximately 60% of the MCH neurons co-express cocaine and
amphetamine regulated transcript (CART). This subgroup send ascending
projections to the septum while the non-CART MCH neurons send
descending projections to the spinal cord (Brichoux et al., 2002). Verret et
al. (2003) found that 58% of the MCH cells are activated after REM sleep
rebound. To better characterize these REM activated MCH neurons, it is
of interest to determine whether they do express CART and therefore send
ascending projections, whether they do not express CART and send
descending projections or they are a mix of both subgroups.

Methods: For this purpose, we undertook a triple immunohistochemical
labeling Fos/MCH/CART in rats REM sleep deprived for 72hr and rats
allowed for a consecutive 2h30 REM sleep rebound. Fos was revealed
using DAB. MCH and CART were labeled by immunofluorescence.

Results: Our preliminary results confirmed our previous data showing
that a large number of Fos labeled neurons are present in the tuberal hypo-
thalamus after REM sleep rebound. A majority of MCH neurons are Fos
immunoreactive after REM sleep rebound. A large proportion of the
MCH neurons co-express CART. In addition, we did not find
MCH/CART/Fos neurons after REM sleep deprivation.

Conclusion: Our preliminary results are in agreement with ours and oth-
ers previous data. This study will allow us to better characterize the REM
activated MCH neurons.

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University of Lyon.

0032 Transgenic Mice Reveal A Network Of Pontine GABAergic Neurons
Regulating REM Sleep
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Introduction: The VLPO and the median preoptic area (mPOA) contain
neurons that are active in NREM sleep. These neurons are hypothesized
to interact with hypothalamic wake-active neurons to generate NREM
sleep and waking. However, the neurons generating REM sleep are local-
ized in the pons. How the hypothalamic neurons interact with REM sleep-
on neurons is not known. One possibility is that such an interaction occurs
via an intermediate group of GABAergic neurons localized in the ventro-
lateral periaqueductal gray (VLPAG) since microinjection of muscimol
(GABA agonist) into this region increases REM sleep (1). Muscimol may
inhibit GABA neurons at the injection site, thus releasing inhibitory input
to the mesopontine REM sleep-on neurons. Identification of the GABA
pons neurons has been difficult because of limitations of the GABA
antibody. An alternative strategy is to utilize transgenic mice where the
GABA neurons are easily evident.

Methods: Mice homozygous for the TgN(GadGFP)4570HSwn transgene
(2) express enhanced green fluorescent protein (eGFP) under the control
of the mouse Gad1 promoter. The retrograde tracer Fluorogold was used
to determine projections from the VLPO and the lateral hypothalamus.

Results: A discrete cluster of eGFP neurons in the VLPAG between 4.9
mm and 5.2 mm posterior to Bregma was clearly evident (Mouse Brain
atlas; Franklin and Paxinos, 1997). This cluster is dense in the VLPAG,
and becomes sparse as it extends laterally into the lateral parabrachial
nucleus. We determined that these neurons are not catecholaminergic,
cholinergic or contain parvalbumin. Using Fluorogold we identified many
retrogradely labeled neurons in the VLPO and surrounding preoptic area.
Some retrogradely labeled neurons were also found in the lateral hypo-
thalamus and other brain areas implicated in wake regulation. We are cur-
cently using c-Fos as a marker of neuronal activity to determine when
these neurons are active.

Conclusion: We suggest that GABAergic control of neurons in the
VLPAG by the hypothalamus could be a potential mechanism of REM
sleep regulation. Input from the hypocretin neurons onto VLPAG GABA
neurons would be excitatory and inhibit REM sleep; lack of hypocretin
would facilitate REM sleep. On the other hand, VLPO GABA input to
these neurons during non-REM sleep would inhibit them and permit the
REM sleep-on neurons to become active. 1. Oliva A et al.,J. Neurosci.,

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0033 Nitric Oxide-A1 Adenosine Receptor Interactions And
Lipopolysaccharide Induced Alterations In Sleep
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Introduction: Lipopolysaccharide (LPS) promotes slow wave sleep and
reduces rapid eye movement sleep and also induces expression of the tran-
scription factor NF-kB. NF-kB regulates several sleep-modulatory sub-
stances, including the A1 adenosine receptor (A1AR) and nitric oxide (NO).
We evaluated relationships among LPS, NO, and A1ARs in vitro using rat
pheochromocytoma (PC12) cells and in vivo using LPS-treated mice.

Methods: In vitro studies: PC12 cells were treated with the NO donor
SNAP (20uM), LPS (3 ug/ml), NF-kB inhibitors (adenoviral vector con-
taining the mutant form of IkB-a or pyrrolidine dithiocarbamate), and/or
SNAP (20uM), LPS (3 ug/ml), NF-kB inhibitors (adenoviral vector con-
taining the mutant form of IkB-a or pyrrolidine dithiocarbamate), and/or
the NO synthase inhibitor L-NAME (1mM), and were analyzed for A1AR
binding both

Results: SNAP increased A1AR binding in PC12 cells,
and in vivo. Blockade of this induction by L-
NAME suggests an interaction between NOergic and adenosinergic sleep
regulatory systems. The altered sleep that occurs in LPS-treated mice may
reflect altered NO-A1AR interactions, possibly mediated via NF-kB.

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Apnea Suppression By Ondansetron And Fluoxetine Alone And Combined

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Introduction: SSRIs have been tested in patients with sleep apnea syndrome, but the results have been disappointing. Conversely, we showed that 5-HT3 antagonists could reduce apnea index (AI) by 50% in an animal model of sleep-disordered breathing. Here, we demonstrate the independent and combined effects of ondansetron and fluoxetine on apnea expression in rats.

Methods: 6 Sprague-Dawley rats were instrumented for cortical EEG and nuchal EMG recording. Sleep and breathing (by plethysmography) were recorded from 10AM - 4PM. After an initial baseline recording, each animal was recorded after i.p. injection of: 1) saline (S), and 2) ondansetron (O; 1 mg/kg), with these recordings separated by 3 days and conducted in random order. Subsequently, each animal was injected daily with fluoxetine (F; 1 mg/kg) and again recorded on the 13th day of injection. On the 14th day, ondansetron and fluoxetine were co-injected (O; 1 mg/kg for each). Sleep and breathing were analyzed by computer algorithms and apneas were scored as breaths longer than 2.5 s. These events represented at least 2 missed breaths, corresponding to 10 s apneas in man.

Results: Average AI during NREM+REM sleep of baseline recordings was 11.4±4.55 (SD) per hour. AI ratio (AI as a fraction of the baseline value) was (mean±SE), for S: 0.98±.19, p = NS (vs baseline); F: 0.93±.26, p = NS; O: 0.53±.13, p = 0.007; O+F: 0.12±.04, p = 0.0001. AI ratio was significantly impacted by treatment (p < 0.004 by ANOVA). Neither saline nor fluoxetine altered apnea expression. In contrast, ondansetron reduced AI by 47% and this effect was potentiated by daily fluoxetine, yielding an 88% reduction.

Conclusion: We conclude that fluoxetine has no consistent effect on apnea expression in rats (as in man), but can significantly potentiate apnea suppression produced by a serotonin antagonist. These findings may have implications for pharmacological treatments of sleep apnea syndrome.

GABA Release In The Orexinergic Perifornical Hypothalamus Is Highest During nonREM Sleep

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Introduction: To investigate the role of GABA in the control of REM sleep, we sampled and measured extracellular levels of GABA from the orexinergic neuron-rich perifornical region of the lateral hypothalamus (LH) during spontaneous sleep-W in freely behaving cats.

Methods: Under standard surgical procedures, male adult cats were implanted with sleep recording electrodes (including PGO electrodes) and microdialysis guides targeted towards the LH. The probes were inserted after post-surgical recovery and habituation. Following 12 hr of post-insertion recovery, behavioral state recording along with artificial CSF (ACSF) perfusion (8 µl/min) and sample collection was begun. At least 2 samples of 6 min each were manually collected during each behavioral state: W, nonREM and REM sleep. Following 2 to 3 days of sample collections for GABA release across spontaneous sleep-W, behavioral states and GABA release were monitored during microdialysis perfusion of GABA uptake blocker nipeotic acid (0.5 mM). The samples were stored in ice until analyzed by HPLC on the same day. GABA assay was carried out using electrochemical detector and standard precolumn derivatization protocol: 5 µl of derivatization mixture (3.7 mM o-phenaldehyde and 22 mM 2-methyl-2-propanethiol in 0.01 M borate buffer, pH 9.5) was mixed with 5 µl of sample and reacted (2 min at room temperature) before injecting in the HPLC. Using the protocol described above, we were able to achieve a sensitivity of 0.04 pmol/sample.

Results: Initial experiments in 4 cats suggest that GABA release in the LH was highest during nonREM (p<0.01, Friedman ANOVA) followed by REM sleep. The lowest levels were observed during W.

Conclusion: These data suggests that GABAergic mechanisms are involved in regulating orexinergic tone during sleep-W.

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GABA Levels Are Increased In The Pontine Reticular Nucleus, Oral Part (PnO) Of Anesthetized Rat By Dialysis Administration Of Hypocretin-1 (Orexin A)

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Introduction: The majority of drugs used clinically to produce sleep, sedation, and anesthesia enhance GABAergic neurotransmission. The effects of GABA on arousal state, however, are site specific within the brain. In cat rostral pontine reticular formation, GABA promotes wakefulness and suppresses sleep (J Neurophysiol 82:2015, 1999). The PnO is the rostral portion of rat pontine reticular formation. The PnO receives input from arousal-promoting hypocretinergic neurons (J Neurosci 18:9996-10015, 1998) and contains hypocretin receptors (Mol Brain Res 88:176-182, 2001). The interaction between hypocretin-1 and GABA in the PnO has not previously been investigated. This study is testing the hypothesis that dialysis administration of hypocretin-1 to the PnO increases PnO GABA levels.

Methods: Adult male Sprague-Dawley rats are anesthetized with halothane and a dialysis probe is aimed unilaterally for the PnO. Dialysis samples (n=6/dialysis condition) are collected every 7 min during sequential perfusion of the probe (2 µL/min) with Ringer’s (vehicle control), hypocretin-1 (1, 3, 10, 30, or 100 µM), and Ringer’s. HPLC with electrochemical detection is utilized to quantify GABA. One-way ANOVA and Tukey-Kramer multiple comparisons test are used to evaluate the effect of hypocretin-1 on GABA levels. Only data from dialysis sites histologically localized to the PnO are included in the statistical analyses.

Results: Hypocretin-1 caused a concentration-dependent increase in PnO GABA levels (F(5, 155)=54.66; p<0.0001). The lowest effective concentration of hypocretin-1 (10 µM) produced a 56% increase in GABA levels (p<0.01). The maximal increase in GABA (184%) was caused by 100 µM hypocretin-1. GABA returned to control levels during dialysis with Ringer’s following hypocretin-1.

Conclusion: The data support the interpretation that hypocretin receptors in the PnO stimulate GABA release. The results suggest that one mechanism by which hypocretin-1 promotes arousal is by increasing GABAergic transmission in the PnO.

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Methods: ICV administration into rat of corticotropin-releasing hormone (CRH) increases wakefulness (W) and decreases NREMS in a dose-related fashion. There are several CRH receptor subtypes; CRH binds preferentially to CRHR1. Conversely, ICV administration of alpha-helical CRH (AhCRH), an antagonist with greater affinity for CRHR2 than CRHR1, reduces W and increases NREMS. Moreover, ICV injection of atraxisin, an antagonist with equal affinity for CRHR1 and R2, also reduces W and increase NREMS. Recently, Urocortin II (UcnII), a CRH-related neuropeptide that binds with high selectivity to CRHR2, was identified and characterized.

Methods: To further elucidate the role of CRH receptors in the regulation/modulation of sleep-wake behavior we administered hUcnII ICV into rats at light onset. Male Sprague-Dawley rats (n=8) were surgically implanted under isoflurane anesthesia with EEG electrodes and a thermometer to monitor brain temperature. The animals were maintained on a 12:12 h light:dark cycle at 23 deg C. ICV injections of vehicle (pyrogen-free saline) or 0.01, 0.1 or 1.0 nmol hUcnII were given at light onset. Recordings of the EEG, body movements, and brain temperature began after injections and continued for 24 hours.

Results: All three doses of hUcnII transiently increased W and decreased NREMS. Relative to control values, administration of 0.01, 0.1, and 1.0 nmol hUcnII resulted in a percent increase of W by 12.1%, 21.7%, and 25.0%, respectively. NREMS decreased by 20.9%, 28.8%, and 32.9%, after these same doses. These effects on W and NREMS were apparent during postinjection hours 1-2. REMS increased after these doses of hUcnII by 26.0%, 56.9%, and 56.5%, respectively. However, these increases in REMS were apparent later, during postinjection hours 4-6.

Conclusion: Our results indicate that selective activation of central CRHR2 by hUcnII increases W. The increase in W after hUcnII is similar to that induced by equimolar CRH. Because CRH binds preferentially to CRHR1, these results suggest activation of either CRHR1 or R2 increases W. However, previous studies in which either CRH itself or CRH receptor antagonists were administered ICV did not reveal effects on REMS. These new data indicate that activation of CRHR2 increases REMS. As such, increases in REMS previously reported to occur in rats subjected to stressors may be mediated by CRHR2.

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0038
A Non-Invasive Method Of Increasing Duration Of Rest In Drosophila
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Introduction: Genetic, mechanical and pharmacological manipulations have been shown to alter the duration of rest in the fruit fly, Drosophila melanogaster. We hypothesized that shortening photoperiod would non-invasively prolong sleep duration.

Methods: Locomotion was individually monitored in young adult wild-type flies at 25°C. For 6 weeks, one group of 48 males and 48 virgin females was maintained on a 12:12 LD schedule (control) and another on an 8:16 LD schedule (experimental). Flies were transferred to new food weekly. The data was analyzed qualitatively for daily rest pattern, and quantitatively for mean total rest (defined as 5 min of no activity), and mean daily rest bout length as a measure of rest consolidation for the 1st and 6th weeks.

Results: In both week 1 and week 6, in both genders, an earlier onset of dark led to an earlier onset of rest. In 8:16 LD conditions, total daily rest in females was 25% greater than in 12:12 LD in week 1, and 20% more in week 6; the effect appeared to be less marked in males, with a 14% increase in week 1 and no effect in week 6 (101% of controls). Further, bout length increased during week 1 in both genders (by 6% in females and by 28% in males), and this effect persisted or was even enhanced after 6 weeks of 8:16 LD conditions, with an increase of 98% in females and 42% in males.

Conclusion: Decreasing photoperiod by 33% is an effective and non-invasive method of lengthening the amount and consolidation of daily rest in the fruit fly. The effects appear to be influenced by gender, and at least some effect of the 8:16 LD conditions persists for several weeks.

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0039
Glutamatergic Control Of Upper Airway Motoneurons During Sleep In Rats
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Introduction: One of the hallmarks of sleep is a potent suppression of skeletal muscle activity that occurs in a stereotypical pattern across the sleep cycle. Understanding the physiological processes that regulate motor activity during sleep is important because most of the major sleep disorders are caused by dysregulation of muscle activity. The neurophysiological mechanisms that mediate muscle activity during sleep are unclear. It is hypothesized that muscle activity is suppressed during sleep because motoneurons are passively disfacilitated by sleep-related neurons in the brainstem. While glutamate is the major excitatory neurotransmitter in the brain, its role in mediating motoneuron excitability during sleep is unknown. This study aims to understand the role that glutamate plays in regulating airway motoneuron excitability across the sleep-wake cycle in rats.

Methods: Glutamate was focally microdialysed onto trigeminal motoneurons while masseter muscle activity was monitored in behaving rats. Male, Sprague-Dawley rats (n=6) were implanted with EEG and EMG (masseter and neck muscles) electrodes to record sleep states. Microdialysis probes were implanted in the left trigeminal motor nucleus for dialysis of artificial cerebral spinal fluid (ACSF) or 25mM glutamate.

Results: Application of ACSF onto trigeminal motoneurons had no effect on masseter muscle activity (P=0.91); however, glutamate application caused a significant increase in masseter activity (P=0.01). Compared to baseline conditions, glutamate application increased masseter muscle activity during wakefulness by 176% (P<0.001) and during NREM sleep by 691% (P<0.001). However, glutamate application during REM sleep had no effect on tonic masseter activity (P=0.91).

Conclusion: While glutamate potently facilitated trigeminal motoneuron excitability and hence masseter muscle activity during waking and NREM sleep, its excitatory effects were abolished during REM sleep. These results suggest that the excitatory effects of glutamate are nullified by powerful inhibitory processes (e.g. glycine) during REM sleep.
0040
Hypocretin-Induced Active (REM) Sleep Is Mediated By Hypocretin Receptor-2 In The Nucleus Pontis Oralis Of The Cat
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Introduction: We have recently reported that microinjections of hypocretins (orexins) into the nucleus pontis oralis (NPO) of the chronic cat induce a behavioral state that is identical to naturally occurring active (REM) sleep (Xi et al., 2002). The present study was undertaken to determine which hypocretin receptors mediate the active sleep-inducing effects of hypocretin in the NPO.

Methods: Three adult cats were prepared for monitoring behavioral states and for drug administration in the NPO. Microinjections of hypocretin-1 (0.25 µl, 500 µM), hypocretin-2 (0.25 µl, 500 µM) and SB-334867-A (0.25 µl, 200-500 µM), a hypocretin receptor-1 antagonist, were carried out in combination or separately. Control solutions of saline (0.25 µl) were injected into the same site that received the injection of drugs.

Results: The microinjection of either hypocretin-1 or hypocretin-2 into the NPO elicited active sleep with a short latency and induced a statistically significant increase in the percentage of time spent in this state during the first hour of recording (hypocretin-1: 19.2 ± 3.1%, n=5; hypocretin-2: 20.0 ± 2.2%, n=4; saline: saline: 9.4 ± 2.1%, n=3, P<0.05). When SB-334867-A was injected into the same area of the NPO 20-30 min prior to the injection of hypocretin-1 or hypocretin-2, it did not block the active sleep-inducing effects of hypocretins (SB-334867A+hypocretin-1: 16.1 ± 2.2, n=5; SB-334867-A+hypocretin-2: 18.3 ± 3.2%, n=3; saline+hypocretin-1: 21.3 ± 2.9%, n=3). The injection of SB-334867-A alone also did not induce any significant change in sleep and waking states.

Conclusion: The present data demonstrate that a preinjection of SB-334867-A, a selective hypocretin receptor-1 antagonist, does not block the induction of active sleep by hypocretin-1 or hypocretin-2. Therefore, we suggest that hypocretnergic processes acting on hypocretin receptor-2 in the NPO play a more important role in the control of the generation of active sleep than those mediated by hypocretin receptor-1.

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0041
Behavioural And Neuronal Activation Following Systemic Injection Of The Adenosine A2a Receptor Antagonist MSX-3 In Rats
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Introduction: Adenosine has been implicated as a sleep promoting factor. In addition to acting at A1 receptors, it has been shown to mediate the somnogenic effects of prostaglandin D2 through A2A receptor activation. Perfusion of an A2A receptor agonist at the ventral surface of the brain induces sleep. To further understand the mechanisms of A2A receptor-mediated sleep-wake regulation, we examined the effects of systemic injections of the novel A2A receptor antagonist MSX-3 on sleep-wake states, and concurrent neuronal activation using c-Fos.

Methods: Adult male Sprague-Dawley rats were instrumented for polygraphic recording of sleep-wake states. After a baseline recording, rats were injected with MSX-3 (2.5, 5, or 10 mg/kg IP) or saline at 08.00 or 20.00 (12:12 LD cycle, lights on at 08.00). After 2 h of recording, rats were perfused and brains processed for dual immunostaining for c-Fos and neurotransmitter markers of known arousal-promoting neurons.

Results: MSX-3 injections at 08.00 increased percent wake time, from 37% after saline (and 33-43% at baseline) to 67, 86 and 76% at 2.5, 5 and 10 mg/kg, respectively. In the same animals, MSX-3 increased the percentage of orexin neurons expressing c-Fos from 0.4% after saline to 21% at 5 mg/kg, with smaller increases after 2.5 and 10 mg/kg. Similar increases in c-Fos immunoreactivity were seen in the medial caudate-putamen and in the core of the accumbens nucleus. MSX-3 induced little or no c-Fos expression in cholinergic, aminergic and melanin-concentrating hormone-containing neurons. Following saline injections at 20.00, percent wake time and c-Fos expression were both high, and there were no further increases after MSX-3 injections.

Conclusion: These results indicate that MSX-3 increases wakefulness and c-Fos expression in orexin neurons and selected neurons in the striatum. These neurons probably play a role in mediating behavioural activation induced by A2A receptor antagonism.

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0042
Activation Of C-FOS In Median Preoptic Nucleus GABAergic Neurons Is Related To REM Sleep
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Introduction: The median preoptic nucleus (MnPN) of the hypothalamus is involved in the regulation of sleep and wakefulness. Immunoreactivity (IR) for c-Fos protein in MnPN GABAergic neurons is positively correlated with the amount of preceding sleep. However, it is unclear whether sleep-induced Fos-IR in the MnPN GABAergic cells is related to nonREM or REM sleep. This study was designed to determine whether or not activation of GABAergic neurons in the MnPN is associated with REM sleep.

Methods: Ten male Sprague-Dawley rats, maintained on a 12/12 L:D cycle (lights-on 08:00 h), were assigned to two groups. One group (n=4) was allowed 2-h spontaneous sleep (SS) before perfusion. The other group was REM sleep restricted (awakened after the first 10-15 sec of a REM episode) for 2-h and then divided into two subgroups: animals (n=3) that were perfused immediately after REM sleep restriction (REMSR) and animals (n=3) that were permitted 90 min recovery sleep (REMrec). All experiments were initiated 30 min after lights on. Brain tissue was processed for double immunostaining for c-Fos protein and glutamic acid decarboxylase (GAD).

Results: Sleep states were assessed for the last 90 min of the recording time. REM sleep occupied 8.5±2.1% of this time in REMSR rats, 17.6±1.4% in SS and 24.9±0.8% in REMrec group. The total number of Fos-immunoreactive cells increased as well (51.5±4.2 in REMSR vs 58.3±15.0 in SS vs 83.2±14.8 in REMrec rats). The median preoptic nucleus (MnPN) of the hypothalamus increased as well (13.6±4.2 in REMSR vs 17.8±1.9 in SS vs 45.3±11.1 in REMrec rats). Percent wake time and c-Fos expression were both high, and there were no further increases after MSX-3 injections.

Conclusion: These results suggest that c-fos activation in the MnPN GABAergic neurons is determined by the amount of preceding REM sleep.

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Introduction: Fur seals display both bilateral and asymmetrical (uni-hemispheric) slow wave sleep. Previously in fur seals, EEG asymmetry has only been evaluated visually. In this study, however, we examined the EEG spectra during sleep and waking, and the degree of EEG asymmetry in different frequency ranges.

Methods: Four juvenile (2-3 years old) northern fur seals (Callorhinus ursinus) were implanted with EEG, EMG, and EOG electrodes. In each seal, data was collected over 2 nights while the animals slept on land. EEG spectral power was computed in two symmetrical bipolar cortical recordings in 20-sec epochs in the range of 1.2-4, 4-8, 8-12, and 12-16 Hz. The degree of EEG asymmetry was computed by the asymmetry index (AI=L-R/L+R; spectral power in left and right hemispheres).

Results: EEG spectral power, in the range of 1.2-4 Hz, during SWS was significantly greater than that during waking and REM. Peaks in the range of 11-15 Hz during SWS and in the range of 4.5-6.5 Hz during waking and REM represented sigma and theta activity, respectively. Unlike other animals and humans, fur seals did not display a decreasing trend in slow wave spectral power over the night, which is the main sleep period in this species. The average percentage of epochs with absolute AI ≤0.3 (considered asymmetrical SWS) was 32+13% (n=8) in the range of 1.2-4 Hz, and 22+9%, 30+11%, 35+15% in the ranges of 4-8, 8-12, and 12-16 Hz, respectively. The percentage of epochs with AI > 0.3 in the slow wave and sigma ranges in high voltage SWS was on average 15% and 48% greater than during low voltage sleep.

Conclusion: EEG asymmetry during SWS in fur seals is expressed in the entire range examined (1-16 Hz), with maximal degree in 1.2-4 and 12-16 Hz ranges.

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0044
The Ontogeny Of Spontaneous Sleep-Related Phasic Activity In The Rat
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Introduction: During early infancy in rats (i.e., before P12), state-dependent neocortical EEG is absent, and so sleep is defined by changes in muscle tone and behavior. The developmental relationship among the several classes of phasic activity, including rapid eye movements and myoclonic twitches, is unknown. We hypothesized that a temporal relationship between rapid eye movements and myoclonic twitches would emerge over the first two postnatal weeks.

Methods: Subjects were P3, P8, and P14/15 rats. EMG electrodes were implanted in the medial and lateral recti (i.e., “eye muscles”) and nuchal muscles, and, in P14/15 subjects, electrodes for recording neocortical EEG were implanted. Eye EMG recordings were filtered to capture both gross horizontal eye movements and eye muscle twitches. Neurophysiological recordings of the LDT were also performed.

Results: During the first two postnatal weeks, eye movements became tightly coupled to eye muscle activity. Twitches of the eye muscles, however, always exhibited a strong temporal relationship with both nuchal and limb twitches. This relationship remained constant throughout the emergence of state-dependent EEG. Furthermore, preliminary data from neurophysiological recordings reveal that twitch-on neurons within the LDT are related to both eye and nuchal twitches.

Conclusion: Rapid eye movements are generated by twitches of the eye muscles, and these eye muscle twitches co-occur with nuchal muscle and limb twitches. The relationship between eye, nuchal, and limb twitches remains unchanged throughout the emergence of state-dependent EEG. These results, coupled with the LDT recordings, support the notion that rapid eye movements are the outward manifestation of eye twitches, and are thus just another form of myoclonic twitching. Furthermore, these data indicate that infant sleep is a highly organized state composed of coherent bouts of phasic activity in multiple muscle groups separated by brief periods of quiescence.

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0045
ERP Differences During Conditioned Lick Response In The Rat
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Introduction: Many investigators report increased cortical evoked response potentials (ERPs) during learning and conditioning. However, ERP amplitude is also sleep dependent, being larger during sleep over waking. Close examination of single trial ERPs show a wide range of amplitudes (0-200uV). Additionally, the rat does not always respond appropriately to the stimulus. Thus, individual conditioned ERP trials may depend on the rat’s moment-to-moment behavioral state. Since we expect a correct conditioned lick response to occur during waking, this state should elicit a smaller ERP when compared to an ERP during an incorrect response assuming a ‘micro-sleep’ state.

Methods: We used the conditioned lick response paradigm with a whisker twitch as a conditioned stimulus and water reward as the unconditioned stimulus. EEG signals from the whisker barrel cortex were continuously recorded using a 25 electrode array. We compared ERP amplitudes after stimuli that elicited a correct lick response to those after which the rat did not respond appropriately. All recordings were also scored for sleep state to assure waking conditions.

Results: We found that the ERP amplitude for an incorrect response was 42% greater than the ERP for the correct response (Paired Student’s t-test, p < 0.05). Peristimulus histograms and reaction time showed sufficient progress of the conditioned learning, indicating waking, learning and that the rat was indeed paying attention to the stimuli.

Conclusion: Our data support the view that micro-sleep observed here might be represented by a sleep-like state within individual cortical columns; as measured by the ERP amplitude. Since the sleep ERP is larger than waking, when the animal does not respond, we conclude that the whisker barrel responsible for processing the twitch may be in an inactive or sleep state even though the whole animal is awake.

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0046
A Phylogenetic Analysis Of Sleep Architecture In Birds And Mammals
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Introduction: Early comparative studies of sleep in mammals identified significant correlations between sleep traits and various morphological, physiological, and ecological variables. Such results helped shape early theories on the function of sleep. These studies, however, were conduct-
ed in the absence of a phylogenetic framework, which considers the statistical complications inherent in common ancestry. Thus, it is not clear whether these early studies will be validated by phylogenetically-based statistical techniques.

**Methods:** Following earlier analyses, we gathered data on sleep, (total sleep time, SWS time, REM sleep time), and morphological (adult body and brain mass), physiological (basal metabolic rate, gestation/incubation period), and ecological (habitat, trophic level, and index of predation risk) variables from the primary literature for mammalian (69 species) and avian (22 species) species. Phylogenetic trees were taken from the literature. Data were analyzed using the phylogenetically-explicit techniques of independent contrasts and spatial autocorrelation.

**Results:** Some correlations identified in early comparative studies hold under a phylogenetic analysis. For example, Allison and Cicchetti (1976 Science 194:732-734) found a significant negative relationship between body weight and total sleep time (TST). When we controlled for the effects of phylogeny, this relationship remained significant in mammals (df=30, r=-0.47, p=0.007), but not in birds (df=10, r=-0.11, p=0.734). Contrary to Allison and Cicchetti (1976), our analysis also provides little support for the relationship between REM sleep time and index of predation risk in mammals (df=30, r=-0.26, p=0.151) and birds (df=10, r=-0.16, p=0.620). Similarly, TST was independent of geographic location in both mammals (df=30, r=0.08, p=0.663) and birds (df=10, r=0.09, p=0.781).

**Conclusion:** Our study suggests that several correlates found in early comparative studies hold under our phylogenetic analysis, but others do not. Overall, further consideration of the evolutionary factors that have shaped sleep architecture in vertebrates may be in order.

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**0047**

**Patterns Of Sleep Disturbance In Rats Exposed To Intermittent Hypoxia**

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**Introduction:** Sleep apnea syndromes are characterized by repetitive, transient episodes of hypoxia and sleep disturbance. Exposing rats to intermittent hypoxia (IH) during the rest period is an animal model of sleep apnea. IH has been reported to cause only transient (1-2 days) sleep loss in rats (Gozal et al., J. Neurosci. 21:2442, 2001). In sleep apnea patients, arousals from sleep occur at the termination of apneas, when hypoxemia is most severe. In the present study, we partitioned intermittent IH cycles into hypoxic and normoxic components, to determine if sleep disturbance in rats was more severe and persistent during the hypoxic phase.

**Methods:** Electrophysiological measures of sleep and wake were performed in 8 male, Sprague-Dawley rats during 12 hours of the lights-on phase of a 12/12 light/dark cycle. Following adaptation, a 12 hour baseline recording was conducted under normoxic conditions, followed by 5 consecutive days of IH. During IH, ambient oxygen was cycled between 21% to 10% (balance nitrogen) for alternating 5 minute intervals. Each IH cycle was partitioned into a normoxic component (oxygen between 17.3-21%) and a hypoxic component (10%-17.2%). Times spent in different sleep-waking-states and EEG delta power values were compared between the normoxic and hypoxic phases.

**Results:** Total sleep time (%TST) for the entire 12 hour IH period was only significantly reduced from baseline values for the first 2 days of IH exposure: 57±2% vs 43±1% (day 1) vs 46±2% (day 2). However, TST during the hypoxic phase remained significantly lower than normoxic values for all 5 days of IH exposure; 36±1% vs 56±2% (day 1) and 50±1% vs 60±2% (day 5). NonREM EEG delta power was also significantly reduced during the hypoxic versus the normoxic phases for the 5 days of IH exposure.

**Conclusion:** Sleep disruption is most severe and persistent during the hypoxic phase of IH in rats.

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**0048**

**Electrophysiological Identification And Behavioral Correlates Of Activity Of Hypocretin/Orexin Neurons In Freely Moving Rats**

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**Introduction:** The behavioral correlates of hypocretin (Hcrt, orexin) neurons are unknown because it has not been possible to identify them in the freely moving animal. We now report on the development of electrophysiological criteria for identifying Hcrt cells in rats and on their behavioral correlates.

**Methods:** Extracellular micropipette recording of antidromic spike with juxtacellular Neurobiotin labeling and immunofluorescent staining for Hcrt were used to identify Hcrt neurons that send projections to the ventral tegmental area (VTA) in urethane anesthetized rats (n=28). Obtained characteristics of Hcrt spikes were used for identification Hcrt neurons during microwire (12.5 µm) unit recording in freely moving rats (n=14).

**Results:** Experiments performed in anesthetized rats demonstrated that all Hcrt cells (n=26) antidromically identified by VTA stimulation (0.2 ms, 300-800 µA, trains of >100 Hz) had spikes with a long lasting positive deflection (LPD) >0.82 ms that was significantly broader than the LPDs of nonHcrt cells (t=12.3, p<0.0001). Hcrt cells responded antidromically with an average latency 5.5±0.48 ms and were located in the medial parts of the perifornical and lateral hypothalamus. Microwire recording from identified Hcrt neurons in anesthetized rats (n=4) revealed that Hcrt spike LPDs ranged from 0.56 ms to 0.7 ms with a mean of 0.62±0.01 ms (n=13). Based on these parameters we identified 9 Hcrt neurons in freely moving rats (n=14). The firing rates of all Hcrt cells positively correlated with both EEG desynchronization and motor activity and reached their highest level during exploratory behavior (8.1±0.57 sp/s, min=3.84 sp/s, max=9.3 sp/s), lower levels during grooming and eating and minimal levels during quiet immobile waking (1.01±0.13 sp/s, min=0.33 sp/s, max=1.5 sp/s). Unit discharge was further reduced during slow wave sleep and tonic REM sleep, but increased during phasic REM sleep.

**Conclusion:** Hcrt neurons are maximally active during alerting and motor activity, less active during grooming and eating and least active during quiet waking and sleep.

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**0049**

**Effects Of Neuropeptide S On The Sleep/Wake Cycle Of Rats After Sleep Deprivation**


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Introduction: The effects of neuropeptide S (NPS) on the sleep/wake cycle after sleep deprivation (SD) have not yet been characterized and it is not known whether it possesses the same arousal potency in SD animals as that seen in non-SD animals. Here we have investigated whether NPS was able to evoke W in rats when the sleep pressure was increased after SD and how this peptide affects the subsequent sleep rebound.

Methods: Sprague-Dawley rats (n=8) were implanted for chronic sleep recordings and with a guide cannula in the lateral ventricle. Rats were recorded for 6 h after ivc administration of saline. One week later, rats were randomly divided and recorded after ivc administration of NPS (0.1 or 1.0 nmol). Two weeks later, rats were SD for 6 h by gentle handling and recorded after ivc injection of saline. Two weeks later, a second SD session was done and rats were treated with NPS (0.1 or 1.0 nmol). The EEG and EMG were analyzed using the SleepSign software (Kissei Comtec America, Irvine, CA). Statistical analysis of the data was carried out using ANOVA.

Results: In SD animals, NPS induced a doses-dependent increase in W and suppression of cortical slow activity during the first hour post injection (p < 0.05), compared to saline. Likewise, after NPS-induced W in SD rats, the evolution of SWS2, REM sleep and power spectra during SWS, were similar to those recorded with saline.

Conclusion: These results indicate that NPS actively induces W and indicates that NPS is effective against the SD induced rebound hypersomnia and blocks subsequent increase in sleep.

MH62261 to SJH and MH58543 to LdL
dopaminergic or non-dopaminergic neural lesions or by night-time motor disability or deleterious effect of anti-PD drugs.

Methods: Using multiple/experimental approaches (EEG and sleep-wake recordings/pharmacological administration/immunohistochemistry) in six cats treated with MPTP, a neurotoxin causing selective dopaminergic neuronal loss, we have studied the possible correlation between the induced effects on the sleep-wake cycle and those on dopaminergic neurons.

Results: MPTP-treatment (5mg/kg/day x 5, i.p.) caused, during the acute period, a severe hypersomnia in slow wave sleep (SWS, up to 80% of recorded time) and a suppression of paradoxical sleep (PS) lasting for 11 days, accompanied with pronounced behavioural somnolence, marked decrease in locomotion and hesitation at moments of movement initiation. SWS hypersomnia, but not PS suppression, was transiently prevented by administration of small doses of dopaminergic agonists like L-dopa or ropinirole. During the chronic period (3rd-4th week post-treatment), whereas the amount of waking and SWS returned to control level, PS showed transitory increase (+30-50% of control over 2-4 days), accompanied with prolonged episode duration and narcolepsy-like episodes. Ex vivo immunohistochemistry of tyrosine-hydroxylase (TH) and choline-acetyltransferase, marker of catecholaminergic or cholinergic neurons, revealed marked decrease in TH-immunoreactivity in the striatum (fibers/terminal-like dots) and substantia nigra (number of labelled cell-bodies) whereas cholinergic cell number in the basal forebrain and mesopontine-territory seemed unchanged.

Conclusion: MPTP-treatment produces in cats the major signs of motor and sleep-wake disorders similar to those seen in PD patients, indicating that the use of MPTP in the cat is an useful animal model for PD. Our results also suggest a possible correlation/causality between the MPTP-induced sleep-wake disorders and the dopaminergic cell loss.

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0053
REM Sleep Enhancing Effect Of Thalidomide Is Dependent On The Availability Of TNF-Alpha
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Introduction: Thalidomide is a unique hypnotic with REM sleep enhancing and immune modulatory effects (such as TNF-alpha modulation). Thalidomide also significantly aggravates cataplexy in canine narcolepsy. In the current study, the sleep-inducing effects of thalidomide were assessed in TNF-alpha knockout (KO) and wild type (WT) mice to examine whether some of the hypnotic effects of thalidomide are mediated through TNF-alpha mechanisms.

Methods: Both TNF-alpha KO (B6;129S6-Tnfltm1Gkl/J) and WT (B6129SF2J) mice were purchased from Jackson laboratory. Eight KO and 8 WT mice were implanted with EEG and EMG electrodes and were maintained in LD12:12 cycle. The mice were administered 3 doses (10, 40, 80 mg/kg, p.o.) of thalidomide and vehicle at ZT6, and the effects on non-REM sleep (NREM) and REM sleep during the 4-hour post treatment were analyzed. In a separate session, the expression of TNF-alpha gene in the hypothalamus and cortex were analyzed using RT-PCR in WT mice 2-hours after the thalidomide was administrated (n=3 for each dose).

Results: Sleep amounts were not different between two groups after the saline injection. Thalidomide dose-dependently increased both NREM (125%, 4-hour after 40 mg/kg) and REM sleep (195%) in WT mice, similar to the effects reported in dogs and humans. However, the effects of thalidomide in TNF-alpha KO were different. Thalidomide enhanced NREM sleep (124%) as seen in WT mice, but no enhancement of REM sleep was observed; REM sleep was reduced by 33% (4-hour after 40 mg/kg). The results of RT-PCR revealed that thalidomide dose-dependently decreases TNF-alpha gene expression in the brains of WT mice.

Conclusion: REM sleep, but not NREM sleep-enhancing effects of thalidomide are dependent on the availability of TNF-alpha. Since thalidomide decreases TNF-alpha production in the brain, the REM enhancing effects of thalidomide is likely to be mediated by the inhibition of central TNF-alpha production. It is interesting to further study the functional significance of REM sleep modulation by TNF-alpha in both normal and pathophysiological conditions.

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0054
Vigilance Change, Hypocretin And Histamine Release In Rats Before And After A Histamine Synthesis Blocker (Alpha-FMH) Administration
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Introduction: Hypocretins are involved in vigilance control and in the sleep disorder narcolepsy. A series of experimental studies has suggested that the histamine system mediates the wake-promoting effects of hypocretins. In this study, we have measured the hypocretin and histamine release together with sleep monitoring, in freely moving rats under 12:12 light cycles, as well as after alpha-FMH, a histidine decarboxylase inhibitor, administration.

Methods: EEG/EMG electrodes and 2 microdialysis probes were implanted in 4 rats, and microdialysis perfusate was collected in a 30-minute sampling bin while sleep was continuously monitored over 108 hours. Saline was injected at ZT11 on day 1 and alpha-FMH (100 mg/kg i.v.) was injected at ZT11 on day 2. Hypocretin content was measured by radioimmunoassay while histamine contents were measured by HPLC.

Results: Both hypocretin and histamine release showed clear diurnal fluctuation patterns; high during the active phase, and low during the resting phase. Alpha-FMH almost completely inhibited the histamine release for over 24-hours from 2-3 hours after the injection. It is, however, the alpha-FMH treatments that do not affect hypocretin release as well as sleep/wake patterns, and the same sleep/wake and hypocretin release patterns were continuously observed.

Conclusion: Acute pharmacological ablation of histamine synthesis did not affect the sleep/wake pattern or hypocretin release. The lack of influence of histaminergic tonus on hypocretin activity is consistent with recent in vitro data showing that histamine does not modify the activity of hypocretin neurons. However, it is difficult to reconcile the results that acute ablation of histamine synthesis does not have an impact on sleep if the histamine system is important for the regulation of physiological sleep. Further studies are necessary to address these questions.

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0055
Chronic Intermittent Hypoxia Reduces Pancreatic MRNA Levels For Secretion-Controlling Proteins MUNC-18 And Syntaxin-1A And Increases Insulin-1 MRNA In Rats
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**Introduction:** The obstructive sleep apnea syndrome (OSAS) commonly coexists with the metabolic syndrome (hypertension, obesity, diabetes), but the mechanisms of this association are unknown. We previously determined that, when tested under anesthesia, chronic intermittent hypoxia (IH), a major pathogenic condition of OSAS, blunts insulin release in response to i.v. glucose load. Our present goal was to assess whether exposure to IH alters pancreatic expression of mRNA for proteins that may regulate insulin release.

**Methods:** Adult Sprague-Dawley rats were subjected to IH for 33-36 days (O2 seen by the animals: 5.5-10% for 70 s followed by 18.9-25% for 80 s, 7:00 am-5:00 pm daily); control rats experienced identical flows of room air. Rats were sacrificed, total RNA extracted from the pancreas, quantified, and selected mRNAs quantified using RT-PCR. The results are expressed as the number of cDNA copies per 1 µg of total RNA ± SE.

**Results:** The mRNA level for Munc-18 decreased from 1140 ± 200 in sham-treated to 450 ± 120 in IH rats (n=5, p<0.02), and for Syntaxin-1A from 620 ± 100 to 215 ± 50 (n=5, p<0.01). In contrast, the pancreatic insulin-1 precursor mRNA level increased from 40 ± 10 x10³ to 200 ± 60 x10³ (n=5-6, p<0.02).

**Conclusion:** Exposure to IH reduces mRNA levels for two proteins that facilitate membrane damping of pancreatic hormone-containing dense-core vesicles and their subsequent exocytosis. This may cause the reduced pancreatic insulin release that we observed in rats exposed to IH.

**IL-074385.**

**0056**

Catecholaminergic Inhibitions Of The Orexin/Hypocretin Neurons By Direct And Indirect Actions

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**Introduction:** Orexin A and B are implicated in the regulation of sleep/wakefulness and energy homeostasis. The human sleep disorder narcolepsy is accompanied by a loss of orexin production due to specific destruction of orexin neurons.

**Methods:** In the present study, patch-clamp recording of green fluorescent protein-labeled orexin neurons in mice showed that NA, dopamine and adrenaline all directly hyperpolarized orexin neurons in a concentration-dependent manner.

**Results:** This response was inhibited by the ∞2 adrenergic receptor (∞2-AR) antagonist, idazoxan (1 µM), and was also inhibited by the ∞2A-AR selective antagonist, BRL44408 (3 µM). A low concentration of Ba2 (30 µM) inhibited NA-induced hyperpolarization suggesting that an activation of G-protein coupled inward rectifier potassium (GIRK) channels is involved in this response. The effects of NA on the glutamatergic and GABAergic synaptic transmissions were also examined. NA application dramatically increased the frequency and amplitude of inhibitory synaptic currents (IPSCs) in orexin neurons, while NA inhibited excitatory synaptic currents (EPSCs). NA also inhibited evoked IPSC and EPSC amplitude by NA presumably by a presynaptic mechanism. Double-label immunohistochemistry showed that tyrosine hydroxylase-immunoreactive neurons were involved in specific neuronal activation.

**Conclusion:** Catecholamines directly hyperpolarize orexin neurons through an ∞2A-AR-mediated activation of the GIRK channel. Catecholamines also indirectly influence the activity of orexin neurons by modulating glutamatergic and GABAergic neurotransmission onto these cells.

**0057**

Effects Of Running Wheel Activity On The Regional EEG Differences During Waking And Subsequent Sleep In Mice

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**Introduction:** Low frequency EEG power in NREM sleep is homeostatically regulated and considered to reflect sleep intensity. Evidence is accumulating that not only the temporal evolution of EEG changes under increased sleep propensity, but also its topographical distribution. The waking EEG is known to be modified by behavior. Regional EEG differences during subsequent sleep may be a consequence of the previous waking activities leading to specific neuronal activation.

**Methods:** The frontal (motor cortex) and parietal EEG, EMG and running wheel (RW) activity of C57BL6 mice were recorded continuously for three days after prolonged adaptation to the RW. After a baseline recording on Day 1 beginning at dark onset, the RW was locked preventing running for the next 24 h. On Day 3 the animals again were allowed access to the RW.

**Results:** The mice made abundant use of the running wheel, especially during the dark period. On Day 1, during epochs when the mice ran, there was a pronounced peak at 8 Hz in the EEG spectrum. During waking epochs without RW-activity on Day 1, as well as on Day 2, theta-activity was lower than during running epochs, while power in the delta frequency band was enhanced. Delta EEG power in NREM sleep initially was enhanced after spontaneous waking bouts, declining gradually, thereby reflecting the well-known effects of sleep deprivation. Moreover, a frontal predominance of delta EEG power in NREM sleep occurred invariably after spontaneous waking bouts on all days. However, the frontal EEG between 2-8 Hz was above the values of Day 1 on Day 2 (no RW). This selective effect was highest during the first 6 h of the dark period, and dissipated on Day 3, when access to the RW was again permitted.

**Conclusion:** Spontaneous running wheel activity contributes to the regional EEG differences in the NREM sleep EEG encountered in mice after wakfulness episodes.

**0058**

Fos Immunoreactivity In The Preoptic Area Of The Cat During States Of Sleep And Wakefulness

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**Introduction:** The preoptic area of the hypothalamus (POA) participates in the control of the wake and sleep cycle. Studies in the rat have shown that neurons in the ventrolateral and median preoptic regions (VLPO, MnPN) of the hypothalamus express c-fos (a marker of neuronal activity) during quiet sleep (QS), while neurons in the “extended-VLPO” are activated during active sleep (AS). In the present study, we analyzed Fos immunoreactivity in the POA of the cat during sleep and waking states.

**Methods:** Cats, which were implanted with electrodes to monitor sleep and waking behaviors, were maintained in the following states for 60-120 minutes before euthanasia: quiet wakfulness (QW, n=3); wakfulness with motor-explorative activity (AW-ME, n=3); active wakfulness without motor activity, in which the animals were restrained but kept alert with loud clicks (AW w/o M, n = 3); QS (n=4) and AS induced by carbachol (AS-carbachol, n=3). Thereafter, immunohistochemical procedures were utilized to detect the Fos protein; the number and distribution of Fos
positive neurons were analyzed in the ventrolateral and median preoptic regions (VLPO, MnPN).

**Results:** In the VLPO, the greatest number of Fos-immunoreactive neurons was present during AW w/o M (33.7 - 5.8, P < 0.05). Fewer Fos-immunoreactive neurons were found during QS (22.2 - 3.6); AS-carbachol (12.7 - 2.3) QW (9.5 - 2.4), or AW-ME (81.2 - 27.1, P < 0.05). In the MnPN, Fos-immunoreactive neurons were detected principally during AW-ME (81.2 - 27.1, P < 0.05); there were smaller numbers of Fos-positive cells during QS (39.2 - 7.2), AS-carbachol (22 - 3.8), AW w/o M (19.3 - 5.7) or QW (8.5 - 2.6).

**Conclusion:** In the POA of the cat, neurons involved in the generation of QS are not as active as those related to specific behaviors that occur during active wakefulness.

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**0059 Chronic Mild Stress, An Animal Model Of Depression, Affects The Expression Of BDNF And 5-HT Levels Over The Sleep/Wake Cycle In Hippocampus In Rats**

**Introduction:** A recent hypothesis suggests a possible interaction between neurotransmitters and neurotrophins in the pathogenesis of depression. Traditionally, a deficiency of serotonin has been suggested as one of the biological bases of affective disorders. Brain-derived neurotrophic factor (BDNF) systems appear to be a downstream target of a variety of antidepressants. Cyclic AMP (cAMP) response element binding protein (CREB) is one of the protein kinases required for the transduction of neurotrophic signals. We investigated whether chronic mild stress (CMS), an animal model of depression, would induce changes in serotonin levels over the sleep/wake cycle and affect the expression of BDNF and phospho-CREB in hippocampus.

**Methods:** Male SPF rats were implanted with EEG and EMG electrodes, and an intracerebral guide cannula in the hippocampus for a microdialysis probe. Rats were divided in a CMS group (n=8) exposed to daily stressors and a Control group (n=5). Sleep was monitored before and after 4 weeks of CMS. As serotonergic neurotransmission in cortical and subcortical areas is state dependent (W>SWS>REM sleep), dialysates were manually collected in the polygraphically defined sleep/wake state. After decapitation, the hippocampal subregions were rapidly dissected and further analysed by sequential western blots.

**Results:** In Controls, 5-HT levels changed with behavioral state (F(2,8)=10.8,p=0.01; waking and SWS>REM sleep), as expected. This was not seen in CMS rats (F(2,14)=3.9,p=0.08). Surprisingly, a higher 5-HT level in SWS (+33%,p=0.03) and REM sleep (+19%,p=0.09) compared to waking was seen. Compared to Controls, levels of BDNF and phospho-CREB protein were down-regulated (-25%,p=0.025; -30%,p=0.002, respectively) in the dentate gyrus of the CMS-treated rats, but not in the hippocampus proper.

**Conclusion:** In an animal model of depression, the state dependent extracellular level of serotonergic neurotransmission in hippocampus was different from Controls over the sleep/wake cycle. Expression of BDNF and phospho-CREB is down-regulated in the dentate gyrus.
Conclusion: The increased apnea index of Tg8 mice and the pharmacological data do not support a role for low central concentrations of 5-HT or NE in apnea genesis.

0062
Altered Sleep Response To 5-HT1B- But Not 5-HT1A-Receptor Activation In Serotonin Transporter Knock-Out Mice
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Introduction: It has been shown by pharmacological and genetic approaches that serotonin (5-HT) exerts a negative control on the state of REM sleep, that is mediated, at least in part, by 5-HT1A and 5-HT1B receptors. However, knock-out mice which do not express the serotonin transporter (5-HTT-) exhibit tonic increase in extracellular 5-HT levels associated with a marked enhancement of REM sleep compared to their wild-type counterparts (5-HTT+). Because such REM sleep facilitation might be due to functional desensitization of 5-HT1A and/or 5-HT1B receptors, we investigated sleep-wakefulness regulations in 5-HTT-/- mutant mice.

Methods: Under general anaesthesia, male mice were implanted with electrodes for polygraphic sleep monitoring. After 10 days of recovery and habituation to the experimental conditions (12h light-dark cycle, light on at 7:00), polygraphic recordings were performed during 8 hours after injection (at 10:00) of selective agonists of either 5-HT1A or 5-HT1B receptors (8-OH-DPAT: 0.2-0.8 mg/kg s.c.; CP 94253: 1-5 mg/kg i.p.).

Results: Activation of 5-HT1A receptors by 8-OH-DPAT induced in 5-HTT+/+ mice, during the first 2 hr period after injection, a dose-related inhibition of REM sleep and SWS, as well as a concomitant increase in wakefulness (W). In 5-HTT-/ mice, we observed the same decrease in REM sleep amounts, but no modification of SWS or W. Activation of 5-HT1B receptors by CP 94253 in 5-HTT+/+ mice, during 2 hrs after injection a dose-related inhibition of REM sleep and an increase in SWS. In contrast 5-HTT-/ mice exhibited no modifications of REM sleep, SWS and W.

Conclusion: The present data suggest that REM sleep enhancement in 5-HT-/- mutant mice is due, at least in part, to desensitization of 5-HT1B, but not 5-HT1A-receptors. The brain structures possibly involved in this phenomenon is the question now addressed currently in our group.

0063
On The Role Of The Basal Forebrain Cholinergic Neurons In Regulation Of Recovery Sleep
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Introduction: Basal forebrain (BF) has been proved as an important site in regulation of sleep need. We have found recently that release of NO in the BF may be a mechanism underling development of recovery sleep after sleep deprivation (SD). To further elucidate the role of BF mechanisms in regulation of recovery sleep we: 1) pharmacologically increased NO level (by infusion of NO donor) outside cholinergic BF area and compared changes in sleep to those observed after NO donor infusion into the BF; 2) destroyed BF cholinergic neurons and compared sleep responses to SD and to pharmacologically increased NO level to those observed in intact animals.

Methods: Male rats were implanted with electrodes for EEG/EMG recording and guide cannulae for microdialysis probes aimed to the BF or non-cholinergic areas. The experimental schedule for each rat included: recording of natural sleep-waking cycle; SD for 3h; infusion of NO donor (DETA NONOate) for 3h. In another group of rats immunotoxin 192 IgG-saporin was injected into the BF and after 2 weeks the same experimental schedule was performed. After the end of experiments brains were taken for estimation of the quality of cholinergic cells lesion and/or for validation of probes locations.

Results: In all intact rats SD induced significant increase in subsequent sleep by 31.2±4%, infusion of DETA NONOate into the BF increased sleep by 37.1±4%, while infusion outside cholinergic region was not effective. After lesion of the BF cholinergic neurons recovery sleep in response to SD was significantly attenuated (9.4±3% increase). Effect of DETA NONOate infusion was totally abolished (3.1±4% decrease as compared with control).

Conclusion: Cholinergic neurons of the BF play a critical role in regulation of the effects of prolonged wakefulness which are mediated by release of NO.

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0064
Unilaterat Cortical Application Of Interleukin 1ß Increases The Number Of Nerve Growth Factor Immunoreactive Cells In The Ipsilateral Horizontal Diagonal Band
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Introduction: Individual neural groups (also called neuronal assemblies) alternate between functional states; these states are posited to be regulated by sleep regulatory substances such as interleukin 1-ß (IL1ß). Unilateral cortical application of 10 ng of IL1ß increases local EEG delta wave power as well as fos-immunoreactivity (IR) in the somatosensory cortex, thereby suggesting that local application of IL1ß activates cortical cells. In this study, we investigated nerve growth factor (NGF)-IR in the somatosensory cortex and the lateral horizontal diagonal band (latHDB), a basal forebrain region implicated in regulating EEG slow wave activity, after a unilateral injection of IL1ß into the somatosensory cortex (SSctx).

Methods: Six male Sprague-Dawley rats (300 to 400 g) received unilateral microinjections of 10 ng in 2 µl of rat recombinant IL1ß into layer VI of the SSctx and saline into the opposite SSctx 2 h before dark onset. (This dose of IL1ß induces EEG asymmetries for 4 h after microinjections). The rats were sacrificed 2 h later. The rats were decapitated, the brains fixed overnight with 4% paraformaldehyde and sunk in 20% sucrose. Coronal sections of the forebrain (30 µ) were prepared using a sliding microtome and IR was performed using a primary antibody against NGF (1:5,000, Chemicon).

Results: The number of NGF-IR cells increased in the latHDB on the side receiving IL1ß relative to the contralateral side that received saline. However, no differences in NGF-IR were observed in layer V of the SSctx near the injection sites at this time point.

Conclusion: The results suggest that IL1ß-induced unilateral increases in NGF-IR occur in the latHDB with a similar time course to the IL1ß-induced unilateral increases in local EEG synchronization. Current find-
ings also suggest that sleep regulatory growth factors are differentially induced in localized brain regions and involved in sleep regulation such as the basal forebrain.

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0065
Excitation Of Cells In The Basal Forebrain Results In Subsequent Increase In Sleep Which Resembles Recovery Sleep Induced By Sleep Deprivation
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Introduction: Increase in extracellular adenosine concentration in the basal forebrain (BF) has been shown to mediate the sleep-inducing effects of prolonged wakefulness. The mechanisms by which prolonged waking activity leads to adenosine production and induction of recovery sleep are not fully characterized. Cells in the BF are modulated by excitatory neurotransmitters, which during prolonged waking activity may contribute to generating the signal for recovery sleep. In the present study we investigated the effect of local neuronal excitation of BF cells with either glutamate, glutamate NMDA receptor agonist or histamine on the subsequent sleep.

Methods: Adult male rats were implanted with EEG recording electrodes and in vivo microdialysis probes aimed to BF. EEG was recorded for 30 h from the beginning of the experiments and normalized to a previous baseline recording. The 3-hour in vivo microdialysis infusions consisted of either 5 mM glutamate or 0.3 mM N-methyl-D-aspartate (NMDA) or 100mM histamine.

Results: All infusions increased the average delta power in NREM sleep during the subsequent recording period as compared with baseline (glutamate 127% ± 13 SEM, n = 14; NMDA 138% ± 11 SEM, n = 16; histamine 188% ± 51 SEM, n = 3; baseline is 100%). NMDA and histamine also induced wakefulness during the 3-hour infusion period whereas glutamate did not.

Conclusion: These results show that histamine and NMDA first induce wakefulness during the infusion, which is then followed by subsequent increase in delta power, the effect of which closely resembles the effect of sleep deprivation. With glutamate infusion, a subsequent increase in delta power was recorded without any immediate effect on behavior during the infusion. These results suggest that increase in sleep resembling recovery sleep can be induced by neuronal activation of BF regardless of the amount of previous wakefulness.

0066
Brain Levels Of BDNF Are Not Changed In A Rat Model Of Depression Induced By Neonatal RSD
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Introduction: Neurotrophic factors, particularly brain derived neurotrophic factors (BDNF), are proposed to operate in mood disorders, with BDNF as a factor in neurotrophic and neuronal plasticity 1. Neonatal treatment with clonipramine (CLI), an antidepressant that suppresses REM sleep, results in a set of behavioral alterations in the adult animal that resemble human depression 2, 3. Our hypothesis would be that BDNF expression in the adult would be induced by neonatal REM sleep depression (RSD). The current study examined brain levels of BDNF in adult rats neonatally subjected to RSD by CLI injection.

Methods: Male Long Evans Hooted rat pups were treated with CLI conventionally (i.e., 20mg/kg, twice daily, s.c., n=8) and equivalent saline (n=10) from age 8 to 21 days. Rats were weaned at 25 days and group housed under the same conditions. Animals were sacrificed at 4 months by decapitation. Brain tissues were collected from multiple regions including frontal cortex, parietal cortex, temporal cortex, occipital cortex, hippocampus, thalamus, midbrain and pons. Tissues were homogenized using ultrasound dismembrator, boiled and centrifuged. Supernatant was used for BDNF quantification according to the commercially provided protocols for ELISA (Promega, Madison, WI). Statistical comparison of groups was performed by t-test.

Results: BDNF levels were the highest in the frontal cortex (CLI: 74.26 ± 3.1 pg/mg and SAL: 73.10 ± 4.91 pg/mg) and the lowest in the pons (CLI: 42.28 ± 4.50 pg/mg and SAL: 39.64 ± 4.69 pg/mg) in both groups. Brain levels of BDNF in hippocampus were CLI: 66.81 ± 6.44 pg/mg and SAL: 64.77 ± 3.74 pg/mg. The largest group difference of BDNF levels was 6.25%, i.e., compared with the SAL rats, CLI rats had 6.25% BDNF reduction. However, no group differences reached statistical significance (p<0.05).

Conclusion: These results do not support a role for BDNF in the pathology in the CLI-RSD model of induced depression.


0067
The Effects Of Diethyl-Lactam On Rodent Sleep
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Introduction: The gamma-butyrolactone derivative diethyl-lactam (3,3-diethyl-2-pyrrolidone) has been shown to potentiate inhibitory GABA_A currents. Due to this action, diethyl-lactam has hypnotic and anticonvulsant properties. The sole anticonvulsant action has been shown to be the result of its GABA_A receptor modulating properties. Data also suggests that diethyl-lactam has potent sophorphic (at low doses) and anesthetic properties (at higher doses) and shares properties of the drug gamma-hydroxybutyrate (GHB). Little work has been done to investigate additional properties GHB may have. The purpose of this investigation was to document the effects of diethyl-lactam on rodent sleep architecture.

Methods: Four Sprague-Dawley rats weighing approximately 375 grams were given a 500mg and 300mg per kg dose of diethyl-lactam dissolved in saline or a saline injection in a counterbalanced design. Sleep was analyzed 24 hours after exposure to diethyl-lactam or vehicle control. Since each animal served as its own control, the effects of the drug were compared to the data obtained during the vehicle injection for each animal.

Results: Diethyl-lactam significantly increased High Voltage (HV) sleep for the first six hours compared to control recordings (mean epochs scored 109 ± 55 and 59 ± 17 p <0.05) respectively. HV replaced waking and Paradoxical Sleep (PS) was reduced during the first 5 hours. There were notable qualitative differences between HV in the treatment compared to the control condition. The amplitude of the HV waves were greater under the diethyl-lactam treatment vs control condition.
Conclusion: Diethyl-lactam shares some properties with GHB and related gamma-butyrolactones. The most notable similarity is its ability to produce prolonged high-amplitude HV sleep. It differs from GHB in that PS is reduced dramatically under diethyl-lactam, while GHB has been shown to maintain fairly normal PS architecture.

**0068**

Influence Of Temporomandibular Joint Pain In Sleep Pattern: Role Of Nitric Oxide

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Introduction: Since nitric oxide is related to nociception and sleep-wake cycle, this study sought to determine its involvement in the altered sleep pattern in temporomandibular joint pain model by investigating the effect of the inhibitor of nitric oxide synthase (L NAME) and of its precursor (L arginine).

Methods: The animals were injected with Freunds adjuvant or saline in temporomandibular joints and their sleep was recorded, and likewise after administration of L NAME and L arginine. L NAME increased REM sleep in the control group.

Results: The orofacial pain group showed reduction in total sleep time and increase in sleep latency compared with SHAM group. L NAME increased sleep time, NREM, REM sleep and reduced sleep latency in the orofacial pain group. L arginine did not alter sleep parameters.

Conclusion: Thus L NAME improved sleep efficiency whereas L arginine did not modify it, suggesting the involvement of nitric oxide in painful temporomandibular joint conditions.

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**0069**

GABAergic Neurotransmission In The Ventral Midbrain On Sleep-Wake Behavior In The Rat

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Introduction: Our previous study found that neurotoxic lesions of the ventral midbrain produce insomnia in the cat, however, the mechanism for this effect is unclear. Because GABAergic neurons in the ventral tegmental area (VTA) display changes in the firing rate correlating with sleep states and GABA receptors are identified in dopaminergic and non-dopaminergic neurons, we hypothesize that the GABAergic mechanism in the VTA is involved in sleep regulation.

Methods: Male rats were implanted with guide cannulae for chemical infusion and electrodes for EEG and EMG recording. Experiments were conducted 2 weeks after the animals recovered from the surgery. Chemicals and artificial CSF (aCSF) were infused into the VTA through a dialysis probe at a flow rate of 2µl/min for 1-h. A baseline control recording was performed with aCSF infusion the day before for the same circadian period.

Results: aCSF infusion into the VTA produced no change in sleep (n=10). Muscimol, a GABA receptor agonist, at the dose of 0.1mM (n=4) and 0.5mM (n=1) infused into the VTA had no effect on total sleep time (90% ± 17% and 88% of baseline sleep respectively). In contrast, bicuculline, a GABA receptor antagonist, infused into the VTA produced a dose-dependent suppression of sleep. Low dose (0.05mM, n=2) of bicuculline at VTA greatly reduced REM sleep (93.5% ± 4.1% from the baseline) without changing NREM sleep, while high dose (1mM, n=3) completely eliminated both NREM and REM sleep at the latency of 4-8 min and this suppression lasted over the entire period of infusion.

**Conclusion:** Our present findings suggest that GABAergic mechanism in the VTA plays an important role in the regulation of sleep. We hypothesize that tonic GABAergic activity in the VTA is required for the maintenance of normal sleep. Inhibition of GABAA receptor activity by bicuculline infusion caused insomnia.

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**0070**

Unilateral Cortical Application Of Interleukin 1-b Increases The Number Of Fos Immunoreactive Nuclei In The Prefrontal And Secondary Motor Cortex

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Introduction: Neuronal assemblies are postulated to exhibit distinct functional states regulated by sleep regulatory substances such as the cytokine, interleukin 1-β. Unilateral cortical application of IL1β increases local EEG synchronization as well as fos immunoreactivity (IR) in the somatosensory cortex. These results suggest that local application of IL1β activates cells within cortical networks. In this study, we investigated fos-IR in the interconnecting regions of the prefrontal cortex after a unilateral injection of IL1β into the somatosensory cortex.

Methods: Six male Sprague-Dawley rats (300 to 400 g) received unilateral microinjections of 10 ng in 2 µl of rat recombiant IL1β into layer VI of the somatosensory cortex and saline into the opposite cortex 2 h before dark onset. (This dose of IL1β induces EEG asymmetries for 4 h after the microinjections). The rats were sacrificed 2 h later. The rats were cardiac-perfused and brains fixed overnight with 4% paraformaldehyde, sunk in 20% sucrose and frozen. Coronal sections of the prefrontal cortex (30 µ) were prepared using a sliding microtome and IR was performed using primary antibodies against c-fos (1:10,000, Oncogene).

Results: The number of fos-IR nuclei increased ipsilaterally in the regions of the prefrontal cortex that interconnect with the somatosensory cortex receiving IL1β relative to the opposite side that received saline. Most of the increase in fos-IR nuclei was evident in layers 2 and 3 of the prelimbic prefrontal cortex and the secondary motor cortex. No changes in fos-IR were observed in the infralimbic prefrontal cortex or the primary motor cortex.

Conclusion: The results suggest that IL1β-dependent increases in fos-IR occur in the interconnecting regions of the prelimbic prefrontal and secondary motor cortex with a similar time course to the increases in local EEG synchronization. Current findings are consistent with the hypothesis that sleep is a localized process.

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**0071**

Nociceptin/Orphanin FQ Modulates Hypocretin/Orexin Neuronal Activity In Mouse Hypothalamus Via Activation Of NOP Receptors

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Introduction: Nociceptin/orphanin FQ (N/OFQ), the endogenous ligand for the NOP (or ORL1) receptor, produces a hyperphagic effect in freely feeding rats but not in food deprived rats. N/OFQ fibers are found in the lateral hypothalamus where hypocretin/orexin (Hcrt) containing neurons
are located. The Hcrt system regulates alertness and modulates feeding behavior. We have investigated the cellular action of N/OFQ on defined Hcrt-containing neurons.

**Methods:** Brain slices (250 µm) containing the lateral hypothalamus were prepared from transgenic mice (3-5 weeks old) in which enhanced green fluorescent protein (EGFP) was linked to the Hcrt/orexin promoter. Slices were perfused with physiological solution containing (mM): NaCl 135, KCl 5, MgCl2 1, NaHCO3 25, glucose 10. Whole-cell recordings from Hcrt/EGFP neurons were made using an Axopatch 1D amplifier. The internal solution contained (mM): KCl 145, MgCl2 1, EGTA-Na3 1.1, HEPES 10, Na2ATP 2, Na2GTP 0.5. Drug applications were via bath perfusion at 2 ml/min flow rate.

**Results:** All Hcrt/EGFP neurons recorded (n = 42) displayed spontaneous firing of action potentials and synaptic activity that was blocked by tetrodotoxin (TTX, 0.5 µM). All Hcrt/EGFP neurons recorded (n = 42) displayed spontaneous firing of action potentials and synaptic activity that was blocked by tetrodotoxin (TTX, 0.5 µM). Application of N/OFQ (0.1 — 3 µm, n=9) caused hyperpolarization of 3 — 10 mV, reduced input resistance and decreased membrane excitability. Spontaneous action potentials were blocked and synaptic activity was depressed. The hyperpolarizing effect of N/OFQ was persistent in the presence of TTX, indicating a direct postsynaptic action. The N/OFQ effects were completely and reversibly blocked by a novel selective NOP antagonist SR14148 (10 µm, n = 4), suggesting mediation by the NOP receptor.

**Conclusion:** These results indicate that functional N/OFQ receptors exist on Hcrt neurons. The N/OFQ-induced responses via activation of NOP receptors in Hcrt cells are consistent with inhibitory cellular actions of the peptide observed in other types of neurons. These data suggest a link between N/OFQ-regulated feeding and states of alertness controlled by Hcrt neuronal activity.

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**0072**

**Inducible Nitric Oxide Synthase In Long-Term Intermittent Hypoxia: Hypersomnolence And Brain Injury**

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**Introduction:** Long-term intermittent hypoxia exposure in adult mice, modeling oxygenation patterns of moderate-severe obstructive sleep apnea, results in lasting hypersomnolence and is associated with nitrification and oxidation injuries in many brain regions, including wake-active regions. We sought to determine if long-term intermittent hypoxia activates inducible nitric oxide synthase in sleep/wake regions, and if this source of nitric oxide contributes to the long-term intermittent hypoxia-induced proinflammatory gene response, oxidative injury and wake impairments.

**Methods:** Mice with genetic absence of inducible nitric oxide synthase activity and wild type controls were exposed to 6 weeks of long-term hypoxia/reoxygenation prior to behavioral state recordings, molecular and biochemical assays and a pharmacological intervention.

**Results:** Two weeks after recovery from hypoxia/reoxygenation exposures, wild type mice showed increased inducible nitric oxide synthase activity in representative wake-active regions (356%, p<0.001), increased sleep times: (mean difference 152 min, t=7.2, p<0.001) and NREM sleep times (mean difference 120 min, t=5.4, p<0.001). REM sleep increased in LTIH exposed wild type mice relative to controls (mean difference 35 min, t=3.0, p<0.05) and average sleep latencies were reduced. In contrast, there was no significant effect of LTIH in iNOS null mice on total sleep time (mean difference 24 min, t=0.9), NREM sleep (mean difference 16 min, t=0.6) or REM sleep (mean difference 0.2 min, t=0.01). Mutant mice showed no effect of long-term hypoxia/reoxygenation on sleep latencies and were resistant to hypoxia/reoxygenation increases in lipid peroxidation and proinflammatory gene responses (tumor necrosis factor-a and cyclooxygenase-2). Systemic inhibition of inducible nitric oxide synthase (1400W) following long-term hypoxia/reoxygenation in wild type mice was effective in reversing the proinflammatory gene response (COX-2 and TNF-a) with strong dose relationships for reduction in gene levels relative to iNOS activity, p<0.001.

**Conclusion:** These data support a critical role for inducible nitric oxide activity in the development of long-term intermittent hypoxia wake impairments, lipid peroxidation and proinflammatory responses in wake-active brain regions and suggest a potential role for inducible nitric oxide inhibition in protection from, and possibly reversal of, proinflammatory responses, oxidative injury and residual hypersomnolence in obstructive sleep apnea.

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**0073**

**Effect In Kittens Of Rapid Eye Movement Sleep Deprivation On Synaptic Plasticity Induced By Monocular Deprivation Are Not Mediated By Stress**

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**Introduction:** The effects of blocked visual input to one eye (monocular deprivation, MD) and induction of in vitro long-term depression (LTD, a form of synaptic plasticity) are both regulated by common mechanisms in the developing visual cortex (Heynen et al., 2003, Nat. Neurosci.). Previous studies in this laboratory demonstrate that REMS-deprivation (REMSDEP) during the critical period heightens developmentally regulated visual cortex synaptic plasticity in young rats. Likewise, when combined with MD, REMSDEP also increases neuronal plasticity in kitten visual thalamus. Here we study stress measures in critical-period, 2-week MD kittens who were being investigated for effects of REMSDEP on induction of in vitro LTD in visual cortex.

**Methods:** Kittens either underwent REMSDEP by gentle cage-shaking (n=6), or were not REMS-deprived, residing in similar cages (control, n=5) or in their home cages (homecage, n=3) during the second MD week. Animals were individually prepared for in vitro LTD experiments. Postmortem measures of stress included radioimmunoassay for serum corticosterone levels and weights of excised spleen, adrenals and thymus glands. Saturation of LTD was based upon the average amplitude of the field potentials recorded in visual cortical layer III in 3 successive LTD inductions, using low frequency stimulation (LFS, 1Hz for 15 min) directed at the white matter below layer III in slices from both sides of brain.

**Results:** ANOVA revealed that saturation was reached in both control kitten cortices after the second LTD-induction. In REMSDEP kittens, saturation was observed after the second LFS of the hemisphere ipsilateral to the patched eye. In the contralateral hemisphere, LFS did not induce LTD. One-way ANOVAS revealed that, of all the stress measures, only thymus weight showed a significant group effect (F=9.05, df = 2.20, p = 0.002). Bonferroni t-tests on thymus weight indicated that the control and REMSDEP groups both differed from the homecage kittens and were not different from each other.

**Conclusion:** These data support our preliminary conclusion that the effects of REMSDEP on synaptic plasticity mechanisms in developing visual cortex are additive to those of MD. Stress does not seem to factor
into the results insofar as, excepting thymus weights in the homecare controls, the three groups showed comparable stress measures. Inasmuch as the two experimental-cage groups did not differ in other respects further suggests that stress is adequately controlled for in these REMSDEP studies.

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0074
The Role Of Adenosine A1 Receptors In Sleep And Arousal
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Introduction: Increases in sleep amount and EEG spectral power in the 0.5-5 Hz frequency band (delta) following sleep deprivation is a feature of homeostatic sleep-control in mammals. Adenosine levels rise in the forebrain with increased wakefulness and is one neural factor implicated in the control of sleep homeostasis. Here, we test for an altered delta-power phenotype in conditional, A1 adenosine-receptor knock out mice (A1R KO) dependent upon the CamKII promoter. CamKII is mainly expressed in the forebrain.

Methods: Pairs of adult male mice (3 A1R KO mice and 3 littermate controls) were used in this experiment. A1R KO mice were generated by crossing A1R floxed (Exon 6) with CamKII-Cre transgenic mice. After implanting electrodes (two for EEG and two for EMG), each mouse was allowed one week recovery and two-three weeks of habituation to the recording leads. Following 24 hours of baseline recording, mice were kept awake by enforced locomotion on a treadmill (2 inches per second) on a schedule of one hour on followed by 5 hours off. This cycle was repeated for 48-hours while the EEG was continuously recorded. The EEG signal was divided into continuous 4 second epochs and subject to spectral analysis (FFT in Rss). Mean spectral power in the 0.5-5 Hz band for each 5-hour recovery period was examined for differences between A1R KO and control mice.

Results: A clear time-of-day effect was not observed in the expression of delta-power. No significant difference was found in delta-power between the A1R KO and control mice within the 48-hour deprivation-rebound cycle.

Conclusion: An effect of knocking out A1 adenosine receptors on homeostatic sleep-control was not detected using the current procedure.

0075
Cortical Protein Profiles Are Altered During Spontaneous Sleep Bouts In Aged Rats
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Introduction: The rat model has been used to study some of the effects of aging on sleep wakfulness. We recently showed that dynamic intracellular changes occur in total protein expression across spontaneous sleep in cholinergic enriched tissue from young rats. Since decreases in choline acetyltransferase with aging are well documented, we tested the hypothesis that changes in total protein signatures would occur in aged rats across spontaneous sleep-wakfulness.

Methods: Young (n=9) and old (n=7) male rats were implanted with EEG/EMG electrodes, a femoral vein catheter, and housed in temperature and light controlled conditions. Animals were euthanized following 10 minutes waking, or 10 minutes non-REM sleep between 3-4 pm (lights on period). Total protein from frontal cortex was separated by two-dimen-

sional electrophoresis. Protein expression was monitored by SYPRO ruby; phosphorylation status was assessed by Pro-Q Diamond staining. Images were scanned and analyzed using PDQuest software.

Results: A total of 826 protein spots were separated. In old rats, there was a 25% increase in protein spots compared to young. Of the 102 phosphorylated protein spots detected, 46 spots exhibited state specificity (waking, n=3; sleep, n=43). Though more protein spots were expressed during sleep, there was a decrease (~46%) in the number of phosphorylated spots expressed during sleep in old rats.

Conclusion: These data indicate that changes in the total cortical protein complement accompany aging. The data suggest that the intracellular response to the signaling associated with spontaneous sleep-wakfulness is affected by age and is consistent with the idea that such changes may occur prior to any electrophysiological or behavioral state alterations under normal conditions. In addition, these data provide a foundation for future investigations designed to elucidate mechanistic consequences of these changes.

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0076
Discharge Of Identified Orexin Neurons Across The Sleep-Waking Cycle
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Introduction: Orexin (Orx or hypocretin) neurons are known to be important for the maintenance of waking since in their absence narcolepsy occurs. However, the way in which they may maintain waking and prevent sleep, including importantly REM or paradoxical sleep (PS) and its associated muscle atonia, is unknown since the neurons identified as containing Orx have yet to be recorded in vivo. Single units recorded in the lateral hypothalamus where Orx neurons are located were reported to discharge in the majority during both waking and paradoxical sleep (PS). According to this conjectural profile of Orx neuronal discharge, it is uncertain how these neurons would prevent the sudden onset of PS. The aim of the present study was thus to determine the discharge of neurons that could be identified as Orx neurons by using juxtacellular labeling with Neurobiotin (Nb) followed by immunohistochemical staining for Orx.

Methods: Units were recorded in head-fixed Long Evans rats (~250 g) in association with EEG and EMG during at least one full sleep-wake cycle before juxtacellular labeling.

Results: All Nb-labeled neurons that were positive for Orx (Nb+/Orx+) (n = 6) discharged maximally during active waking. They fired in a slow tonic manner during periods of tonic neck muscle tonus but also increased their discharge in association with movements. They significantly decreased their firing during quiet waking in absence of movement. They became virtually silent during SWS and PS except for sporadic spikes associated with muscle twitches or occurring at the end of PS preceding waking. Nb-labeled neurons that were negative for Orx (Nb+/Orx-) included Wake/PS-active neurons (n = 3) and PS-active neurons (n = 5).

Conclusion: These results demonstrate for the first time that Orx neurons may stimulate arousal in association with muscle tone and movement and thus serve to maintain an active waking state.

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A Learning And Memory Center Promotes Sleep In Drosophila

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Introduction: The fruit fly Drosophila melanogaster exhibits many of the cardinal features of sleep. While changes in neural activity are thought to be central to sleep mechanisms and functions, the neuroanatomical loci regulating sleep have not been identified in this model organism.

Methods: We exploited a dominant temperature sensitive blocker of synaptic transmission (shits) to manipulate the activity of neural circuits. Using the GAL4/UAS system, we drove shits expression in multiple adult brain regions defined by 100 distinct GAL4 lines and assayed the consequences on sleep.

Results: We identified five short-sleeper (S-S) GAL4 lines that in combination with shits inhibited sleep at the restrictive temperature (29oC). Transient disruption of synaptic transmission during sleep using a 6-hour heat pulse (29oC) resulted in sleep rebound, consistent with the notion that these regions promote sleep. While these lines had diverse anatomical expression patterns within the brain, they shared expression in the mushroom bodies (MB), a region of the fly brain important for learning and memory. Chemical ablation of the MB resulted in a S-S phenotype. Additionally, MB ablation in one S-S GAL4 line did not enhance the S-S phenotype, indicating MB inhibition is primarily responsible for its phenotype.

Conclusion: Our results strongly implicate a specific and central role for the mushroom bodies in promoting sleep in Drosophila.
Altered Choline Acetyltransferase (Chat) Immunoreactivity And Nicotine Binding Are Associated With Intermittent Hypoxia (IH) Exposure In The Rat

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Introduction: Exposure to IH, such as occurs in sleep disordered breathing (SDB), is associated with cognitive impairment, regional neurodegeneration, oxidative stress, and inflammatory responses in the brain rat. In rodents, one region in which oxidative damage following IH exposure has been observed is the basal forebrain. Loss of basal forebrain cholinergic neurons has been correlated with working memory deficits in a number of neurodegenerative disorders, suggesting that involvement of cholinergic systems may also contribute to the working memory impairments observed after IH exposures. We therefore examined working memory, basal forebrain CHAT immunohistochemistry, and nicotinic binding in the prefrontal cortex (PFC) of male rats exposed to either room air (RA) or intermittent hypoxia (IH).

Methods: Sprague-Dawley male rats (8 weeks of age; 175-200g) were exposed to 14 days of RA or IH (consisting of alternating 90 second epochs of 21% and 10% O2) and tested on a delayed matching to place (DMP) task in the water-maze. Following behavioral testing, brain tissue was harvested for CHAT immunohistochemistry and assessment of nicotinic receptor binding.

Results: IH-treated animals displayed impaired working memory with respect to controls and significant reductions in CHAT stained neurons were observed in the medial septal nucleus (p < 0.04), in both the vertical and horizontal limbs of the diagonal band (p < 0.01), and the substantia innominata (p < 0.03) after 14 days of IH exposure. Increased nicotinic receptor binding in the PFC was observed at 14 days IH.

Conclusion: Loss of cholinergic neurons in the basal forebrain may contribute to the cognitive impairments associated with IH exposure. It is possible that compensatory mechanisms may also be activated in other brain regions, and may provide potential therapeutic targets for the cognitive deficits associated with SDB.

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Burst Synchronization To Auditory Stimuli Under Isoflurane

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Introduction: The electroencephalogram (EEG) shows characteristic patterns under different anesthetics. A burst suppression pattern can be recognized during deep isoflurane anesthesia, with periods of high amplitude (bursts) followed by periods of near ‘silence’ (suppression). The duration of both periods is in the range of seconds. The bursts observed during isoflurane anesthesia (2% or higher) suggests epochs of cortical activity that occur with a regular period due to the burst characteristics of thalamic neurons. If external stimuli can drive the bursting thalamic neurons and elicit the appearance of cortical burst, then somatosensory input to the cortex is possible during isoflurane anesthesia.

Methods: In order to investigate the relationship between the burst suppression state and the auditory evoked responses, rats were chronically prepared to record cortical EEG and the electromyogram under movement restrained conditions. During 2% isoflurane anesthesia we provided single click (0.2 ms) random stimulation (1-2s ISI) from a speaker placed in front of the animal. After the recording, we calculated the time from each stimulus to the presence of the next burst during the burst suppression anesthetic state.

Results: Our results show that the burst during burst suppression state occurs consistently about 167 ms after auditory stimuli. The delay time increases with increasing anesthesia depth to approximately 200 ms.

Conclusion: We found consistent burst activity occurring after auditory stimuli, even though the evoked response was nearly absent. Since external auditory stimuli can drive the appearance of bursts, we speculate that neural responses to external stimuli might be possible without evoking motor output. This finding suggests the possibility of sensory processing during burst periods, which may be due to delayed activation of thalamocortical circuits during this state. The delayed burst activation may also parallel an underlying mechanism for arousal from sleep, which is more distinct during isoflurane anesthesia. Under unanesthetized conditions this mechanism may invoke sleep regulatory circuitry.

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0082

A New In Vitro Model For The Study Of Rapid Eye Movement (REM) Sleep: Ngf-Induced Effects In The Rat Brainstem Slice Preparation

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Introduction: The ponto-mesencephalic junction in the brainstem contains the neuronal circuits that are necessary for the generation of REM sleep. The latero-dorsal and pedunculo-pontine tegmental nuclei (LDT and PPT), and the nucleus pontis oralis (NPO), have been proposed to be responsible for the orchestration of the physiologic processes that result in the expression of REM sleep. However, it has been difficult to obtain a comprehensive understanding of the subcellular and interneuronal processes that promote the expression of this state. Accordingly, we sought to develop an in vitro slice model that contains all of the structures that are necessary for the generation of REM sleep, which could then be used to examine the interactions among the relevant critical structures utilizing pharmacological, electrophysiological, and imaging techniques.

Methods: Pontine slices that included the LDT/PPT, NPO, and the trigeminal motor nucleus (MV) were obtained from 9-15 day old rats. Electrical stimulation was delivered to the ipsilateral LDT/PPT. Intracellular recordings from NPO neurons and MV motoneurons were obtained prior to and following the application of NGF into the ipsilateral NPO (0.4 µg/µl in PBS with 0.5% BSA, ejected at 5-30 PSI during 0.3-4 s).

Results: Stimulation of the LDT/PPT evoked EPSPs in both NPO neurons and MV motoneurons. NGF depolarized and increased the discharge rate of NPO neurons and hyperpolarized and decreased the firing rate of MV motoneurons. In some motoneurons, IPSPs were recorded that were similar to previously described REM sleep specific inhibitory postsynaptic potentials.

Conclusion: We conclude that NGF induces patterns of activity in the NPO and motoneuron pools that are similar to those which occur during naturally-occurring REM sleep. Based upon these data, we believe that this in vitro model of REM sleep will open new avenues for understanding the complex mechanisms that underlie the physiologic pattern of activities that characterize this behavioral state.

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0083

Intermittent Hypoxia (IH)-Induced Oxidative Damage Is Attenuated Following Moderate Physical Activity In The Rat

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Introduction: Exposure to IH, such as occurs in sleep-disordered breathing (SDB), is associated with substantial cognitive impairments and increased neuronal cell loss in brain regions underlying learning and memory in rats. The degenerative mechanisms include free radical generation, calcium overload, cytotoxicity, apoptosis, and the activation of inflammatory pathways. Physical activity (PA) is protective in excitotoxic, ischemic, and oxidative models of neuronal injury and degeneration, and attenuates the behavioral impairments associated with IH. Therefore, in the present study we examined the effect of a PA regimen on the degree of oxidative damage in brain regions underlying learning and memory of animals exposed to 14 days of IH exposure.

Methods: Sprague-Dawley male rats were given a six-week PA regimen (PA) on a motorized treadmill. Control animals were placed in the apparatus for the same duration, but were given no activity (NA). Animals were then exposed to intermittent hypoxia (IH) consisting of 90 sec alternations of 10% O2 and 21% O2, or room air (RA) for 14 days (12 hours/day during light phase). All rats underwent cognitive assessment in the water maze, after which their brains removed for immunohistochemical detection of 8-OHDG, a marker of DNA/RNA oxidative damage.

Results: PA-IH animals displayed marked attenuation of IH-induced spatial learning deficits, and post-hoc analyses revealed the PA-IH were not significantly different from either control group (NA-RA or PA-RA). In comparison to NA-IH, the PA-IH group had a significant reduction in 8-OHDG immunoreactivity in both the hippocampus and cortex (p<0.05).

Conclusion: Behavioral modifications aiming to decrease oxidative stress, such as physical activity, are associated with decreased susceptibility to intermittent-hypoxia-induced spatial task deficits. These findings may have important implications for interventional strategies targeting behavioral modifications in patients with SDB.

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0084

A Gender Comparative Analysis Of Sleep In Neonatal And Juvenile Mice

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Introduction: We have previously showed that there are pronounced differences in the sleep-wake cycle of male and female mice under baseline conditions which can be at least partly attributed to adult gonadal hormone levels. In mice, puberty begins at approximately 21 days of age and sexual maturation is attained at about 6 weeks of age. To investigate the influence of the hormonal environment in mediating the effects of gender on sleep, either early in life or near the time of puberty onset, we compared the states of vigilance of male and female C57BL/6J mice at the age of 9 days (neonates) and 23 days (juveniles).

Methods: In neonates, behavioral states of wake, quiet sleep (QS) and active sleep (AS) were measured in 12 males and 10 females by recording EMG activity with temporary fixed nuchal electrodes for a 2-3 hour period. Juvenile mice were implanted with EEG/EMG electrodes at the age of 21 days (just after weaning) and 2 days later sleep recordings were collected for a 24-h period. In this group, preliminary data have only been obtained in 3 males and 2 females.

Results: No gender differences were found in the amounts of wake, QS and AS across a 2-h recording period during the light phase in neonatal mice. At 23 days of age, clear diurnal rhythms in the amounts of wake, NREM and REM sleep were observed in both males and females, and the percentage of time spent in REM sleep was twice that observed in adults during both the light and dark phases. In this small sample size, no gender differences were observed in any sleep-wake parameters.

Conclusion: Unlike in adults, there were no gender differences in the behavioral states of vigilance in neonatal mice. While more data are needed before any firm conclusions can be made, our preliminary findings indicate no sexual dimorphism in the sleep-wake cycle near the onset of puberty.

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0085

Ionotropic And Metabotropic GABA Receptors On Orexin/Hypocretin Neurons

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Introduction: Several lines of evidence suggest that Orexin/Hypocretin (Orx/Hcr1 or Orx) neurons are active in association with behavioral arousal during waking and inactive in association with behavioral quiescence during quiet waking and sleep. Since Orx neurons are excited by multiple transmitters of the arousal systems and also endowed with intrinsic properties to maintain spontaneous activity, their silence is likely actively imposed by an inhibitory input. The aim of the present study was to examine whether the Orx neurons are endowed with ionotropic, GABA_A, and/or metabotropic, GABA_B, receptors by immunohistochemical and electrophysiological means.

Methods: Adult male Wistar rats were employed for immunohistochemistry and young Sprague-Dawley rats for in vitro electrophysiology. Immunofluorescent dual-staining was performed on frozen sections using antibodies against Orexin-A together with those against the β-chain subunits of GABA_A receptor or the GABA_B receptor. GABA agonists (muscimol or baclofen) were applied upon identified Orx neurons in the slice under conditions of synaptic uncoupling as well as normal transmission.

Results: Orx neurons were lightly immunostained along their somatodendritic membrane for the GABA_A β-chain subunit. They were heavily stained over their cytoplasm for the GABA_B receptor. Identified Orx neurons were hyperpolarized by both GABA_A and GABA_B agonists in the slice. The hyperpolarization was proven to be post-synaptic for both agonists.

Conclusion: Given a previously documented GABAergic innervation and the presently illustrated presence of GABA receptors on Orx neurons, GABA likely plays an important role in inhibiting the Orx neurons during quiet behavioral states including sleep. This inhibition may occur through ionotropic GABA_A receptors, which by opening chloride channels could exert a rapid phasic inhibition possibly in association with different behaviors during waking. The inhibition may also occur through metabotropic GABA_B receptors, which by indirectly opening potassium channels could exert a slower long-lasting inhibition possibly in association with prolonged behavioral quiescence including sleep.

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0086
EEG Sleep, Locomotor Activity And Body Temperature During Chronic Treatment With Gamma-Hydroxybutyrate (GHB) In Rats
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Introduction: Gamma-hydroxybutyrate (GHB) can promote slow wave sleep in humans with no evidence of tolerance during chronic treatment in narcoleptic patients. In rats, acute administration of GHB induces an initial period of EEG hypersynchrony in wake followed by an increase in NREM sleep time and NREM delta power. Here, we investigated whether tolerance and/or withdrawal effects would occur on EEG sleep, activity and temperature measured in rats chronically treated with GHB.

Methods: Adult male Sprague-Dawley rats were implanted with EEG/EMG electrodes and transducers for recording of sleep, locomotor activity and body temperature. At the onset of the dark phase, the animals received a daily i.p. injection of GHB (200 mg/kg) or vehicle (saline) for 10 days, then a vehicle injection for the next 2 days. EEG sleep, activity and temperature values obtained on days 1, 4, 7, 10, 11 and 12 were compared with those measured under baseline conditions (vehicle injection before GHB administration was started).

Results: On the first day of GHB administration, animals showed an elevated delta power during wake in the first hour followed by an increase in NREM and REM sleep time associated with an increased NREM delta power in hours 2 and 3. A similar increase in NREM and REM sleep time was maintained during the 10 days of chronic treatment, whereas the increase in delta power during wake and NREM was attenuated from day 4 onwards. The decrease in locomotor activity and body temperature was present during the entire chronic treatment. Upon withdrawal (days 11 and 12), all parameters returned to baseline values except NREM delta power which was decreased.

Conclusion: We previously showed that GHB increases NREM sleep time through interactions with specific GHB receptor sites, whereas the enhanced NREM delta power is mediated by the GABA-B receptor system. The present results indicate that chronic GHB administration induces tolerance in the increase of NREM delta power only, supporting the hypothesis that the effects of GHB on EEG sleep may be mediated through two different mechanisms.

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0087
The Effect Of Systemic And Intra-Acb Amphetamine On Break Point In A Progressive Ratio Task In REM Sleep Deprived Rats
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Introduction: REM sleep deprivation (RSD) decreases operant responding suggesting that RSD decreases motivation for food reward. Since stimulants are often used to reverse the effects of sleep deprivation, we investigated the effect of systemic and intra-nucleus accumbens (Acb) amphetamine on break point in a progressive ratio operant task in RSD rats.

Methods: The multiple platform method was used to produce RSD (D rats), which were compared to a home cage controls (H rats). Animals were trained in a progressive-ratio 2 (PR2) schedule. Rats were reinforced for the first lever press, and then had to increase responding by two presses for each subsequent sugar pellet. D and H groups were tested on each of the 5 days of RSD. Systemic Amphetamine: Rats received saline on day 1 of RSD and then received an intraperitoneal (i.p.) injection of either 0, 0.1, 0.5, or 2.5 mg/kg of amphetamine. Intracerebral Microinfusions: Rats received saline on day 1 of RSD and then received either 0, 0.1, 10, or 30 ?g of intra-Acb amphetamine on days 3 and 5 of RSD.

Results: D animals decreased responding over 5 days of RSD. Systemic amphetamine did not reverse the effects of RSD, and the higher doses decreased responding in both D and H rats. Preliminary results suggest that intra-Acb amphetamine may not act the same as systemic amphetamine, in that it did not reduce responding further and might have enhanced responding in some D rats.

Conclusion: RSD impairs motivation for food reward and systemic amphetamine does not reverse deficits in responding. Since systemic amphetamine may suppress appetite and thus decrease responding, we are also administering amphetamine into the Acb, where it typically increases responding. Preliminary data suggests that intra-Acb amphetamine may tend to restore effects of RSD, which implicates deficits in dopaminergic systems as mediating some of the behavioral effects of RSD.

0088
Diurnal Variation In The Response To Sleep Deprivation In Young And Old Rats
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Introduction: In this study, we compared baseline sleep patterns in young and old rats and the response to sleep deprivation at different times of day.

Methods: Young (3-6 months) and old (19-22 months) male F344 rats (N=8 and N=7, respectively) were entrained to a 12:12 light:dark cycle. Following 2 days of baseline EEG/EMG recording, animals were sleep deprived for 24 hrs in a slowly rotating wheel beginning either at light or dark onset, and given a 24-hr ad libitum sleep opportunity.

Results: Young and old rats had similar amounts of wake, NREM and REM sleep time over the 24-hr baseline period. Old rats had less sleep during the light phase and more during the dark phase. Old rats also exhibited decreased sleep intensity, as measured by relative NREM delta power (NDP), as well as less sleep consolidation, as measured by bout number and duration. During 24-hr sleep deprivation, all animals showed less than 4% total sleep time. When the recovery opportunity began at light onset, old rats had a larger rebound of NREM sleep (% change from baseline) during the 12-hr light phase and a smaller rebound in the 12-hr dark phase compared to young animals, even though the 24-hr recovery amounts were the same. Similarly, NDP showed a larger positive rebound in the light phase and a smaller negative rebound in the dark phase in old vs. young rats. When recovery began at dark onset, old rats had a notably smaller rebound in REM sleep and a slight reduction in NREM sleep during the 12-hr dark phase.

Conclusion: These data indicate that old rats exhibit alterations in the circadian control of both baseline sleep and the homeostatic response to 24-hours of sleep deprivation.

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0089
Gene Expression In The Rat Cerebral Cortex: Comparison Of Recovery Sleep And Hypnotic-Induced Sleep
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Introduction: Recovery sleep (RS) that follows sleep deprivation (SD) is...
accompanied by alterations in electroencephalographic (EEG) qualities, timing of sleep stages, and gene expression in the brain. GABAergic hypnotics induce EEG changes that are similar to those induced by SD. To determine whether hypnotics induce molecular changes similar to those induced by SD, we measured gene expression in the cerebral cortex after administration of three hypnotics and during RS.

**Methods:** EEG, electromyographic, body temperature and locomotor activity data were collected from 30 WKY rats in a light/dark 12:12 cycle. Rats were assigned to one of five groups (n=6/group): either RS (6 h of SD starting at lights-off followed by 2 h of RS), or one of four intraperitoneal injections- vehicle, gamma-hydroxybutyrate (300 mg/kg), triazolam (1.6 mg/kg) or zolpidem (20 mg/kg) at 6 h after lights-off. Rats were killed by decapitation 8 h after lights-off. Real-time polymerase chain reaction was used to quantify the relative expression levels of the heat shock protein grp94 and the immediate early genes fra-2, and egr-3, all of which were previously demonstrated to be upregulated in the mouse cerebral cortex during RS in the light phase of the LD12:12 cycle.

**Results:** ANOVA indicated significant effects of treatment on sleep time, body temperature and EEG spectra. As in the mouse, grp94, fra-2 and egr-3 were upregulated (60, 42 and 178% respectively; p<0.02, unpaired t test) in RS rats relative to vehicle control. Among hypnotic-treated groups, fra-2 expression was significantly upregulated (88%; p=0.002, unpaired t test) in GHB-treated rats only, and grp94 was upregulated (31%; p=0.041, unpaired t test) in triazolam treated rats only.

**Conclusion:** The upregulation of grp94, fra-2 and egr-3 during RS is not time of day dependent. Some but not all of these molecular correlates of RS are produced by GABAergic hypnotics.

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0090

**Respiratory Disturbance Induced By Glutamate Injection Into The Intertrigeminal Region Is Abolished By An NMDA Receptor Antagonist In Rats**

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**Introduction:** Respiratory disturbance, including apnea, can be induced by microinjection of glutamate (GLU) into the intertrigeminal region (ITR) of the lateral pons in rats. Previously, we antagonized this effect by microinjection of kynurenic acid (KYN), a broad spectrum GLU receptor antagonist. The aim of the present experiment was to determine whether this effect can be abolished by a specific NMDA receptor antagonist AP5.

**Methods:** Respiratory movements were recorded in 7 Sprague Dawley rats anesthetized with ketamine/xylazine (80/5 mg/kg i.p.). In 4 rats, 3-barrel micropipettes were filled with GLU (10mM), AP5 (1mM) and oil red-O dye. In the other 3 rats, AP5 was replaced with KYN (50mM). At ITR sites, microinjection of GLU produced immediate apnea followed by tachypnea. After recovery of the breathing pattern, AP5 or KYN was microinjected, followed by an additional GLU microinjection. The respiratory response was quantified as coefficient of variation for breath duration (CVTT) over 30 s intervals during baseline, and immediately preceding and following each microinjection.

**Results:** The mean values of CVTT before all injections, reflecting baseline pattern variability, were equivalent in the two groups of rats (x=2.86; p=0.72, Kruskal Wallis ANOVA). GLU injection significantly increased CVTT by 908% (t=4.04; p<0.03) in animals subsequently injected by AP5 and by 636% (t=9.6; p=0.01) in the group of rats injected by KYN. These increases were equivalent (z=0.35; p=0.72). AP5 (t=1.55; p=0.22) and KYN (t=0.33; p=0.77) did not impact CVTT, but each antagonist fully blocked GLU induced respiratory disturbance (CVTT remained equivalent to preinjection levels; p>0.25 for AP5 and KYN).

**Conclusion:** NMDA receptor mechanisms are important for ITR induced respiratory disturbance.

This work was supported by NIH Grants HL70870 and AG16303.

0091

**Muscarinic-2 And Orexin-2 Receptors On GABAergic And Other Neurons Of The Mesopontine Reticular Formation**

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**Introduction:** Acetylcholine (ACh) and its action through muscarinic type 2 receptors (M2R) in the mesopontine reticular formation (MPRF) play a key role in initiating paradoxical sleep (PS). Conversely, orexin (Orx) and its action through Orx 2 receptors (Orx2R) play a critical role in preventing the occurrence of PS and associated muscle atonia, as evident by the appearance of narcolepsy in absence of Orx or the Orx2R. Within the MPRF, ACh and Orx may act upon reticular neurons at different levels subserving different roles or upon GABAergic neurons that serve to inhibit reticular neurons, including those which generate PS. The aim of the present study was to examine by immunohistochemical staining the presence of M2R and Orx2R on GABAergic and other neurons of the MPRF.

**Methods:** Brains of adult Wistar rats were employed for dual and triple immunofluorescent staining of M2R and/or Orx2R neurons with glutamic acid decarboxylase (GAD) or with neuronal nuclei (NeuN).

**Results:** M2R immunostaining was evident over many GAD+ cells, particularly those located rostrally, and it was evident over a large number of NeuN+ neurons through the mesencephalic, oral pontine and caudal pontine reticular fields. In contrast, OrxR2 was expressed in a small number of GAD+ cells, but was expressed in a substantial number of NeuN+ neurons, particularly large reticular neurons located caudally, some of which were also immunostained for the M2 receptor.

**Conclusion:** Through M2R, which are associated with hyperpolarizing responses, ACh appears to influence many neurons in the MPRF. It could initiate PS by inhibiting particular GABAergic neurons that normally inhibit PS-generating cells. It could also exert an inhibitory influence upon large reticular neurons that normally facilitate muscle tone. Through Orx2R, which is associated with depolarizing responses, Orx may act predominantly upon the same large reticular neurons to facilitate muscle tone during waking and prevent PS.

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0092

**Functional Neuroanatomy Of Gamma-Hydroxybutyrate Action**

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**Introduction:** Gamma-hydroxybutyrate (GHB) is a hypnotic compound used in the treatment of narcolepsy/cataplexy (Xyrem®, Orphan Medical). GHB has been shown to reduce sleep latency and fragmentation, and enhance slow wave activity, in contrast to benzodiazepine hypnotics, which suppress slow wave activity. Endogenous GHB is synthesized from the inhibitory neurotransmitter GABA and acts as an agonist at GABAB receptors. The neural mechanisms of action underlying the hypnotic response to GHB are not known, although it is hypothesized that
GHB interacts with known sleep-regulating pathways such as the hypocretin (Hcrt, also known as orexin) system. In the present study, we used the immediate-early-gene product Fos as a marker of neuronal activation, to determine whether behavioral state-regulating neuronal groups are activated/deactivated by GHB administration.

**Methods:** Xyrem® (300 mg/kg, i.p.) or sterile saline was administered to rats (adult male Harlan Sprague-Dawley, n=8 per group) at ZT3. Rats were sacrificed 60-90 min following the injection and perfused with fixative. Brains were removed, equilibrated in sucrose, and sectioned on a freezing microtome. Fos and Hcrt immunohistochemistry (IHC) was performed on 30 um brain sections. Fos-immunoreactive (-ir) neurons contained black precipitate (Ni+-DAB in the nucleus, and Hcrt-ir neurons contained amber/brown precipitate in the cytoplasm (DAB). Fos/Hcrt-ir neurons contained both. Cell counts (Hcrt-ir and Fos/Hcrt-ir neurons) were made in the perifornical hypothalamus at 3 rostrocaudal levels within a 400 x 200 um counting box that was consistently placed with the fornix at the bottom center of the box. Counts were averaged and t-tests were performed to assess significant differences among treatment groups.

**Results:** Both groups showed a mixture of Fos/Hcrt-ir and Hcrt-ir neurons. The total number of Hcrt-ir neurons did not differ between groups. No difference was seen in the proportion of Hcrt-ir neurons that were Fos/Hcrt-ir, which ranged from 7-31% (mean = 17.9 ± 3.7) for saline and 6-40% (mean = 24.3 ± 4.2) for GHB.

**Conclusion:** Our results indicate that decreased Fos activity does not occur in the Hcrt neuron population during GHB-induced sleep, suggesting that many Hcrt neurons are active during this state. It remains to be determined whether differences might exist within subregions of the Hcrt population, and what effects are seen in other sleep-modulating neuronal groups.

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**0093**

**Prenatal Ethanol Exposure Changes Non Rapid Eye Movement Sleep In Adult Male Rats**

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**Introduction:** Abnormal sleep patterns are observed in human infants exposed to prenatal alcohol. In female rats prenatal exposure to alcohol results in a reduction in rapid eye movement sleep (REMS) in juvenile and adults. At present there is little additional evidence either in human, rodents or male rats about the nature, extent, or duration of non-rapid eye movement sleep (NREMS) sleep in adults following prenatal exposure to alcohol. In the present study we determined the changes in NREMS and REMS in adult male Sprague-Dawley (SD) rats after they had been exposed to alcohol prenatally.

**Methods:** Pregnant female SD rats were treated with ethanol (6% in liquid diet) from day 8 to day 20 of gestation. Controls were pair fed liquid diet. At birth, the offspring were counted, weighed, and culled to 8 pups per litter and returned to the dam. The offspring were weaned at 21 days of age, separated by gender, and group housed (2-3 per cage). The rats were kept on a 12:12 hr light/dark cycle at 23 ±2 C. Surgery for electrocorticogram and intracerebroventricular canula implantation was done as described before (Kubota et al 2002) at 8-10 months of age. After recovery from surgery, rats were placed in sleep-recording chambers, acclimated for 3 days, and then 23 hour sleep recordings were done.

**Results:** We found a significant increase of NREMS in both light and dark cycle in fetal alcohol exposed males compare to males from non alcohol pair-fed mothers (ANOVA, p=0.0045, N=7). There was no difference in REMS duration or the spectral power density (0.5-4 Hz) in either NREMS or REMS.

**Conclusion:** Prenatal exposure to alcohol can cause permanent changes of sleep in male SD rats.

**Grants AA 13248, and NS 25378 and NS 31453.**

**0094**

**Sleep Alterations In Ob/Ob Mice Are Reversed With Chronic Leptin Repletion**

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**Introduction:** Recent data from epidemiological, as well as experimental human and animal studies indicate that sleep loss is associated with alterations in metabolic regulation. Leptin is a critical adiposity signal, and levels of this hormone are decreased following sleep deprivation. In this study, we examine sleep in the ob/ob mouse, a well-characterized rodent model of leptin-deficient obesity, hyperphagia, hyperglycemia, hyperinsulinemia, and insulin resistance.

**Methods:** Male C57Bl/6J (N=6) and ob/ob (N=6) mice (3-4 months of age) were maintained on a 12L:12D cycle and were implanted with EEG/EMG electrodes and a transmitter for body temperature recording. Animals underwent 48-hr of baseline recording following 2 weeks of continuous saline administration (subcutaneous osmotic mini-pump) and after 2 weeks of continuous leptin (100μg/kg/day) administration.

**Results:** Following saline administration, ob/ob mice had significantly higher amounts of 24-hr NREM sleep time compared to wild-type animals. Additionally, ob/ob mice had significantly more sleep fragmentation (measured by stage shifts, p<.05) and lower body temperature (p<.01). Interestingly, leptin administration decreased NREM sleep time in ob/ob mice (saline, 49.7±1.4 vs. leptin 44.3±2.0, p<.01), without changing sleep time in wild-type animals (saline, 42.6±1.4 vs. leptin, 44.8±2.0%, NS). In ob/ob mice, leptin administration increased REM sleep time (p< .01), decreased the number of stage shifts (p<.05) and increased body temperature (p<.05) but did not affect these measures in wild-type controls.

**Conclusion:** These data show that leptin deficiency is associated with a number of alterations in sleep-wake regulation. Following chronic leptin administration, the sleep-patterns in ob/ob mice are corrected and comparable to wild-type animals. Leptin may represent an important mechanism that communicates information about peripheral metabolic status to hypothalamic and brainstem regions involved in sleep-wake regulation.

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**0095**

**Basal Forebrain GABAergic Neurons Relays Pontine Signals To The Neocortex And Hippocampus To Activate EEG During REM Sleep**

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**Introduction:** Although it is generally believed that the thalamus relays signals from the pons to activate the EEG during REM sleep, this assertion has never been proven. On the other hand, the basal forebrain contains the two major classes of corticopetal neurons: cholinergic and GABAergic neurons. It is not clear how and whether these neurons are involved in the control of REM sleep, or if they are, how REM signals reach the basal forebrain.

**Methods:** Lesions were placed in the thalamus with ibotenic acid and in the basal forebrain with orexin-saporin or 192-saporin. To identify the pathway from the pontine region to the basal forebrain, we injected a ret-
rograde tracer, CTb, into the basal forebrain.

**Results:** Large thalamic lesions did not affect sleep-wake behavior or EEG patterns. Moreover, Fos expression in athalamic rats following wakefulness showed the same high levels in the neocortex and arousal systems as in waking controls. Basal forebrain lesions caused a significant slowing in EEG, doubling delta power during wakefulness and REM sleep, compared to the same rats prior to the lesions. These rats showed very low levels of Fos expression in the cerebral cortex after waking behavior, even though high levels of Fos expression were seen in the thalamus and other arousal systems. By contrast, selective destruction of cholinergic neurons by 192-saporin did not cause any alteration in EEG pattern or sleep-wake cycle, and showed the same high levels of Fos expression in the cerebral cortex and arousal systems as the waking controls. After injection of CTb into the medial septum or into the substantia innominata, retrogradely labeled cells in the REM-on region were concentrated in the pre-coeruleus region and most of these cells were glutamatergic.

**Conclusion:** In conclusion, we hypothesize that forebrain REM sleep originates from the pre-coeruleus region and is relayed to the cerebral cortex and hippocampus by non-cholinergic basal forebrain corticopetal neurons, resulting in cortical desynchronization and hippocampal theta rhythms.

**HL60292**

**0096**

**Intermittent Hypoxia Causes Deficits In Copulatory Erections Without Affecting Serum Testosterone Levels**

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**Introduction:** There is a strong clinical association between obstructive sleep apnea (OSA) and erectile dysfunction (ED). Hypogonadism has been hypothesized to be a cause of ED in OSA. However, the cause of ED in OSA is unclear, particularly given the numerous cardiovascular consequences, comorbid conditions or concomitant medications commonly seen in OSA patients that can directly influence erectile function. We recently reported that erectile activity significantly decreases in rats exposed to 8 weeks of intermittent hypoxia (IH). We now report on the effects of IH on copulatory erections and testosterone levels.

**Methods:** Twelve male rats were implanted with a telemetric transducer for chronic recordings of penile tissue pressure and erections. This technique has been validated for a recording of penile erections across behavioral states. After 4 days of continuous recordings, animals were placed into chambers that cycled O2 concentrations between 21% and 10% every 90 seconds during 12 hours of daylight (sleep period). Erectile activity was recorded for 8 weeks in the IH protocol. Mating and reflex erection tests were performed before and following 4 and 8 weeks of IH exposure. Testosterone levels were drawn at the same circadian time for all rats at the end of the study and compared with 6 room-air controls.

**Results:** Erectile activity in freely behaving rats decreased from 63.1±3.3 erections per day during baseline to 28.7±4.7 following 8 weeks of IH (p<0.001). We found a trend of fewer males achieving intromission with receptive females (8/12 in control, 6/12 at week 4, and 5/12 at week 8). An analysis of the erectile pressures during intromission demonstrated a decrease in the mean and maximum pressures during copulatory erections from baseline to week 8 post IH (mean pressure: 78.0±7.2 at baseline to 36.2±0.8 mmHg at week 8, p<0.05; maximum pressure: 415.0±22.7 at baseline to 346.5±81.9 mmHg at week 8, p<0.05). No differences in pressure parameters were observed regarding reflex-induced erections. Finally, total and free serum testosterone levels did not differ from controls.

**Conclusion:** IH lead to a significant decrease in 24-hour erectile activity and penile pressures during copulation, including a trend of fewer males achieving intromission, following 8 weeks of IH exposure. These changes occurred even though serum testosterone levels failed to differ from room-air controls. Our data suggest that IH may be a cause of ED in OSA independent of serum testosterone levels.

**Supported by NIH HL69932, HL63912, and the Sleep Medicine Research Foundation**

**0097**

**A Collection Of cDNAs Selective For The Hypocretin-Containing Neurons In Mice**

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**Introduction:** The identification of novel genes selective for hypocretinergic neurons is critical for our understanding of the etiology of hypocretin cell loss in narcolepsy. We used subtractive hybridization to isolate transcripts differentially expressed in wild-type (WT) versus hypocretin neuron-ablated narcoleptic mice (Tg) (orexin-ataxin-3 transgenic mice provided by Dr. Sakurai and bred at Stanford).

**Methods:** Multiple cDNA libraries were constructed from fresh cytoplasmic PolyA+ RNA isolated from dissected posterior hypothalami (WT and Tg, n =25/group). Directional Tag PCR Subtraction was applied. One µg of trace-labeled tagged target (WT) was hybridized with an excess of 40 µg of Driver cRNA (Tg) for 24h at 68C. Following hydroxylapatite chromatography, the single-stranded target cDNA was used as template for PCR and the amplicons were cloned to generate subtracted libraries.

**Results:** Validation of the subtraction process: 1) Real time PCR experiments showed that hypocretin expression was approximately 100 fold lower in Tg versus WT libraries, and demonstrated an enrichment of about 100 fold in subtracted versus WT libraries. Beta actin, an endogenous control gene, as well as MCH, a neuropeptide expressed in cells located in the vicinity of hypocretin-containing neurons were equally amplified in WT and Tg libraries and were absent in subtracted libraries. 2) Sequencing data: 1.5 % of the clones corresponded to hypocretin in subtracted libraries, indicating significant enrichment in hypocretin cell containing genes. Forty candidate genes (22 known; 18 unknown) were enriched, but most were less abundant than hypocretin itself in subtracted libraries. Whether these novel genes are selectively expressed in hypocretin-containing cells is currently under investigation (real time PCR; combined in situ hybridization and immunocytochemistry).

**Conclusion:** The high efficiency of the subtraction method, combined with the use of cell ablated models, may be ideal to identify novel low abundance transcripts in selected cell population. A series of candidates were identified and are being validated through functional analysis and possible involvement in human narcolepsy.

**0098**

**Ghrelin-Induced Sleep Responses In Ad Libitum Fed And Food-Restricted Rats**

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Introduction: Ghrelin is an endogenous ligand for the GH secretagogue receptor and stimulates GHRH release. GHRH is a part of a hypothalamic network regulating non-rapid eye movement sleep (NREMS). Ghrelin is produced by gastrointestinal endocrine cells and by hypothalamic neurons. Ghrelin may modulate sleep through stimulating GHRH system and/or food intake. Ghrelin-induced sleep responses in free-feeding and in feeding-restricted rats are reported here.

Methods: Rats received icv injections of physiological saline (baseline) and ghrelin (0.2, 1, 5 µg in 2 µl, n=8, n=6, n=9, respectively) at light onset. Another group of rats was injected with saline or ghrelin before dark onset (n=11, n=8, n=13, respectively). Sleep-wake activity, motor activity and brain temperature were recorded for 12 h. Food intake and behavioral responses after 1 µg ghrelin were also recorded during the light period. A third group of rats (n=5) was food-restricted for the entire recording period after injection of 1 µg ghrelin.

Results: Light onset injection of ghrelin suppressed NREMS and REMS for 1-2 h followed by significant increases in NREMS in response to the 1 µg dose. Ghrelin administration at dark onset also elicited NREMS and REMS suppression for 1-2 h but the effect was not as marked as in the light period. The 5 µg dose given at dark significantly increased NREMS in post-injection hours 3-12. Food intake was higher during the first post-injection h. In the food-restricted rats, ghrelin did not suppress NREMS or REMS in 1-2 h post-injection nor was NREMS affected in later post-injection hours, although a significant REMS decrease was observed.

Conclusion: The results suggest a dose-dependent somnogenic effect of central administration of ghrelin. Data from food-restricted animals show that feeding activity may have an important role in the immediate sleep suppression and in the subsequent sleep-promoting effects of ghrelin.

OTKA T043156 and ETI 10304/2003 to FO and NIH NS27250 to JK.

0099

Median Preoptic Nucleus Modulates C-FOS Expression In Hypocretin And Other Perifornical-Lateral Hypothalamic Area Neurons In Anesthetized Rats

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Introduction: The perifornical-lateral hypothalamic area (PF-LHA) has been implicated in the regulation of behavioral arousal. The PF-LHA contains several cell types, including neurons expressing the peptides, hypocretin (HCRT) and melanin-concentrating hormone (MCH). A majority of neurons within PF-LHA, including HCRT neurons, are active during waking and quiescent during non-rapid eye movement sleep. The median preoptic nucleus (MnPN) of the preoptic region is a sleep-promoting structure. Sleep-active neurons within MnPN are GABAergic and MnPN constitutes a significant source of afferents to the PF-LHA. We hypothesized that MnPN neurons promote sleep, in part, by inhibiting wake-active neurons within the PF-LHA.

Methods: Experiments were conducted on Ketamine + Xylazine (80 mg/Kg + 10mg/Kg) anesthetized rats. Anesthetized rats were injected with artificial cerebrospinal fluid (aCSF; injected volume 0.2 µl in 10 min; n=3) or muscimol (10 mM, n=4), a GABA receptor agonist, into MnPN and sacrificed after 90 min of microinjection. The numbers of HCRT+, MCH+ and non-HCRT/non-MCH neurons exhibiting Fos-IR also increased after muscimol microinjection into MnPN (165±50 vs. 68±19). Very few MCH+ neurons exhibited Fos-IR after either aCSF or muscimol microinjections into MnPN (0.96±0.21 vs. 0.64±0.12).

Conclusion: These preliminary results suggest that MnPN neurons exert inhibitory influences on PF-LHA neurons, including a subpopulation of HCRT neurons, during anesthesia. These findings support the hypothesis that PF-LHA neurons are inhibited by MnPN GABAergic neurons during spontaneous sleep. These results further suggest that MCH neurons are not under MnPN inhibitory control.

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0101

Distribution Of Neurons In The Preoptic Hypothalamus That Project To Both The Perifornical Lateral Hypothalamus And The Locus Coerulescens

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Introduction: The preoptic hypothalamus contains neurons that display...
assessed the effect of the GABAA receptor antagonist, gabazine, on hypo-
Using this model, we now tested whether release from endogenous
Introduction:
Inhibition mediated in the posterior hypothalamus by
Department of Animal Biology and Center for Sleep and Respiratory
were processed for visualization of tracers and immunostaining for GAD.
Methods:
were placed for visualization of tracers and immunostaining for GAD.
Results:
In two cases. Double-labeled, FITC+RhoRed, neurons were most frequent-
ventrolateral preoptic area (VLPO). VLPO did contain several neurons
Localized tracer injections were placed in the PFLH and LC in
to the locus coeruleus (LC). The goals of the present study
were to determine if individual preoptic area neurons project to both the
and to characterize the distribution of dual projection neu-
were found that, in hypothalamic slices

Category A—Basic Neuroscience

elevated discharge rates during sleep compared to waking, and neurons
that are immunoreactive (IR) for c-Fos protein following sleep. Sleep-
related Fos-IR is co-localized with glutamic acid decarboxylase (GAD), a
marker of GABAergic neurons. Anatomical tracer studies demonstrate
projections from the preoptic area to the perifornical lateral hypothalamus
(PFLH) and to the locus coeruleus (LC). The goals of the present study
were to determine if individual preoptic area neurons project to both the
PFLH and LC, and to characterize the distribution of dual projection neu-
rons within the preoptic area.

Methods: Under anesthesia and stereotaxic guidance, rats received tracer
injections targeting the PFLH and LC. FITC fluorospheres were injected
into the PFLH (volume 0.2µl, delivered over a 20 min period) using a com-
puter-controlled pressure injection system. Rho-Red fluorospheres (0.2 µl)
were similarly injected into the LC. Rats were permitted a 10 day survival
period after injections. One series of sections (40µ in thickness) was col-
glected to localize tracer injections sites. Sections through the preoptic area
were processed for visualization of tracers and immunostaining for GAD.

Results: Localized tracer injections were placed in the PFLH and LC in
two cases. Double-labeled, FITC+RhoRed, neurons were most frequent-
ly observed in the median preoptic nucleus (MnPN), the dorsal lateral
preoptic area (DLPO) and the bed nucleus of the stria terminalis (BnST).
Few double-labeled cells were observed in the medial preoptic area or the
ventralateral preoptic area (VLPO). VLPO did contain several neurons
retrogradely labeled from LC. Triple-labeled, FITC+RhoRed+GAD, neu-
rons were observed in the MnPN, DLPO and BnST, but in all areas com-
prised only 20-40% of the dual projection neurons. Triple-labeled cells
were most numerous in the MnPN.

Conclusion: Dual projection neurons in the preoptic area may function to
co-ordinate sleep/wake state-dependent changes in neuronal activity in the
PFLH and LC.

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0102

Endogenous Activation Of GABA<sub>A</sub> Receptors In Posterior
Hypothalamic Slices In Vitro Decreases GABA<sub>A</sub> Receptor Subunit
MRNA Expression

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Introduction: Inhibition mediated in the posterior hypothalamus by
GABA<sub>A</sub> receptors contributes to the regulation of sleep. We previously
found that, in hypothalamic slices in vitro, exogenous activation of
GABA<sub>A</sub> receptors by muscimol reduces mRNA levels for selected
GABA<sub>A</sub> receptor subunits in the hypothalamic perifornical (PF) region.
Using this model, we now tested whether release from endogenous
GABAergic inhibition also elicits transcriptional changes. For this, we,
assessed the effect of the GABA<sub>A</sub> receptor antagonist, gabazine, on hypo-
thalamic expression of genes important for GABAergic transmission.

Methods: Hypothalamic slices, 600 µm thick, were obtained from the level
caudal to the optic chiasm from six adult rats. One half of each slice was
superfused for 90 min at 34°C with a medium containing 20 µm gabazine
and 20 µm GABA uptake blocker, NO-711, and the other with NO-711
only. Two 700 µm punches were cut from each half-slice, one from the PF
region and the other from adjacent dorsomedial/paraventricular (DM)
region. RNA was extracted from each sample, quantified, reverse-trans-
scribed and subjected to quantitative PCR. Individual cDNAs were quanti-
fied as the number of copies per 1 ng of total RNA in each sample.

Results: In the PF region, the mRNA levels for the <i>α</i>, <i>β</i>1, <i>β</i>3 and
<i>α</i> subunits of GABA<sub>A</sub> receptor and for GAD-65 were 2-3 times higher
following incubation with gabazine than with NO-711 only (percentage
increases: 196, 203, 178, 177, 300, and 178%, respectively; <i>n</i>=6 pairs,
p=0.01-0.04 each). The changes for the <i>α</i>1 and <i>α</i>2 GABA<sub>A</sub> receptor sub-
units, GAD-67, prepro-orexin and tubulin were not significant. In the DM
region, the basal levels of all these mRNAs except prepro-orexin were
similar to the PF region, but none was significantly altered by gabazine.

Conclusion: Endogenous GABA causes a transcriptional downregulation
of perifornical GABA<sub>A</sub> receptors and GAD-65 in vitro. The changes
induced by gabazine are generally opposite to those that we previously
observed with muscimol. Taken together, these data suggest that the
strength of GABAergic inhibition is regulated in the PF region by local
feedback mechanisms. This may also play an important role in the regu-
lation of the timing and intensity of sleep in vivo.

HL-071097 and ASMF #26-CA-04

0103
WITHDRAWN

0104

Urethane Differentially Modulates Subtypes Of Ventral Tegmental
Area Non-Dopaminergic Neurons

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Introduction: Presumed VTA GABAergic cells have been linked to corti-
ical and behavioral arousal, displaying higher discharge rates during periods
of cortical arousal in the freely-moving animal. Anatomical evidence indi-
cates projections to the basal forebrain area. Urethane, widely used in non-
survival preparations due to its relatively minimal effects on autonomic
function, is thought to enhance GABA function. We recorded the activity
of VTA neurons while simultaneously recording the cortical electroen-
cephalogram (EEG) in anesthetized rats under both halothane and urethane.

Methods: Tracheotomized adult male Sprague-Dawley rats were placed in
a stereotaxic device and maintained under halothane (37 oC core body
temp.). A skin incision and skull openings permitted access by glass
micropipettes. Fast firing neurons in the VTA exhibiting short duration
action potentials were identified on-line, and firing rates were recorded on
computer. The cortical EEG (obtained from skull screws) was also digi-
tized and recorded. Urethane (1.4g/kg in saline, ip) was injected after sta-
ble baseline neuronal recordings were obtained under halothane.
Halothane was discontinued and EEG and neuronal discharge were
recorded continuously.

Results: Non-dopaminergic (GABAergic) neurons exhibited at least 3
distinct types of response to urethane. A “stabilization” of irregular firing
was observed in one group of cells, while other cells displayed a dramat-
ic reduction in firing rate. The third major type of response, often seen in
slower-firing cells, was characterized by an apparent entrainment of neu-
ronal discharge to the phasic, spiking cortical EEG wave pattern produced
by urethane. This relationship was not seen under halothane.

Conclusion: Urethane significantly affects firing patterns and firing rates
of subgroups of VTA non-dopaminergic neurons. In particular, one sub-
type of VTA neurons begins firing in synchrony with the EEG under ure-
thane. Experiments to determine the mechanism by which urethane exerts
these effects are underway.

DA12444, MH62261
**0105**

**Selective Spatial Learning Impairment Following Randomly Timed Auditory Stimulation Within The Sleep Period**

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**Introduction:** There is mounting evidence that sleep serves a role in learning. For example, total sleep or selective REM sleep deprivation results in learning impairment on spatial tasks. Alternatively, increasing REM sleep by auditory stimulation has been shown to result in improved learning on certain tasks in humans. The effects of NREM sleep manipulations on spatial learning are unknown, however presentation of a conditioned stimulus during NREM results in learning impairment (Hars and Hennevin, 1987). We tested the hypothesis that randomly timed auditory stimulation across states, including NREM, would impair spatial learning.

**Methods:** Two groups of male F344 rats were tested on the Poe 8-box spatial task for 20 min/day and a procedural task for 10 min/day across 7 days. One group (n=5, stim) received auditory stimulation (80 dB clicks at 0.2 Hz) randomly with respect to behavioral state for 4 hours following training, while another group (n=5, control) had no manipulation following training. More than 10 days prior, animals were implanted with EEG and EMG electrodes under surgical anesthesia. After recovery, signals were recorded while rats were in their home cage in order to determine sleep-waking state.

**Results:** Auditory stimulation across the 4 hour period occurred mostly during NREM sleep and waking. Animals in the stim group showed delayed learning compared with controls. However, there was no difference between groups on learning the procedural task.

**Conclusion:** Auditory stimulation across sleep/waking states following daily training disrupted learning of a spatial task, but not learning of a procedural task. The impairment may have been due to the disruption of NREM sleep by the stimulation, although some waking effect cannot be ruled out. It is unlikely that stimulation during REM is responsible for the disruption as we have previously shown that auditory stimulation during REM sleep results in normal to enhanced spatial learning.

**Supported by MH60670 and the Department of Anesthesiology**

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**0106**

**Diurnal Fluctuations In Ventral Tegmental Area Impulse Activity**

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**Introduction:** The ventral tegmental area (VTA) contains dopamine (DA) and GABA neurons known to be involved in motivated behaviors, and more recently, implicated in behavioral state regulation. These phenome- na are also influenced by circadian factors. Our aim was to explore possible diurnal fluctuations in VTA neuron impulse activity as a potential mechanism for the circadian influence on these behaviors.

**Methods:** Extracellular recordings of VTA neurons were obtained from male neonatal rat pups assigned as audio exposure (AE) and control (AC) groups. At age 14 (P14), rats were implanted with EEG and EMG electrodes 1. 48 hours polygraphic recording and audio treatment were started the next day. During the treatment, loud rock music was played for 2 hours followed by 2 hours without music. The sound level was 90dB -100 dB in the cage of AE rats and less than 55 dB in the cage of AC rats during music playing time. After treatment and recording, rats were sacrificed and brain tissues were collected for the measurement of BDNF and CRF using ELISA method.

**Results:** EEG Spectrogram showed that EEG power was decreased in Delta (-22.24%), Beta (-22.96%), Delta (-43.04%) and Theta (-21.03%) bands in the period of audio-on compared with that of audio-off in AE rats. These alterations were not seen in AC rats. The mean hypothalamic levels of CRF were 16.42 ng/mg in AC rats and 15.24 ng/mg in AE rats. The mean hippocampal levels of BDNF were 13.94 pg/mg in AC rats and 11.18 pg/mg in AE rats. The AE rats had a 20.15% decrease in BDNF compared with the AC rats.

**Conclusion:** Over exposure to high level music on EEG and brain levels of CRF and BDNF in neonatal rats.

**Supported by MH60670 and the Department of Anesthesiology**

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**0107**

**Alterations Of EEG Power Band And Brain Levels Of BDNF In Neonatal Rat Over-Exposed To High Level Music**

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**Introduction:** Increased environmental stimulation such as loud sound, white noise impacts human health significantly. Excessive or extended exposure to entertainment systems may also impact human health. This may be critical if it is applied in the developmental period, which has a much higher neural plasticity. The current study reports the effects of over exposure to high level music on EEG and brain levels of CRF and BDNF in neonatal rats.

**Methods:** Male neonatal rat pups were assigned as audio exposure (AE) and control (AC) groups. At age 14 (P14), rats were implanted with EEG and EMG electrodes 1. 48 hours polygraphic recording and audio treatment were started the next day. During the treatment, loud rock music was played for 2 hours followed by 2 hours without music. The sound level was 90dB -100 dB in the cage of AE rats and less than 55 dB in the cage of AC rats during music playing time. After treatment and recording, rats were sacrificed and brain tissues were collected for the measurement of BDNF and CRF using ELISA method.

**Results:** EEG Spectrogram showed that EEG power was decreased in Alpha (-22.24%), Beta (-22.96%), Delta (-43.04%) and Theta (-21.03%) bands in the period of audio-on compared with that of audio-off in AE rats. These alterations were not seen in AC rats. The mean hypothalamic levels of CRF were 16.42 ng/mg in AC rats and 15.24 ng/mg in AE rats. The mean hippocampal levels of BDNF were 13.94 pg/mg in AC rats and 11.18 pg/mg in AE rats. The AE rats had a 20.15% decrease in BDNF compared with the AC rats.

**Conclusion:** Over exposure to high level music suppresses power of all EEG band particularly the delta band and may also suppress hippocampal BDNF but not affect hypothalamic CRF.

**Work was supported by NIMH grant MN 069854 to Feng. 1. Feng P, Vogel GW. A new method for continuous, long-term polysomno- graphic recording of neonatal rats. Sleep 2000; 23:9-14.**
0108
EEG Slow-Wave Synchronization During Sleep
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Introduction: Sleep EEG shows nonlinear structure for briefs periods during NREM, correlated with the appearance of the so-called “cyclic alternating pattern” (CAP). The aim of this study was to analyze EEG spatial synchronization to test the hypothesis that the occurrence of CAP induces high levels of synchronization in the slow-wave sleep activity.

Methods: We characterized the different levels of EEG synchronization during sleep (in the 0.25-2.5 Hz band) of 5 normal controls by means of the synchronization likelihood (SL) algorithm and analyzed its oscillations by means of the determined fluctuation analysis (DFA).

Results: We found higher levels of SL during CAP sleep than during non-CAP with a small but significant difference between its A and B phases. A high degree of oscillations corresponding to the single EEG slow-wave elements. DFA showed the presence of 2 linear scaling regions in the double-logarithmic plot of the fluctuations of SL level as a function of time scale. This indicates the presence of a characteristic time scale in the underlying dynamics which was very stable among the different subjects (1.2-1.3 s). We also computed the DFA exponent of the 2 scaling regions; the first, with values ±1.5, corresponded to fluctuations with period 0.096-0.77 s and the second, with values ±1, corresponded to fluctuations with period 1.54-24.65 s. Only the first exponent showed different values during the different sleep stages.

Conclusion: All these results indicate a different role for each sleep stage and CAP condition in the EEG synchronization processes of sleep which may play a complex structure correlated with the neurophysiological mechanisms. Very slow oscillations in spatial EEG synchronization might play a critical role in the time-long range EEG correlations during sleep which might be the chain of events responsible for the maintenance and correct complex development of sleep structure during the night.

0109
Effects Of Low-Dose Acetazolamide On Sleep And Sleep-Disordered Breathing During A Controlled Trial At High Altitude
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Introduction: Acetazolamide is widely used to treat acute mountain sickness; however, a common side effect at high doses is paresthesias in the extremities that may adversely affect climbing skills. At base camp of Mt. Everest (17,800 ft), a randomized, double-blinded, placebo-controlled study was conducted to determine if a single low dose of acetazolamide at bedtime would improve sleep and sleep-disordered breathing (SDB) yet minimize paresthesias and other side effects.

Methods: Twenty-two subjects at least 18 years old and in good health were consented and enrolled. Exclusion criteria included sulfa allergy, high-dose aspirin use, low blood sodium or potassium, kidney and liver disease, glaucoma, and pregnancy. Validated sleep questionnaire and Epworth data were obtained at baseline, as well as ambulatory sleep respiratory data (Stardust, Respironics). Following ascent to base camp, subjects were randomized to either placebo or 125 mg of acetazolamide at bedtime. Sleep log and actigraphy data were then collected for 10 nights and ambulatory sleep respiratory data for 3 nights.

Results: There were 21 men and 1 woman with a mean age of 40.3 years. They self-described their sleep at least “fairly good” and denied SDB symptoms. The Epworth scores for the two groups were not statistically different with an overall mean of 7.7. The actigraphy data revealed improved total sleep time*, number of awakenings, sleep latency, sleep efficiency*, and wake after sleep onset* (* p < 0.05) for those on acetazolamide vs. placebo. Subjects on acetazolamide reported better sleep in 4 out of 5 sleep parameters (except for sleep latency) compared to their actigraphy data vs. subjects on placebo who reported better sleep in only their number of awakenings. For the ambulatory sleep respiratory data, there were no differences in the number of Cheyne-Stokes-like events, apneas, hypopneas, or desaturations at base camp between the two groups. The subjects had mild SDB with apnea-hypopnea indices for the acetazolamide and placebo groups of 8.0 and 8.5, respectively. No significant side effects were reported in either group.

Conclusion: Low-dose acetazolamide had no effect on SDB compared to placebo at high altitude. However, subjects reported better sleep with acetazolamide, a finding that was confirmed by actigraphy. In those without risk factors for SDB who can tolerate the development of mild SDB at high altitude, low-dose acetazolamide may provide benefit in improving sleep with low probability of side effects.

Supported by Respironics, Inc.

0110
As Predicted By The Neuronal Transition Probability Model The Time Between Sleep Onset & Maximum Spindle Power Is Equal To The Time Constant Of The Concurrent Fall In Beta Power
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Introduction: Sequential spectral analysis data show that power in the beta band (β) of sleep EEG falls rapidly after sleep onset while there is a concurrent rise in spindle power (σ) reaching a maximum while delta is still rising. Only the neuronal transition probability (NTP) model has proposed a possible explanation for this relationship. The model predicts that the fall in β should be exponential e–t/τ and that the delay between sleep onset and the arrival of the σ maximum should be identical to the time constant τ of that exponential. The shape of the σ time-course is given by the model as τ(e–t/τ – e–τ) / (τ – p) with τ ≈ p, which gives a maximum σ power at time t = τ. Here we focus on the β and σ time-courses in the 25 min interval following sleep onset, with the aim of measuring these time delays and verifying the predictions of the model.

Methods: Data were obtained from the F4-CZ derivation of 14 healthy subjects aged 20-30 years. For each subject, power spectra were computed by FFT for consecutive 4-sec epochs over the range 0-30 Hz and the β (11-15 Hz) and σ (18-30 Hz) band time-courses extracted. Polynomial curves were fitted to individual subject β data to obtain the times at which they reached their maxima and hence the mean time and its standard error. Similarly, individual β data were fitted by exponential curves and combined to obtain a mean β time-constant with its error. Individual curves were then normalised to their maxima and combined to give normalised average time-courses for comparison with the theoretical curves obtained using these means.

Results: We show that the average time delay between sleep onset and the
0111  Alcohol Increases Nasal Resistance And P3 Latency Of The Cortical Evoked Response To Brief Pulses Of Negative Airway Pressure In Healthy Males And Females During Wakefulness

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Introduction: Alcohol has been shown to increase upper airway (UA) resistance and snoring in healthy males and augment the severity of sleep disordered breathing in obstructive sleep apnea patients. These findings are less consistent amongst female subjects. Alcohol has also been shown to impair cortical evoked potentials to non-stimuli. The aim of this study was to test the hypotheses that alcohol 1) decreases UA negative pressure genioglossus (EMGgg) reflex activation and increases UA resistance to a greater extent in males compared to females and 2) decreases the P3 (cognitive processing) component of the respiratory related evoked potential (RREP).

Methods: 19 healthy individuals (10 males) breathed via a nasal mask and pneumotachograph. UA negative pressure pulses (-12 cmH2O choanal pressure, 200 msec) were delivered via a computer-controlled rapid actuating solenoid valve system every 3-7 breaths during early inspiration before and 45-min after acute alcohol administration (1.5ml.kg-1 body weight of 100 proof vodka). EEG (C3-A1) was measured to monitor wakefulness and record RREPs. UA collapsibility (peak choanal-epiglottic pressure), EMGgg (bipolar intramuscular electrodes) reflex responses (latency and peak amplitude) and the P3 component of the evoked response (peak latency and amplitude) were generated by ensemble averaging ~60 pulses per subject in each condition. UA resistance was measured (slope of the change in pressure versus flow) across the collapsible portion of the UA during relaxed breathing. Between gender effects were explored before and after alcohol using ANOVA for repeated measures.

Results: Neither alcohol nor gender affected baseline EMGgg, EMGgg reflex responses or UA collapsibility to negative pressure pulses. Nasal resistance significantly increased after alcohol (1.3±ε 0.16 vs. 1.8±ε 0.18 cmH2O.L-1.s, p=0.04), but there were no gender differences. Pharyngeal and total UA resistance remained unchanged after alcohol in both genders. RREP P3 latency was prolonged following alcohol (275.3± 7.6 vs. 291.1± 7.7 msec, p=0.03).

Conclusion: These data support previous findings that alcohol increases nasal resistance, an effect likely to be a key contributor to alcohol-induced sleep disordered breathing. These data also suggest that cognitive processing of respiratory neural information is delayed with alcohol. Further experiments are required to determine whether early components of the RREP, reflecting primary respiratory afferent traffic, are affected.

NIHMRC of Australia

0112  Onset Of Human Tongue Retractor Muscle Activity Is Independent Of Negative Pressure During Hypoxia/Hypercapnia

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Introduction: Preliminary studies in humans have shown that tongue retractor muscles are activated in response to changes in chemical stimuli (hypoxia/hypercapnia), independent of the application of negative pressure. Given this finding, we were interested in determining whether activation of human retractor muscles precedes the initiation of negative pressure on a breath-by-breath basis and whether these muscles are activated earlier in response to alterations in chemical stimuli. Moreover, we were interested in determining if tongue retraction is coupled to the onset of retractor muscle activity.

Methods: Fine wire electrodes were inserted into the interdigitation between the styloglossus and hyoglossus muscles in seven (5 males and 2 females) healthy subjects in the supine position. A Millar catheter was inserted into the epiglottal region of the upper airway and a fiber-optic bronchoscope was positioned 2-3 cm above the tip of the epiglottis to capture video images of the retroglossal lumen. Subjects breathed through a sealed face mask that was attached to a pneumotachometer that measured inspiratory and expiratory flow and volume. Mask pressure, epiglottal pressure, end-tidal oxygen and carbon dioxide levels, oxygen saturation, as well as, raw and integrated electromyographic (EMG) activity from the retractor muscles were recorded under conditions of normoxia and hypoxia/hypercapnia (10 % oxygen and 7 % carbon dioxide).

Results: Phasic retractor muscle activity was not observed during normoxia. During hypoxia/hypercapnia, phasic retractor activity (peak amplitude = 14.5 ± 3.8 % of maximum) was observed consistently and was characterized by a decrementing discharge pattern. The onset of discharge preceded the negative deflection in epiglottic pressure (-367.1 ± 109.5 ms). At the onset of retractor muscle activity the tongue area within the bronchoscope field of view was increased compared to the area at the termination of retractor activity (30.1 ± 4.3 vs. 20.4 ± 3.7 mm2 x 102). The increase in tongue area coincided with a decrease in epiglottic cross-sectional area.

Conclusion: We conclude that retractor muscles are activated during hypoxia/hypercapnia and that activation of these muscles occurs prior to the generation of negative pressure. Additionally, a brief tongue retraction might coincide with the onset of retractor muscle activity prior to forward movement of the tongue during inspiration.

VA Merit, American Heart Association and National Institutes of Health

0113  The Autonomic Perspective Of Sleep Stages

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Introduction: Transitions between sleep states are not always well delineated, and some overlap in electrophysiological, cognitive and behavioral
patterns is frequently encountered during both normal and abnormal sleep. It is well accepted that autonomic and cardiorespiratory regulation are essentially different during Wakefulness, NREM and REM. Our objective was to evaluate the usefulness of the quantitative parameters representing autonomic function during sleep that can be readily derived non-invasively from the analysis of Heart Rate Variability (HRV).

**Methods:** 12 Normal Adults (AN); 12 Adults with Obstructive Sleep Apnea (OSA); 10 Normal Children (CN); 11 Children with OSAS (COSA) underwent sleep studies scored according to gold standards. Autonomic function was evaluated by applying time-dependent HRV analysis and computing the following parameters: VLF- vasomotor, LF- combined sympathetic-parasympathetic, HF- mainly parasympathetic modulations; LF/HF - sympathovagal balance. Paired t-tests were performed for each parameter to compare different sleep stages. The distribution of each parameter was evaluated and compared between subject groups.

**Results:** Significant differences were detected in VLF and LF/HF between SWS and REM in all groups (* for p<0.05, paired t-test), indicating increased sympathetic vasomotor fluctuations and a predominantly sympathetic balance during REM. VLF and LF differed (*) between SWS and LS, but not between LS and REM, whereas HF was different(+) between LS and REM, but not between LS and SWS. The average values of VLF, LF during LS were between those during SWS and REM respectively. The average values of the same parameters during SWS and REM fall within 2STD from their averages during LS. AOSA showed increased sympathet-ic activity during all sleep stages (+) as compared to AN, whereas these differences were less obvious when comparing CN with COSA.

**Conclusion:** Autonomic control operates at different levels during SWS and REM, whereas LS displays overlapping SWS-REM characteristics. The differences are more accentuated in subjects of all ages with sleep disordered breathing. Thus non invasive evaluation of autonomic function during sleep adds another dimension to the evaluation of normal and abnormal sleep.

### 0114

**Gender Differences In SWA Response To A 3 Hour Sleep Delay In Healthy Adults**

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**Introduction:** Several studies have shown that sleep deprivation is associated with an increase in slow-wave activity (SWA) during non-rapid eye movement (NREM) sleep. Moreover there is a systematic relationship between SWA and the amount of prior wakefulness. Recent work has suggested that women may show a greater SWA response to sleep deprivation than men. The present study evaluated potential gender differences in SWA response to a 3 hour sleep delay.

**Methods:** Forty-seven medically-fit 20-40 year olds (27 men, 20 women) with no personal or family history of psychiatric illness participated in study. Subjects maintained an 11pm-6am schedule for 1 week prior to study, verified by diary and actigraphy, followed by three consecutive nights in the lab. Night 1 served as adaptation, followed by a baseline night and delay night (2am-9am). Seven hours of available sleep time were available throughout the protocol. Power spectral analysis quantified modulations; LF/HF - sympathovagal balance. Paired t-tests were performed for each parameter to compare different sleep states. The distribution of each parameter was evaluated and compared between subject groups.

**Results:** Significant differences were detected in VLF and LF/HF between SWS and REM in all groups (* for p<0.05, paired t-test), indicating increased sympathetic vasomotor fluctuations and a predominantly sympathetic balance during REM. VLF and LF differed (+) between SWS and LS, but not between LS and REM, whereas HF was different(+) between LS and REM, but not between LS and SWS. The average values of VLF, LF during LS were between those during SWS and REM respectively. The average values of the same parameters during SWS and REM fall within 2STD from their averages during LS. AOSA showed increased sympathet-ic activity during all sleep stages (+) as compared to AN, whereas these differences were less obvious when comparing CN with COSA.

**Conclusion:** Autonomic control operates at different levels during SWS and REM, whereas LS displays overlapping SWS-REM characteristics. The differences are more accentuated in subjects of all ages with sleep disordered breathing. Thus non invasive evaluation of autonomic function during sleep adds another dimension to the evaluation of normal and abnormal sleep.

### 0115

**End Tidal Carbon Dioxide In Sleep After Sleep Deprivation In Cat Orem JM, Geric M, Tilton Orem B**

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**Introduction:** End tidal CO2 levels increase from light to deep NREM sleep. We hypothesized that sleep deprivation caused by exposure to a cold environment would increase the amount and depth of subsequent deep NREM sleep and that this would increase end tidal CO2 levels.

**Methods:** Electrodes for recording electroencephalograms were implanted and attached to a headcap in 2 cats. A tracheostomy was also performed. The animals were studied 3 times wk-1 following 15 h of exposure to 10o, 30° or 50°F. A Latin Square design was used to vary these temperatures on days before recordings for 6 (2 Latin Square blocks) and 3 wks (1 Latin Square block) respectively for the two animals. Recording sessions were 3 h in duration and occurred within 2 h after release from the cold. A tracheal tube was placed through the fistula, and the head was immobilized atraumatically. Airflow, tidal CO2 , and EEGs were recorded, digitized and analyzed using Spike2 and DataView software. States were discriminated based on the EEG and patterns of breathing. Delta power (0.5 to 3 cps) was quantified. The Friedman test was used to determine statistical significance.

**Results:** End tidal CO2 increased with increasing delta power and was therefore lowest in REM sleep and wakefulness and highest in deep NREM sleep. Deep NREM sleep and REM sleep increased in inverse proportion to temperature in the pre-recording period. That is, animals had more deep NREM sleep and REM sleep following 10°F than following 30°F. However, end tidal CO2 levels in sleep increased in one animal and decreased in the other with prior exposure to colder temperatures.

**Conclusion:** The results are inconsistent with the idea that prior depriva- tion increases end tidal CO2 levels in sleep. This indicates that deprivation increased the amount but not the depth of subsequent sleep.

### 0116

**Closing The Eyes: A Signal For Thermoregulation And Sleep**

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**Introduction:** Increases in distal skin temperatures have been associated with the attempt to sleep. However, it is not known which aspects of the attempt to sleep are responsible for these increases. This paper presents two studies that investigated specific sleep behaviors, cognitions and events, and their effects on distal skin temperature and sleep onset.

**Methods:** Study 1 employed 34 good sleepers (mean age = 26.7 (10) yrs) in a counterbalanced, repeated measures design comprising manipulations of four sleep behaviors: laying down, pulling covers up, placing contra-lateral (left) hand under covers, and closing the eyes. Distal skin tem-perature was measured from the right fingertip, and this remained outside the covers. Study 2 employed 15 good sleepers (mean age = 19.6 (1.5)
yrs) with three conditions counterbalanced: lights off, close eyes, and attempt sleep. Finger temperature (Tf), EEG and EOG were measured in study 2. Sleep onset latency was measured from lights out to Stage 1 sleep onset.

Results: In study 1, laying down and placing the contra-lateral hand under the covers did not significantly increase Tf (both p>.05), but pulling the covers up, [t(95)=1.78, p<.01], and closing the eyes did, [t(99)=4.10, p<.0001]. In study 2, lights off increased Tf [t(164)=2.79, p=.006], with closing the eyes contributing a further Tf increase [t(164)=2.15, p=.03]. However, the intention to sleep, and actually falling asleep, did not evoke any further significant Tf change (p>.05). The likelihood of falling asleep was also affected by conditions, with sleep onset occurring <1% of trials in the lights off condition, significantly increasing to 36% in the close eyes condition (p<.0001) (despite being instructed in both conditions to remain awake). With instructions to attempt sleep, no further significant increase in sleep likelihood occurred (p>.05).

Conclusion: The stimuli of lights out and closing the eyes evoked thermoregulatory responses, with closing the eyes also increasing sleep propensity.

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0117

Eye Movement Stereotypy In Stage REM
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Introduction: Patterns of eye motion provide a window on spontaneous neural activation in sleep. EOG sequences have recently been analyzed using simple mathematical waveform description. In hypnagogic stage 5/6 and in Stage REM, “looped” EOG trajectories can be articulated as waveform translation (often with stretching or compression) or as reflection around waveform coordinate axes. Such pattern repetition and approximate symmetry produce distinctive EOG waveform stereotypy. Easily demonstrated within subjects, translation and reflection in the Stage REM EOG are currently under investigation across subjects. It is predicted that eye movement stereotypy in Stage REM, as in hypnagogic Stage 5/6, will generalize across subjects.

Methods: During polysomnography in eight human subjects, the DC EOG was recorded using BIOPAC hardware. EOG pattern characteristics were then digitally quantified according to (1) segment duration; (2) mathematically derived waveform length; (3) local peak-to-peak amplitude, standard deviation, and waveform area; (4) physical likeness calculated by (a) waveform template application and (b) point-to-point waveform correlation.

Results: Preliminary data analysis suggests strong local similarities among Stage REM EOG waveforms produced by different subjects on different nights. Extended “loop envelopes,” similar to those traced by hypnagogic SEMs, translate approximately but reliably among subjects. Within trajectory envelopes, local waveform translation yields high intersubject correlations (representative Pearson r = 0.90 to 0.97). By increasing or decreasing waveform area with respect to zero voltage, stretching or compression predictably decreases intersubject correlation (representative r = 0.75 to 0.85). Also as predicted, initial and final segments of reflected waveforms can be excised and reinserted among records (representative r = 0.90 to 0.95), resulting in good approximation to original waveforms.

Conclusion: Eye motion in Stage REM reveals oculomotor stereotypy among subjects. Within subjects, a mechanism akin to velocity storage may contribute to predictable waveform transformation. To account for waveform stereotypy among subjects, a more fundamental mechanism may be in play.

0118

Indoor Exposure To Natural Bright Light Reduces Afternoon Sleepiness
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Introduction: Strong sleepiness/drowsiness in the afternoon often disturbs work efficiency in our business life. Although a short nap (< 30 min) is a useful tool to reduce sleepiness, not everyone can have enough time or space to take a nap in a work setting. Thus, we tested the effect of short time exposure (30 min) of natural bright light (NBL) as a more convenient tool.

Methods: Participants were 16 healthy women aged 33 to 43 (38.1 ± 2.68) years. The arousal level was measured by the psychomotor vigilance task (PVT), the alpha attenuation test and the Karolinska sleepiness scale (KSS). The tasks were repeated in every 30 min from 11.00 to 16.30. Participants took part in the three experimental conditions: (1) the NBL condition in which they carried out the task sitting by a window side (1077-9200 lux) from 12.40 to 13.10, (2) the nap condition in which they took a nap for 20 min from 12.40, and (3) the control condition in which they continued the tasks in a semi dark environment (< 100 lux). The ambient light intensity was set to less than 100 lux, except for NBL exposure and napping periods.

Results: Compared with the control condition, KSS score was significantly improved during the NBL exposure (t(15) = 2.28, p < 0.05), but no effect was shown in alpha attenuation coefficient (AAC). After NBL exposure or nap, AAC was significantly higher than the control condition (F(2, 30) = 4.59, ε = 0.97, p < 0.05). There were no significant differences in PVT performance between conditions.

Conclusion: Our results demonstrated that short time exposure to NBL improved arousal level in the afternoon, suggesting the use of natural light as an alternative to a short nap.

0119

Does The N350 NREM Event-Related Potential Waveform Reflect Cognitive Processing During Sleep?
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Introduction: Event-related potentials (ERPs) are stimulus-elicted changes in brain activity. P300, a positive potential thought to reflect cognitive processing, can be elicited using an oddball paradigm when subjects attend but not ignore stimuli. With sleep, P300 to the oddball stimulus disappears replaced by the prominent negativity, N350. N350’s functional significance is currently unknown but it does vary with physical and psychological properties of the eliciting stimulus. With an omitted stimulus (OS) paradigm, the oddball is the omission of an expected stimulus. An ERP to stimulus omission reflects the psychological significance of the event. In the present study, ERPs to an OS are examined in wakefulness and sleep.

Methods: EEG was recorded from scalp electrodes for 10 healthy subjects at bedtime during 1000 Hz tone presentation (1 stimulus/second). Stimuli were omitted pseudorandomly (p=0.2). The procedure was repeated as subjects attended or ignored stimuli and attempted to remain awake or to sleep (intention). Up to 60 trials were selected for averaging for each subject where an OS was immediately preceded and followed by a tone, during four wake/sleep states (Awake/Alpha, Awake/Mixed, Stage1, Stage2). Peak waveform amplitude was compared to baseline averages.
Category B—General Physiology

Results: As expected, during Alpha, the OS elicited large P300s when subjects attended (M=51.28 µV, SD=34.5; t(9) = -4.70; p<.05) and were significantly reduced when subjects ignored (t(9) = -3.218; p<.05). These findings were consistent regardless of subject intention. N350 was clearly present following tones as theta activity appeared (M=-50.687, SD=21.63; t(7) = 2.59; p<.05) regardless of subject attention. N350s were also present following OS in drowsiness (Awake/Mixed-- M=26.55, SD=21.16), Stage1 (M=50.29, SD=38.52) and Stage2 sleep (M=48.04, SD=29.31).

Conclusion: The elicitation of N350 by OS indicates that this NREM ERP waveform reflects an ongoing monitoring of the environment during sleep and is not simply a sensory response modified by other potentials.

0120

Effect Of Potent Anxiolytic Doses Of The 5-HT2C Receptor Antagonist SB-242084 And Chlordiazepoxide On Vigilance States In Freely Moving Conscious Rats

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Introduction: Benzodiazepines have limited clinical benefits as anxiolytics due to their sedative effects. Recently, it has been proposed that 5-HT2C receptor antagonists may have anxiolytic properties but the effects of 5-HT2C receptor antagonists on sleep and EEG are still controversial.

Methods: To compare the effects of benzodiazepines and subtype-selective 5-HT2C receptor antagonists on anxiety and vigilance, social interaction test and 8 h polygraphic recordings were performed in male Sprague-Dawley rats after chlordiazepoxide (CDP, 4.0 mg/kg i.p) and SB-242084 (0.1, 0.3 and 1.0 mg/kg, i.p.) treatment.

Results: In social interaction test of anxiety, CDP and SB-242084 (0.3 and 1.0 mg/kg) had similar anxiolytic effects under high-light unfamiliar test condition. Although lower doses of SB-242084 (0.1 and 0.3 mg/kg) did not affect considerably the amount of vigilant states, the highest dose (1.0 mg / kg i.p.) of the drug increased wakefulness and decreased deep slow wave sleep in the first hour. CDP markedly increased intermediate stage of sleep (IS) in the second h and a trend for decrease in paradoxical sleep in the first h and increase in light slow wave in the second h was found.

Conclusion: In conclusion, our studies show that the subtype-selective 5-HT2C receptor antagonist SB-242084 at low, but potent anxiolytic doses did not affect considerably the length of vigilance states, while CDP decreased IS at a relatively low dose. These effects could be explained as GABA agonist action by CDP and blockade of 5-HT-induced, 5-HT2C receptor-mediated activation of GABA neurons by SB-242084. Therefore, our data provide evidence for an anxiolytic agent without sedative-hypnotic side effect.

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0121

Excitability And Effective Connectivity Of The Human Cerebral Cortex Across The Sleep-Wake Cycle: A TMS/EEG Study

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Introduction: Many studies have examined how the transmission of information from the sensory periphery to the cortex changes as a function of behavioral state. However, very little is known about how information is transmitted between cortical areas in the sleeping brain. To answer this question we directly stimulated the cerebral cortex of humans using Transcranial Magnetic Stimulation (TMS) and we recorded the evoked response by means of high-density electroencephalography (hd-EEG).

Methods: Low frequency (<1 Hz) TMS was delivered together with masking noise while subjects (n=8) lied on a reclining chair. An infrared positioning system and a 60-channel TMS-compatible EEG amplifier were used to target precisely and reproducibly the cortical region of interest while recording TMS-evoked potentials over the entire scalp. In some subjects, different areas (both frontal and parietal) were stimulated during separated sessions. In each subject, we calculated the strength and the spread of cortical evoked activity by solving the inverse problem on a realistic head model. We also analyzed evoked activity on a single trial basis.

Results: All subjects progressed from wakefulness to slow wave sleep while stimulation was delivered. Consistently, TMS evoked a series of high-frequency oscillations (15-45 Hz) during wakefulness while, during sleep, the same stimulation elicited a higher amplitude, slower component. This changes in cortical responsiveness were also evident on a single-trial basis during transition between behavioral states. In all subjects, source modeling of the average response revealed the presence of recurrent cortical activations that propagated amongst anatomically connected cortical regions during wakefulness. During sleep, an initially stronger cortical activation progressively dissipated while remaining localized.

Conclusion: Compared to wakefulness, the reaction of the sleeping brain to a direct cortical perturbation is initially stronger, but remains local and is not sustained over time. These changes possibly reflect a substantial decrease of cortico-cortical effective connectivity.

0122

The Role Of Type I Interferons In Sleep And Body Temperature Responses In A Model Of Acute Viral Infection

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Introduction: Type I interferons (IFNs) such as IFNα and IFNβ are known to play a role in host defense against viruses. These IFNs are pyrogenic and somnogenic in large doses, but their role in the viral acute phase response is undetermined. This study employed IFN receptor type 1 (IFN-RI) deficient mice to define the role of type I IFNs in a model of acute viral disease.

Methods: We challenged wild-type 129 SvEv mice and IFN-RI knockout (KO) mice intratracheally (IT) with poly[riC] (synthetic double-strand RNA) and IFNα, a model that we have shown to simulate an acute viral infection with respect to body temperature and locomotor activity responses. The mice were surgically fitted with EEG and EMG electrodes or intraperitoneal radio-telemetry temperature sensors, and allowed to recover in a 29 C environmental chamber with 12:12 hr light/dark cycles. IFN-RI KOs or their 129 SvEv controls were challenged IT at light onset with combined poly[riC]/IFNα (or IFNα alone in controls) and monitored for sleep and temperature changes over 48 hr.

Results: Hypothermic responses to IT poly[riC]/IFNα were more exaggerated in the IFN-RI KO mice than in controls. The NREMS response to IT poly[riC]/IFNα was enhanced earlier in the IFN-RI KO mice than in controls, though the total time spent in NREMS was reduced in the KOs and the return to baseline NREMS occurred more rapidly in the KOs. The quality of NREMS was altered more extensively in the control than in the KO mice. Spontaneous REMS was suppressed in IFN-RI KOs as previously reported, but was not substantially altered in either strain by IT poly[riC]/IFNα challenge.

Conclusion: Our results implicate type I IFNs as inhibitors of the
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0123
The Role Of Type I Interferons In Sleep And Body Temperature Responses To Influenza Virus Infection
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Introduction: Type I interferons (IFNs) are elevated in acute viral infections, but their role in mediation of the acute phase response (fever, somnolence, anorexia, etc.) to viruses is unknown. Therefore sleep and body temperature responses to influenza virus infection were assessed in mice deficient in the type I IFN receptor.

Methods: IFN receptor type I (IFN-RI) knockouts (KOs) or their 129 SvEv controls were housed in an environmental chamber at 29 C with 12:12 hr light/dark cycles. The mice were surgically implanted with EEG and EMG electrodes or with intraperitoneal radio-telemetry temperature sensors. After recovery mice were challenged intranasally with a low dose of X-31 influenza virus at light onset. Animals were monitored for 24 hr prior to infection to determine baseline temperature and sleep profiles, and then for 9 days following infection.

Results: Hypothermic responses to virus were less exaggerated in the IFN-RI KO mice than in controls, and tended to return to normal on day 5 while control values continued to decline until the end of the observation period. An increase in NREMS was detected earlier in infected IFN-RI KO mice than in controls and approached baseline values sooner in the KO mice. REMS, reduced 35% in uninfected KOs, declined comparably in both X-31-infected strains. Relative slow wave amplitude values were suppressed briefly only in infected control mice. During both NREMS and REMS in infected mice, subtle differences were seen in EEG power density measurements, with increased power in NREMS and decreased power in REMS occurring in the IFN-RI KOs relative to controls. The KOs appeared to survive better than did the controls.

Conclusion: Type I IFNs contribute to the hypothermic response to virus and modulate EEG power density but they delay and slightly suppress total time spent in NREMS.

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0124
Differential Effects Of Caffeine On Quantitative Sleep EEG In Moderate And Light Caffeine Consumers
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Introduction: Surprisingly, there are only very few studies in humans on the development of tolerance to the effects of caffeine on sleep. The aim of this study is to evaluate if the sleep of moderate caffeine consumers is less sensitive to the effects of caffeine than the sleep of light consumers.

Methods: 24 healthy subjects (20-30 y) were assigned to two groups according to their habitual caffeine consumption: moderate (125-400 mg per day) and light (less than 65 mg per day). All were submitted to caffeine (200 mg) and placebo conditions in a double blind crossover design, separated by a one week pause. They received 100 mg of caffeine (or placebo) in capsule form three hours before bedtime and the remaining dose (100 mg) one hour before bedtime. Sleep stages were scored and spectral analysis was performed on C3 EEG. Mixed ANOVAs evaluated condition (caffeine, placebo), group (moderate, light) and interaction effects.

Results: Compared to placebo, caffeine lengthened sleep latency (p<0.001) and decreased sleep efficiency (p=0.07) in both groups. Total sleep time (p=0.01), minutes of stage 2 (p=0.04) and SWS (p<0.001) were reduced following caffeine consumption. Compared to placebo, spectral power between 0.25-3.00 Hz (p<0.04) was significantly reduced while power between 18.00-32.00 Hz was enhanced (p<0.01) in caffeine condition. Caffeine consumption produced a more pronounced increase of spectral power between 14.00-16.00 Hz in light compared to moderate caffeine consumers (p<0.03).

Conclusion: While caffeine consumption habits did not influence the effects of caffeine on polysomnographic sleep parameters, light consumers showed a higher sensitivity to the effects of caffeine on sigma power than moderate consumers. Whether this difference is due to the development of a tolerance or to a pre-existing lower sensitivity to the effects of caffeine in moderate consumers still needs to be determined.

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0125
Night Weight Loss And Delta Sleep. A Preliminary Study
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Introduction: New evidences suggest that sleep habits influence weight loss. A strong inverse association between sleep hours and obesity in adults and children was found. Some authors suggest that the chance to become obese is 24% less for each additional hour of sleep. A possible explanation is the effect of sleep deprivation on hormonal levels, causing insulin resistance, higher cortisol and lower growth hormone levels. There are no studies, up to present date, relating weight loss during sleep and sleep structure assessed by polysomnography.

Methods: Twenty-two healthy volunteers, 17 females and 5 males, aged 18-29 were included. Females were not in menstruation period. Volunteers received a 487 kcal 430g meal and 200 ml water at night. During the experiment, they were weighed four times in a high precision balance. The first, after meal and the fourth after 5 hours daytime. They were not allowed to eat, drink, urinate or defecate between first and second weighing and between third and fourth. Room and body temperature were controlled. Regression analysis was performed considering daytime and nighttime weight loss rates (grams per hour) as dependent variables, polysomnographic and environmental data as independent ones.

Results: A significant positive correlation was found between sleep stage 4 duration and night weight loss rate (R=0.64, R2=0.63). No other significant correlation was found.

Conclusion: Increase delta sleep stage 4 duration correlated with night weight loss rate in healthy young volunteers. Previous reports found increased fat oxidation and weight loss in experimental models. Our finding could possibly be explained by growth hormone secretion occurring during delta sleep, although further confirmation is needed.

AFIP - FAPESP
0126
Cardiovascular Correlates Of Sleep Quality In Healthy Subjects
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Introduction: Systolic blood pressure (SBP), diastolic BP (DBP) and their variability (standard deviation, sd) are all parameters of high clinical relevance, and highly influenced by the autonomic nervous system. In the present study we examined whether indices of sleep quality are associated with such parameters of the cardiovascular system during sleep and the subsequent day.

Methods: Seven subjects (1 women, aged 30-55 years, 5 suffering from primary insomnia) without any medical or psychiatric history, underwent 24 hour continuous recording of 3 lead ECG, beat-to-beat non-invasive blood pressure (Portapres), and respiration along with 2-lead EEG in daytime, and full polysomnography during sleep. The analyses of the cardiovascular parameters was performed by Beatscope software on consecutive 15-minute segments. Mean HR, SBP and DBP obtained in each segment were then averaged to obtain daytime (from 8 AM to 10 PM) and night time (from sleep onset to last awakening) values. The final mean HR, SBP and DBP and their standard deviation were considered for the analysis.

Results: A significant negative correlation was found between sleep efficiency (SE) and both nocturnal mean SBP (R=.78, p<0.04) and DBP (R=-.74, p=0.056). No relationship was found between SE and nocturnal HR. No correlation were found between sleep parameters and mean values of diurnal HR, SBP and DBP. Conversely, a significant negative correlation was found between SE and diurnal sdSBP (R=-.89, p=0.008) and sdDBP (R=-.90, p=0.005). As expected, age also was associated with SE (R=-.69, p=0.09), mean SBP (R=0.77, p=0.04) and diurnal sdSBP variability (0.75, p=0.52). However, the main effect of the association between SE on these cardiovascular parameters resulted to be independent from age (after correction, all p<0.05).

Conclusion: Indices of poor sleep quality are clearly associated with higher BP and BP variability which persist over the 24 hour period. These alterations suggest a link between sleep and vascular function and/or autonomic control of BP.

0127
Intratracheal Polyriboinosinic:Polyribocytidyl Acid (Poly rI:rC) Induces Sleep But Not Body Temperature Or Locomotor Activity Changes
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Introduction: It is posited that viral double-stranded (ds) RNA triggers the acute phase response in viral infections. Previously we reported that intraperitoneal (IP) challenge with the synthetic dsRNA poly rI:rC induced pyrexia and suppression of locomotor activity, but that intratracheal (IT) poly rI:rC has no effect on these parameters unless co-injected with interferon (IFN)γ. In the current study, we determined whether sleep responses characteristic of a viral acute phase response are elicited by IT poly rI:rC administration without IFNγ priming.

Methods: C57BL/6 male mice (9-12 weeks old) were implanted IP with radio transmitters and monitored for core body temperature and locomotor activity by telemetry. Recordings were taken every 6 minutes for two days of baseline and two days following IT inoculation with 160 μg poly rI:rC. Sleep recordings were conducted on separate mice fitted with electroencephalogram (EEG) and electromyogram (EMG) electrodes and challenged as above. Sleep recordings were also taken for two days of baseline and two days following poly rI:rC challenge.

Results: Body temperature and locomotor activity responses were absent following IT poly rI:rC inoculation, thereby confirming previous studies. In contrast, the time spent in non-rapid eye movement (NREM) sleep increased during the first post-inoculation day. The amount of time spent in rapid eye movement (REM) sleep did not change significantly.

Conclusion: IT inoculation of poly rI:rC alone enhances NREM sleep but not REM sleep, hypothermia or locomotor activity. The priming agent, IFNγ, was not needed for poly rI:rC-induced sleep responses, thereby indicating that the mechanisms responsible for the sleep responses are distinct from those responsible for temperature and locomotor activity response changes.

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0128
Evoked K-Complex Elicitation And Auditory Evoked Potentials At Transitions From Stage 2 To Slow Wave Sleep And Stage 2 To Rapid Eye Movement Sleep
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Introduction: Increased spontaneous K-complex activity has been reported during stage 2 NREM sleep prior to transition to SWS, compared to stage 2 prior to the transition to REM sleep. This suggests that although the EEG in both cases is visually scored as stage 2, the underlying network is in a state more conducive to delta frequency EEG generation prior to SWS than prior to REM sleep. However, while prior work has addressed the incidence of delta frequency events, it has not investigated their amplitude, or speed of elicitation. Averaging evoked K-complexes and evaluating the N550 component produces an amplitude measure which reflects the number of neural units available for production of the synchronized response and a latency measure, providing both another measure of ease of elicitation, and an assessment of the speed of cortical synchronization. The present study reports an investigation of evoked K-complexes, and the K-complex-related N550 component in stage 2 sleep, prior to SWS and REM sleep transitions.

Methods: Data were collected from 10 healthy young males (mean age = 24.8 ± 2.15 years) on three nights. During one of the nights, tones (1kHz, 50msec, 80dB) were presented with a random ISI (20-35sec) during sleep, irrespective of sleep stage. Evoked K-complexes and sleep evoked potentials were analyzed from the 10 minutes of stage 2 NREM prior to SWS and REM transitions. EEG was recorded from 12 scalp sites using Neuroscan amplifiers and software with a 1000Hz sampling rate. K-complex elicitation probability, and N550 amplitude and latency in the KC+ averages were compared between SWS and REM transitions using paired t-tests.

Results: KC elicitation probability was significantly greater (p = .009) prior to SWS (0.88 ± 0.11) than prior to REM (0.63 ± 0.22). N550 latency was significantly faster (p = .004) prior to SWS (538 ± 53ms) than prior to REM (623 ± 53 ms). N550 amplitude did not differ between the two conditions (p > .2).

Conclusion: The K-complex probability data support the earlier findings that spontaneous K-complexes were more likely to occur prior to SWS than REM. The N550 latency difference reflects the relative ease of K-complex production in this state. The K-complex triggering mechanism is thus becoming more active prior to the onset of SWS. The lack of an amplitude difference highlights the all-or-none quality of K-complexes.
and indicates that if triggered, the same number of neural units are available for synchronization in stage 2, regardless of the following sleep state.

0129

Gender Differences In Heart Rate Variability During Nocturnal Wakefulness And Sleep

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Introduction: Heart rate variability (HRV) studies during wakefulness show that men have greater sympathetic and less parasympathetic activity as compared to women. However, few studies have characterized these autonomic gender differences during sleep. The purpose of this study was to evaluate gender differences in HRV during nocturnal wakefulness and sleep.

Methods: Fourteen men and 10 women were enrolled in the study and did not differ in age (38 ± 9.2 years old) or body mass index (23.9 ± 4.2 kg/m2). Following two nights of adaptation at the UCLA General Clinical Research Center, continuous all night polysomnography was recorded and included ECG monitoring. ECG signals were spectral analyzed to produce HRV variables (HF, LF, LF/HF and R-R interval). Data were stratified by pre-sleep wakefulness, stage 2, and REM sleep.

Results: Men and women were similar on total sleep time (405 min), sleep onset (26 min), sleep efficiency (80%) and NREM sleep (316 min). Women had more REM sleep than men, F(1,22)=4.7, p<.05. For HRV variables, repeated measures ANOVAs indicated significant main effects for gender, with men having decreased HF power (F[1,22]=9.8, p <.01), increased LF power (F[1,22]=6.2, p <.05) and greater LF/HF ratio (F[1,22]=7.2, p <.01) as compared to women across wakefulness, stage 2 and REM sleep. In contrast, men had a longer R-R interval than women, F(1,22)=16.7, p <.0001 across these states.

Conclusion: These findings show that men have decreased parasympathetic and increased sympathetic activity during wakefulness that persists into sleep. Given that this pattern is associated with deleterious effects on the cardiovascular system, and given that men have higher rates of cardiovascular disease than pre-menopausal women, it would be of great interest to examine mechanisms accounting for gender differences in HRV.

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A Comparison Of Placebo And No-Treatment During A Hypnotic Clinical Trial

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Introduction: Sleep commonly improves with placebo in insomnia clinical trials. We examined whether the improvement seen with placebo was related to taking pills or other non-specific factors.

Methods: Ninety-five persons with primary insomnia (40.4 +/- 12.3 years old, 81% women) participated in this 12 week trial. They were instructed to take study medication (a placebo pill) on at least 3 nights and no more than 5 nights per week, on nights of their choosing. Sleep diaries were completed daily, assessing sleep latency, number of awakenings, wake after sleep onset, total sleep time (TST), and whether or not they had taken a pill. Analyses were conducted as repeated-measures ANOVAs for each dependent sleep variable, comparing the nights when pills were taken (pill+) against nights when pills were not taken (pill-). The independent variables for each ANOVA were Condition (2: pill+ vs. pill-) and Time (7: baseline & 6 bi-weekly time increments). Baseline values were included. Inference for the repeated measures ANOVA was provided by the Generalized Estimating Equation procedure.

Results: Pills were consumed on about half of the nights. Consistent improvement was seen with reduced reported sleep latency, wakefulness after sleep onset, number of awakenings, and TST over the 12 weeks for both the pill+ and pill- condition (all p < 0.05 for “Time”). A difference between pill+ and pill- was detected only for TST, showing an increase in TST of 7 minutes for the pill+ condition (chi-square = 6.1, df = 1, p-value = 0.014)

Conclusion: This study suggests that improvement seen during placebo treatment is related more to non-specific factors of participating in a clinical trial than to pill-taking behavior. However a small effect specific to pill-taking may be present for TST. The findings should be tested in a randomized comparison of the pill+ and pill- conditions.

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Ventilatory Safety Of Zaleplon During Sleep In Patients With Obstructive Sleep Apnea On CPAP

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Introduction: While on CPAP therapy, OSA patients report difficulty falling asleep as one of the contributors to poor sleep quality and, further, is one of the factors associated with diminished long-term therapy compliance. A potential remedy would be to administer a hypnotic agent, but this has often raised concern due to the potential for reducing respiratory center drive. A preliminary study indicated that the non-benzodiazepine zaleplon did not worsen ventilation in patients with chronic obstructive pulmonary disease (George, 2000). In order to expand the findings to other respiratory conditions, we present data that evaluates the use of zaleplon in patients with mild to moderate OSA while on CPAP.

Methods: Patients (N=15; n=9 men; age=57.5±13.8 yrs; BMI=33.9±5.2 kg/m2) with OSA who complained of poor subjective sleep quality despite receiving appropriately titrated CPAP were enrolled in the study. Entry criteria for the study were a history of mild to moderate OSA as defined by polysomnography indicating an apnea-hypopnea index (AHI) of 10-20 events/hr, a minimum oxygen saturation of less than 89% but greater than 70%, and CPAP therapy for at least 90 days prior to the start of the study. Patients underwent a baseline cardio-respiratory home sleep study (LifeShirt®, (LS), VivoMetrics, USA). The first eligible patient was randomly assigned and subsequent patients were alternately assigned to one of two treatment sequences in a single-blind, crossover design (two nights of zaleplon (Z) 10 mg, followed by two nights of placebo (P) [Sequence A], or two nights of PL followed by two nights of ZN 10 mg [Sequence B]). During the four experimental nights, patients self-administered ZN or PL 30-minutes prior to their normal bedtime and underwent a home cardio-respiratory LS sleep study.

Results: No statistically significant treatment differences between zaleplon and placebo were observed for apnea-hypopnea index (AHI) (mean±SE) (Z=7.2±0.8; PL=7.5±1.0; p=0.602), apneas (ZN=15.2±2.7; PL=21.6±6.0; p=0.888), hypopneas (ZN = 41.0±4.2; PL = 36.0±3.5; p=0.266), or mean SpO2 (ZN=94.6±0.3; PL=94.7±0.2; p=0.859). A difference was observed between ZN (79.2±1.3) and PL (82.1±0.9) for nadir SpO2 (p=0.008), but this difference is of questionable clinical significance.

Conclusion: These data support the hypothesis that zaleplon may be used safely in middle-aged patients with mild to moderate OSA while receiving CPAP therapy in the home environment.

This study was supported by Elan Pharmaceuticals

Ramelteon And Triazolam In Humans: Behavioral Effects And Abuse Potential

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Introduction: Ramelteon is a novel selective melatonin MT1/MT2 receptor agonist being studied for the treatment of insomnia. This study evaluated behavioral effects and abuse potential of ramelteon and triazolam, a classic benzodiazepine sedative-hypnotic, in subjects with histories of sedative drug abuse.

Methods: In this double-blind crossover study, 14 adult subjects with known histories of sedative drug abuse received a once-daily oral dose of ramelteon (16mg, 80mg, 160mg), triazolam (0.25mg, 0.5mg, 0.75mg), or placebo. Abuse potential was inferred from widely used subjective effect questionnaires. Behavioral and cognitive performance were also assessed.

Results: Compared to placebo, ramelteon (16mg, 80mg, 160mg) showed no significant effect on primary outcome questionnaire item “drug liking” at any time point (0.5-24 hours postdose) or on items “drug strength,” “drug liking,” “good effects,” and “street value” at 24 hours postdose. Similarly, ramelteon had no effect on Word Recall/Recognition Task, Enter and Recall Task, Balance Task, Digit Symbol Substitution Task, and Circular Lights performance at any dose compared to placebo. In contrast, triazolam (0.5 and 0.75mg) showed dose-related effects on all these subjective and behavioral measures, consistent with its profile as a sedative drug with known abuse potential.

Conclusion: Ramelteon demonstrated no abuse potential or behavioral impairment under these study conditions at doses up to 20 times the anticipated therapeutic dose.

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0133
Ramelteon Does Not Have Benzodiazepine Agonist-Like Discriminative Stimulus Effects In Normal Or Diazepam-Dependent Rhesus Monkeys

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Introduction: Ramelteon is a selective MT1/MT2 receptor agonist under investigation for the treatment of insomnia. Two studies were conducted to determine if ramelteon produces benzodiazepine agonist-like discriminative stimulus effects in monkeys.

Methods: In the first study, 4 rhesus monkeys were trained to reliably discriminate between subcutaneous injections of vehicle and midazolam (benzodiazepine) by using a standard 2-lever procedure for shock avoidance. In 120-minute test sessions, ramelteon was administered intravenously in lieu of midazolam at doses of 0.32, 1.0, 3.2, 5.6, and 10.0 mg/kg. Responses on the midazolam-associated lever were recorded to assess the ability of ramelteon to substitute for midazolam. In the second study, 4 rhesus monkeys dependent on diazepam were trained to reliably discriminate between subcutaneous injections of vehicle and flumazenil (benzodiazepine antagonist) by using a standard 2-lever procedure for food presentation. In testing sessions, ramelteon was administered intravenously at doses of 3.2, 5.6, and 10.0 mg/kg/15 minutes prior to increasing doses of flumazenil. Responses on the flumazenil-associated lever were recorded to assess the ability of ramelteon to attenuate flumazenil-precipitated withdrawal effects.

Results: In the first study, monkeys responded primarily on the vehicle-associated lever after receiving ramelteon, indicating that these animals did not generalize ramelteon to midazolam. In the second study, ramelteon did not attenuate the discriminative stimulus effects of flumazenil.

Conclusion: In rhesus monkeys, ramelteon (up to 10 mg/kg) did not produce benzodiazepine agonist-like discriminative stimulus effects. This study supports the view that ramelteon is not likely to have benzodiazepine-like abuse or dependence liability.

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0134
Lack Of Primary Physical Dependence Effects Of Ramelteon In Rhesus Monkeys

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Introduction: Ramelteon is a novel highly selective MT1/MT2 receptor agonist being studied for the treatment of insomnia. This study was conducted to determine if ramelteon produces any behavioral changes indicative of physical dependence in monkeys.

Methods: Four adult rhesus monkeys received ramelteon (10 mg/kg, i.g. catheter) daily for 1 year. During weeks 14, 27, and 40, treatment was temporarily discontinued for 5 days to assess effects of treatment discontinuation on operant behavior (conditioned lever pressing to obtain food and avoid shock) and observable clinical signs (such as yawning and grooming) by using a paradigm sensitive to benzodiazepine dependence. Behavior and clinical signs were also monitored when treatment was terminated at the end of the study.

Results: Daily treatment with ramelteon had no overall effect on monkey behavior to obtain food or avoid shock. Operant response rates in individual monkeys did not systematically change over the course of the study. In addition, there were no apparent changes in body weight, motor activity, posture, or behavior observed during the periods of treatment or after discontinuation of treatment.

Conclusion: Ramelteon, when given daily and when temporarily discontinued, had no statistically significant effect on spontaneous or learned behavior in monkeys. These results suggest that ramelteon is not likely to have physical dependence liability.

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0135
Reinforcing Effect Of Ramelteon Assessed By Intravenous Self-Administration Experiments In Rhesus Monkeys

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Introduction: Ramelteon is a novel selective MT1/MT2 receptor agonist under investigation for the treatment of insomnia. This abuse liability study was conducted to assess a possible reinforcing effect of ramelteon by monitoring intravenous self-administration in rhesus monkeys.

Methods: In daily 2-hour sessions, 4 rhesus monkeys were allowed to self-administer sodium pentobarbital at 0.125, 0.25, 0.5, and 1.0 mg/kg/infusion, vehicle control (30% PEG400 glucose solution), or ramelteon at 0.025, 0.05, 0.1, 0.2, and 0.4 mg/kg/infusion for 4-6 days each by pressing a lever (fixed ratio, 50). Around-the-clock continuous self-administration of ramelteon at 0.025, 0.1, and 0.4 mg/kg/infusion (fixed ratio, 5) was also recorded for 2-4 weeks per dose.

Results: The number of self-administrations of pentobarbital (0.5 and 1.0 mg/kg/infusion) was statistically significantly greater than that of vehicle, whereas no significant differences were noted in the number of self-administrations of ramelteon at any dose compared to vehicle control. In the continuous self-administration experiment, ramelteon showed no positive reinforcing effect, as defined as 11 or more self-administrations per day for 5 or more consecutive days.

Conclusion: Under the conditions of this study, ramelteon showed no positive reinforcing effect at doses of 0.025-0.4 mg/kg/infusion in rhesus monkeys, whereas the positive control substance (pentobarbital) produced the expected reinforcing effect. This study suggests that ramelteon has no abuse potential, a supposition that needs to be confirmed in human studies.

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0136
Open-Label Assessment Of The Pharmacokinetics And Pharmacodynamics Of Warfarin In The Presence Of Multiple Doses Of Ramelteon In Healthy Adults

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Introduction: Ramelteon is a selective MT1/MT2 receptor agonist under investigation for the treatment of insomnia. This study examined the effect of multiple doses of ramelteon on the steady-state pharmacokinetics of stabilized doses of warfarin and on the steady-state pharmacodynamic measures prothrombin time (PT) and international normalized ratio (INR).

Methods: Twenty-four subjects (mean age, 34.5 yrs) received 16 mg ramelteon and stable doses of warfarin once daily for 7 days. Following a
Category C—Clinical Pharmacology

7-9 day titration period, subjects were considered stabilized on warfarin when their PT values were 1.2 to 1.7 times their respective baseline values. Blood samples were obtained over 24 hours following dosing on Day 7 for pharmacokinetic analyses of ramelteon, R-warfarin, and S-warfarin. Blood samples were also collected for anticoagulant analyses (PT and INR at 15 minutes predose and 12 hours postdose).

**Results:** Compared with warfarin alone, coadministration with ramelteon had no clinically relevant effect on the dose-normalized systemic exposure of R-warfarin (AUC0-24: 3871 vs. 3798 ng/h/mL/mg; 90% CI: 93.3%, 103%; Cmax: 238 vs. 228 ng/mL/mg; 90% CI: 90.6%, 101%; Cmin: 133 vs. 128 ng/mL/mg; 90% CI: 89.9%, 104%) or S-warfarin (AUC0-24: 2731 vs. 2569 ng/h/mL/mg; 90% CI: 89.4%, 99.0%; Cmax: 188 vs. 174 ng/mL/mg; 90% CI: 88.5%, 97.4%; Cmin: 84.0 vs. 76.5 ng/mL/mg; 90% CI: 84.6%, 98.1%). No differences in mean PT values were found with warfarin alone (14.1 seconds predose, 14.1 seconds postdose) vs. combination therapy (13.0 seconds predose, 13.3 seconds postdose). No differences in mean INR were found with warfarin alone (1.44 predose, 1.45 postdose) vs. combination therapy (1.33 predose, 1.36 postdose).

**Conclusion:** Multiple-dose administration of ramelteon did not affect systemic exposures of R-warfarin and S-warfarin or PT values and INR in subjects stabilized on warfarin. These results suggest that ramelteon is neither an inhibitor nor an inducer of CYP1A2 and CYP2C9.

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**0138**

**The Effect Of Tiagabine On Sleep In Adult Patients With Primary Insomnia**

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**Introduction:** Tiagabine, a selective gamma-aminobutyric acid (GABA) reuptake inhibitor (SGRI), increases synaptic GABA availability via selective inhibition of the GAT-1 GABA transporter. Since GABA plays a central role in promoting sleep, increased availability of GABA may have therapeutic use in insomnia. In initial studies tiagabine has been shown to have sleep-consolidating effects in healthy elderly subjects and adult patients with primary insomnia. In this study, the effect of tiagabine on objective sleep measures in adult patients with primary insomnia was further evaluated.

**Methods:** 232 adult patients (18-64 years) with DSM-IV-TR-defined primary insomnia were randomized to receive tiagabine 4, 6, 8, 10 mg, or placebo on two consecutive nights of polysomnography.

**Results:** Polysomnography data were obtained from 230 patients. The mean change from baseline in minutes of slow wave sleep (SWS) was greater with tiagabine than with placebo (4 mg, +18.6 min; 6 mg, +31.7 min; 8 mg, +39.6 min; 10 mg, +52.9 min; placebo, +10.5 min). A three higher doses being significant vs. placebo (P <0.001 for each). The mean reduction from baseline in minutes of stage 1 sleep was significantly greater with tiagabine than with placebo (4 mg, -5.7 min; 6 mg, -7.1 min; 8 mg, -7.3 min; 10 mg, -15.5 min; placebo, +1.8 min; P <0.01 for each). No significant effect on latency to persistent sleep or total sleep time was observed. The tolerability profile of tiagabine was good, with dizziness, nausea, and somnolence being the most common adverse events, primarily at the two higher doses.

**Conclusion:** Tiagabine increased SWS and reduced stage 1 sleep in adult patients with primary insomnia. The clinical importance of these sleep architecture changes, such as potential resistance to perturbation, warrants further investigation.

**Research supported by Cephalon, Inc.**

**0139**

**Sleeping Pills And Decreased Longevity**

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**Introduction:** Kripke (2002) reported, in a replication of his 1979 study, an increased risk of death in sleeping pill users aged 30-102 and expressed a particular concern for those over 65 because they are the heaviest users of sleeping pills.

**Methods:** A review was done of the English language literature on sleeping pill use and mortality between 1979 and 2004 focused on studies of sleeping pills users age 65 and older.

**Results:** Kripke (2002) in a study of 1.1 million participants aged 30-102 after controlling for 32 variables, found, in sleeping pill users a 1.25 increase in mortality risk in 6 years. Kojima (1999) in a study of 5,322 participants aged 20 to 67 after 12-year follow-up found an increased morality risk of 1.81 both in female and in male sleeping pill users. No relationship between sleeping pill use and longevity was found in four studies focused on users over age 65 (Pollak, 1990; Rumble, 1992; Brabbins, 1993; Hays, 1996;) with over 8,000 participants ranging in age from 65 to 98 and a median follow-up period of 4 years. One study (Rumble, 1992) found a

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Effect Of Lorazepam On Activity, Actigraphic Sleep, Cognitive And Psychomotor Performance

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Introduction: Historically actigraphy has been developed as a non-invasive tool for assessing sleep-wake patterns, however, there are little data on whether the technology is sensitive to the sedating effects of medication. The aim of this study was to evaluate the effect of a single dose of the sedating benzodiazepine, lorazepam (LZP) (2.5mg), compared with placebo, on activity, actigraphic sleep parameters, cognitive and psychomotor performance.

Methods: Healthy male and female volunteers (n=24, aged 19-37 yrs) were randomised to a double blind, placebo-controlled, cross-over study with a 6-day wash out period. After dosing at 18:00 hrs psychomotor and cognitive tests were conducted at 1, 2, 3, 4 and 14 hrs post dose. The volunteers were required to wear actigraphs (Actiwatch) for the duration of each test period.

Results: All results were analysed using repeated measures ANOVA. Following LZP administration reaction time was significantly impaired (p < 0.05) compared with placebo for both the Choice Reaction Time (CRT) and Continuous Tracking Task (CTT) at 2, 3, 4 and 14 hrs, respectively. Tracking accuracy was also significantly impaired (p < 0.02) at 2, 3, 4 and 14 hrs. Subjects felt more sedated (Line Analogue Rating Scale LARS) at 4 (p=0.01) hrs post dose. Activity levels after LZP were significantly reduced (p < 0.02) between 1.5-2.0, 2.5-3.0, 4.5-5.0, 13.0-13.5 and 13.5-14.0 hrs post dose. In addition, various actigraphic sleep parameters showed a significant change following LZP: increased Actual Sleep Percent (p=0.01); reduced Mean Activity Score (p=0.03) and reduced number of Wake Bouts (p=0.02).

Conclusion: This study showed that general activity and sleep, as monitored by actigraphy, mirrored changes in cognitive function and psychometric performance following dosing with a sedative benzodiazepine, LZP. Actigraphy may therefore be a useful tool to assess the sedative properties of medication.

GABApentin Improves Sleep In The Presence Of Alcohol

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Introduction: GABApentin (GBP) is widely used in epilepsy and pain, however studies with chronic use have shown beneficial effects on sleep including increased slow wave sleep (SWS), decreased awakenings, and increased sleep efficiency. GBP might therefore represent a novel agent for improving sleep continuity. This study looks at the ability of a single dose GBP to improve sleep disruption with alcohol consumption.

Methods: This was a double-blind, randomized, single dose, crossover study of normal subjects free of sleep disorders or contraindications to alcohol or GBP (age 21-45). Following informed consent, subjects received baseline history and examination followed by polysomnography and subjective scales measuring drowsiness, alertness, and function. After 1-2 weeks, they returned and consumed 4 ounces of 40% alcohol (vodka) one hour before bedtime, and GBP (300 or 600 mg) or placebo (P). Polysomnography and subjective scales were repeated. 1-2 weeks later, subjects returned for crossover treatment and repeat testing. Differences between baseline and P (alcohol) results were compared to differences between baseline and GBP (alcohol) by paired t-test (p<0.05).

Results: Thirteen subjects were enrolled, twelve completed. There were no adverse events. Mean age was 30.8 years (range 25-37). There was no effect of alcohol compared to baseline. GBP (300 or 600 mg, compared to P) showed improvement in stage 1 (9.3 vs. 5.5%), sleep efficiency (93 vs. 96.2%) and number of awakenings (11 vs 6). 600 mg GBP compared to P increased %SWS (20 vs. 30%), and decreased %Stage 1 (7.6 vs. 4.0%), %REM (20.2 vs. 16.0%), awakenings (9 vs. 5) and arousals (29 vs. 17). No differences were seen in subjective tests of drowsiness and performance.

Conclusion: In this study, alcohol did not disrupt sleep; this could result from baseline disruption due to first night effect. GABApentin use resulted in decreased sleep disruption, and the higher dose subgroup showed increased slow wave sleep. REM was decreased with 600 mg. GBP could be useful in the treatment of conditions with frequent awakenings and decreased sleep efficiency; further controlled trials are warranted.

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Acute Effects Of MDMA On Sleep And Daytime Alertness

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Introduction: Recreational use of 3,4-methylenedioxyxymethamphetamine (MDMA), an amphetamine derivative with serotonergic toxicity, is reported to cause insomnia, and abstinent MDMA users are reported to have sleep difficulties. However, the acute effect of MDMA on sleep and daytime alertness has not been studied in the sleep laboratory.

Methods: Five recreational MDMA users, 18-25 yrs, without psychiatric disease or drug dependence and in good health participated. On 3 sessions, with 3 nights (baseline, treatment, and recovery) and 2 days (after night 2 and 3) per session, participants on the treatment night (night 2) received placebo, or 2 mg/kg MDMA at 1800 hr, or a restricted bedtime (0300-0700 hr). Bedtime was 8 hrs on non-restriction nights and standard NPSGs and MSLTs were collected.

Results: No baseline differences were seen on NPSG measures prior to treatment nights. Total sleep time was reduced with MDMA relative to placebo by 32% (5.0 vs 7.4 hrs, p<0.05) due to increased sleep latency (123.9 vs 7.7 min, p<0.04) and not increased wake after sleep onset (38.3 vs 34.6 min, NS). Percent stage 1 was slightly Increased (8.9 vs 7.4%, p<0.05) and percent stage REM was reduced (4.9 vs 17.4%, p<0.02). Sleep time in the bedtime restriction was 50% (3.7 hrs) of placebo. On recovery all measures returned to baseline. Mean daily sleep latency on the MSLT was reduced after 4 vs 8 hr bedtime by 54% (7.0 vs 15.1 min, p<0.02) and the MDMA mean daily sleep latency was reduced by 24% (13.0 min). Daytime sleepiness in MDMA users is likely due to the MDMA-associated reduction of sleep time.

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Category C—Clinical Pharmacology
0143
Circulating Norepinephrine Levels In Response To Severe Sleep Deprivation, Caffeine, And Modafinil

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Introduction: A series of experiments were performed to determine the effects of caffeine and modafinil on circulating norepinephrine (NE) levels in healthy adults undergoing severe sleep deprivation (SD).

Methods: Four randomized, double-blind, placebo-controlled trials involving 88h SD were completed. N=85 subjects spent 10 days in the laboratory. In two trials, subjects were randomized to either sustained low-dose caffeine (0.3mg/kg/h) or placebo. One trial involved 0h sleep, and the other two 2h naps per 24h (TIB: 0245-0445h; 1445-1645h) across the 88h. In another two trials, subjects were randomized to either modafinil (200mg or 400mg per 24h) or placebo. One trial involved 0h sleep, and the other one 2h nap per 24h (TIB: 0245-0445h) across the 88h. Subjects completed a 30-min computerized neurobehavioral battery every 2h of wakefulness. Plasma samples were taken every 0.5h via an indwelling venous catheter, and assayed for NE (blind to condition) using RIA. Linear mixed-effects ANOVA was used to evaluate the effects of 0, 1, or 2 naps per 24h; time of SD; and drug condition, on NE.

Results: Significant main effects were found for SD day (p=0.001), time of day (p<0.001), and drug condition (p<0.004). An interaction of drug condition by nap by time of day (p=0.004) revealed that caffeine during 88h SD without naps produced significantly higher plasma NE, especially during the diurnal period. Naps attenuated this effect in subjects who received caffeine. Modafinil appeared to have no effect on NE.

Conclusion: Sustained low-dose caffeine during SD resulted in a marked increase in plasma NE to levels well beyond those observed for modafinil or placebo. The effect of 2h naps in attenuating the NE increase due to caffeine suggests that homeostatic pressure for sleep contributed to the elevated NE levels; and the confinement of the effects to diurnal periods suggests that the circadian system also influenced NE release.

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0144
The Pharmacokinetic Properties Of Gaboxadol, A New Hypnotic, In Young And Elderly Men

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Introduction: Gaboxadol is a selective extrasynaptic GABA agonist in development for the treatment of insomnia. An extensive pharmacokinetic and tolerability study was performed. This abstract presents results from young and elderly men.

Methods: Thirty-six young men (18-45yrs) were randomised to receive doses of gaboxadol (10, 20, 30 and 40mg/day) or placebo in four groups. Six received gaboxadol and three received placebo per group. In a group of 6 elderly men (more than 65yrs), four received 20mg and two placebo. Gaboxadol was administered in the morning for five consecutive days following overnight fasting. Full pharmacokinetic serum profiles were obtained on Days 1 and 5. Safety parameters were measured regularly during treatment.

Results: Gaboxadol was rapidly absorbed and eliminated in young men at all dose levels (mean tmax range: 0.5 to 0.9h; mean apparent terminal half-life (range: 1.4 to 1.6h) with similar results on both days. Apparent terminal half-life, tmax and the apparent oral clearance (CL/F) (range: 34 to 39L/h) were independent of dosage. Mean apparent volume of distribution (Vz/F) was 70 to 87L. After treatment with 20mg gaboxadol, tmax (range 0.7 to 1.1h) in elderly men was similar to young men. AUC0-inf and Cmax were approximately 40% higher in the elderly. Mean apparent terminal half-life was longer in elderly (approx. 2h vs. 1.5h in young men). Mean Vz/F was similar to young men and CL/F was approximately 40% lower in elderly men. Up to 20mg gaboxadol was well tolerated in young and elderly men. In young men, 30mg was moderately well tolerated and 40mg was not well tolerated. Dizziness, somnolence and headache were the most common adverse events.

Conclusion: The pharmacokinetic properties of gaboxadol, with its rapid absorption and short apparent terminal half-life, demonstrate an optimal profile for a hypnotic. Younger men have higher apparent clearance than elderly men and a slightly longer half-life.

This research was part of a larger study to be reported later and was supported by H. Lundbeck A/S.

0145
Effects Of RS-86 And Donepezil On EEG Sleep In Healthy Subjects

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Introduction: In the present study we investigated the effects of the M1 agonist RS-86 and the acetylcholinesterase inhibitor donepezil on the sleep EEG in healthy subjects. By doing this we aimed to establish both substances for further investigations of sleep regulation and sleep abnormalities in depressive disorders. Based on the reciprocal interaction model of sleep regulation and previous studies we hypothesized that both drugs would lead to an increased production of REM sleep and a shortening of REM latency.

Methods: In a double-blind, placebo-controlled sleep laboratory study we investigated the effects of 1.5 mg RS-86 and 10 mg donepezil on sleep in n=20 healthy volunteers (18-35 years) by polysomnography and EEG spectral analysis.

Results: RS-86 lead to a significant reduction of REM-latency, slow wave sleep and slow wave activity compared to placebo. After donepezil we observed a significant increase in REM % and REM density. Both substances were very well tolerated.

Conclusion: Like in previous studies RS-86 was more effective in shortening REM latency than donepezil. However, donepezil enhanced REM % and REM density. The differential effects of the two substances seem to be promising for future research into the regulation of NREM/ REM sleep and for modulating sleep in depressive disorders.

0146
Neurobehavioral Functioning During 88 Hours Of Sustained Wakefulness: Modafinil As A Countermeasure

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Introduction: Severe sleep restriction over multiple circadian cycles produces wake-state instability, with attentional lapses; neurocognitive performance decrements; increased sleepiness, fatigue and exhaustion; and elevated homeostatic drive for sleep. This study examined the effectiveness of a split daily 2 x 200mg dose of modafinil across 4 days of total
sleep deprivation for mitigating neurocognitive, subjective and physiological impairment as pressure for sleep increased.

**Methods:** A double-blind, placebo-controlled, randomized parallel-groups trial was performed in N=25 healthy volunteers (19m, 6f; aged 22-45y) who lived for 10 days in the laboratory. Following a baseline period, subjects remained awake for 88h (4 days). Subjects received 200mg modafinil (n=14) or placebo (n=11) at 12:00 and 00:00 each day (i.e., 400mg per 24h) during sleep deprivation. Eight neurocognitive performance and subjective tests and eight subjective scales were administered every 2h of wakefulness. Physiological parameters (core body temperature; plasma cortisol, melatonin, noradrenaline) were also measured. Subjective adverse experiences were evaluated every 2h throughout the 88h sleep deprivation. Active drug vs. placebo responses were compared using mixed-effects regression models that accommodated non-linear changes over days as well as inter-subject variability in response magnitudes.

**Results:** Relative to placebo, modafinil significantly attenuated impairments in psychomotor vigilance lapses (P<0.009), cognitive throughput (P<0.013) and other neurocognitive performance functions (P≤0.05), for up to 76h of wakefulness. Modafinil had fewer effects on subjective ratings, but improved alertness post performance testing (P<0.013). No serious adverse experiences were reported.

**Conclusion:** During 4 days of sleep deprivation, a split daily dose of 400mg modafinil was effective in attenuating decrements in a range of neurobehavioural functions, without producing significant physiological side effects or serious adverse experiences. The cognitive effects of sustained twice-daily modafinil administration persisted in the face of escalating sleep drive.

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0147

**The Arousal Threshold And Neurocognitive Effects Of Sodium Oxybate**

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**Introduction:** There is concern about the peak dose effect of sodium oxybate on arousal threshold and neurocognitive function in patients during sleep. There are no published studies that address the effect on auditory arousal threshold and neurocognitive function at peak dose. Our study is meant to assess these two issues regarding the use of sodium oxybate for cataplexy in patients with narcolepsy.

**Methods:** A total of six patients currently using stable doses of sodium oxybate (dose range 4-5-9.0 g/day) for cataplexy associated with narcolepsy were chosen for this study. The patients were asked to fall asleep without their usual medication and were awakened by a 1000 Hz escalating decibel pulsed tone 45 minutes to 75 minutes after sleep onset. The auditory arousal threshold was noted and the patient was asked to perform parts A and B of the Trail Making Test. The patient then was asked to take their usual dose of sodium oxybate and once again awakened 45 to 75 minutes later using the same procedures.

**Results:** Pre-drug arousal threshold values ranged from 30-80 decibels (mean 53.3 ± 16.3), with peak drug dose arousal threshold values ranging from 60-90 decibels (mean 78.3 ± 11.3). Using the Wilcoxon Sign Rank Test the pre- and post-drug decibel difference were significant (p<0.05). There was no significant difference between the pre- and post-drug states on the Trail Making Test.

**Conclusion:** There was no measurable acute cognitive impairment using the Trail Making Test at the approximate peak dose of sodium oxybate. There may be an increased auditory arousal threshold comparable to published reports for benzodiazepine hypnotics. The arousal threshold during approximate peak drug doses of sodium oxybate falls within range of typical alarm devices. Further investigation is warranted utilizing a larger sample size and individual nights comparing sodium oxybate to placebo on auditory arousal threshold.

0148

**Effects Of An Evening Caffeine Administration On Vigilance, Melatonin And Cortisol Levels In Young And Middle-Aged Subjects**

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**Introduction:** Caffeine enhances vigilance in young subjects. However, few have studied the effects of caffeine on biochemical substrates associated with alertness such as melatonin and cortisol, and there are no comparative studies on middle-aged and younger subjects with regards to these parameters. The objective of this study is to evaluate age-related effects of an evening dose of caffeine on subjective and objective measures of vigilance and on melatonin and cortisol concentrations.

**Methods:** Moderate caffeine consumers (N=26), were assigned to two age groups, young (mean: 23.8y) and middle-aged (mean:49.8y). All were submitted to a caffeine (200 mg) and a placebo condition in a double blind cross over design, separated by a one week. They received a 100 mg capsule of caffeine (or placebo) three hours before bedtime and the remaining dose, one hour before bedtime. Vigilance and neuroendocrine measures were repeated during the evening.

**Results:** No condition by group effect was found for any variable showing that the effects of caffeine were similar in the young and middle-aged subjects. In the caffeine condition, subjective alertness (p<0.01) and psychomotor performance (p<0.01), were significantly higher whereas spectral power in delta, theta and beta frequencies of waking EEG were significantly lower compared to placebo (p<0.05). Melatonin concentration increased (p<0.01) and cortisol levels diminished (p<0.04) in the caffeine condition.

**Conclusion:** Caffeine produced similar arousing effects in both age groups. It also enhanced melatonin and reduced cortisol concentrations likewise in young and middle-aged subjects. While these neuroendocrine effects are usually associated with a decrease in vigilance, caffeine significantly raises subjective and objective measures of vigilance. The dissociation between neuroendocrine changes and increased vigilance following caffeine suggests that the effects of caffeine on vigilance are not modulated via its effects on melatonin and cortisol concentration.

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0149

**The Effect Of Risperidone On The Slow-Wave Sleep Of Normal Subjects**

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**Introduction:** Slow-wave sleep (SWS) deficits have been associated with schizophrenia. The serotonin type 2 receptor (5-HT2) antagonist
ritanserin, an experimental compound, increases SWS in humans. The atypical antipsychotic risperidone, an effective medication with fewer extrapyramidal side effects than traditional antipsychotics, also antagonizes 5-HT2. This similarity between risperidone and ritanserin led us to hypothesize that risperidone would increase SWS.

Methods: Twelve healthy medication-free subjects maintained a regular sleep schedule for five days prior to three consecutive nights of in-lab over-night polysomnographic recordings. A full clinical-polysomnogram (PSG) montage was recorded the first night. On the second and third nights only EEG, chin EMG, and EOG were recorded. All of the subjects were randomized to receive risperidone 1 mg 30-minutes prior to one of their three PSGs, half of the subjects prior to their second PSG and half prior to their third PSG. Placebo was given prior to the other PSGs. PSGs were scored using standard criteria while blinded to the subject’s medication status. A single-tailed paired-sample Student’s t-test was used to compare SWS across nights.

Results: Eight of 12 subjects (age 28.92±2.97) were male. No sleep disorders were identified on the screening night. The percent of SWS (%SWS) did not differ significantly from placebo nights (6.90±3.99%) to risperidone nights (5.78±3.69%) (p=0.11). In fact, SWS% of all but one subject decreased on risperidone. The total number of REM sleep epochs, but not %REM, changed significantly from placebo (180.17±36.16) to risperidone (156.00±33.76) (p=0.034).

Conclusion: Low-dose risperidone did not acutely affect the %SWS or any sleep architecture parameters other than REM sleep. Fewer total epochs of REM sleep occurred on risperidone, but %REM sleep did not differ. It appears that a single low-dose of risperidone does not acutely affect the SWS of normal subjects, but it may suppress REM sleep.

Janssen Pharmaceutica Products

0150
Low-Dose Doxepin In The Treatment Of Primary Insomnia
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Introduction: Doxepin HCl is a dibenzoxepin tricyclic compound approved for the treatment of depression. The purpose of the present study was to explore the efficacy and tolerability of low-dose doxepin for treatment of primary insomnia.

Methods: This was a randomized, multicenter, double-blind, placebo-controlled, four-way crossover dose-response study in which three dose levels (1 mg, 3 mg, and 6 mg) of doxepin were assessed in adult patients from 18-64 years with primary sleep maintenance insomnia. Randomized patients reported ? 3 months of DSM IV primary insomnia, ? 60 minutes of Wake Time During Sleep (WTDS) and ? 10 minutes of Latency to Persistent Sleep (LPS), confirmed by screening polysomnography (PSG). Each of four treatment periods consisted of two consecutive nights of study drug dosing separated by a 5 or 12-day drug free interval. Primary endpoint was WTDS.

Results: Doxepin 3mg and 6 mg demonstrated significant improvement in sleep maintenance by PSG-defined WTDS vs. placebo. Other sleep maintenance measures including Wake After Sleep Onset (WASO), Wake Time After Sleep (WTAS) and Total Sleep Time (TST) showed similar results. In addition, LPS showed a dose-dependent reduction, although not statistically significant. In a third-of-the-night analysis, doxepin improved sleep efficiency in each third of the night. Patient-reported data paralleled the PSG results. Objective and subjective measures of next-day residual effects were not statistically different from placebo. There was no difference in adverse events reported for doxepin vs. placebo.

Conclusion: Low-dose doxepin was efficacious in the treatment of primary insomnia. Relative to placebo, low-dose doxepin was well-tolerated and devoid of residual effects.

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0151

Insomnia And Dream Recall Frequency - Differential Effects Of Obstructive Sleep Apnea (OSA)
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Introduction: Nightmares occur in higher frequency in patients reporting insomnia. One study indicates that insomniacs report higher dream frequency based on diary reports (Schredl et. al. 1998). This study correlates questionnaire reports of dream and night frequency with self-reported insomnia in patients undergoing full night polysomnography.

Methods: Patients being evaluated with full night polysomnography in an AASM accredited sleep laboratory (N=290) completed an intake questionnaire assessing reported dream and nightmare recall frequency (1=never, 2=1/month, 3=1/week, 4=2/week, 5=nightly), and self reports of chronic disrupted sleep/insomnia. That data is correlated with a spectrum of polysomnography variables including: sleep latency (sl), wake after sleep onset (waso), sleep efficiency (se), REMS min., Epworth scale (0-24), and apnea-hypopnea index (ahi).

Results: For the entire grouping, no difference in dream recall was found between insomniacs (N=142, mean=2.68) and those reporting no insomnia (N=148, mean=2.66). Dream recall was significantly lower in those with (sl) > 30 min., (se) < 65%, (waso) > 60 min., (ahi) > 15, and Epworth < 10. Nightmare recall was significantly higher (p<0.01) in patients reporting insomnia. Nightmare recall was significantly lower in those with < 60 min. REMS, (se) < 65%, Epworth < 10, and (waso) > 60 min. For the grouping without OSA (ahi<15, N=156) dream recall frequency was significantly lower (p<0.05) in the insomnia grouping. In the grouping with OSA (N=92) both dream and nightmare recall were significantly higher (p<0.01) for the grouping reporting insomnia (N=36), despite significant negative correlation for (waso) > 60 min. and (se) < 65%.

Conclusion: (1) Insomniacs report increased nightmare recall frequency. (2) Reported dream frequency declines with declining sleep quality. (3) In patients with sleep apnea, dream recall is increased for those patients reporting insomnia (a finding not seen in the grouping without OSA). These findings demonstrate that reported dream recall frequency declines with diminishing sleep quality. In patients with OSA, however, dream recall increases with self-reported insomnia suggesting that increased arousal in these patients is associated with increases in dream recall.

0152

Affect Frequency And Valence In Manifest Dream Reports Or Associations In Psychoanalytic Therapy
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Introduction: Question has been raised as to whether it is the affective or narrative aspect of dreaming that is central to its development. In both laboratory and spontaneous dream reporting affect has been reported as low as 35% and as high as 80%.

Methods: We examined the first and last manifest dream report of 24 patients, 14 women and 10 men who had completed psychoanalytic therapy, for the presence and valence of affect. If no affect was found, the dream associations were examined for affect and valence. Two raters scored each dream report.

Results: The agreement between the two raters in scoring the presence or absence of affect in the dream report was 93.8% (45/48). The agreement for scoring the valence of affect, positive or negative was 100% (94/94). We found affect in 58.3% (28/48) of dream reports. Affect was present in 65% (13/20) of men’s dream reports and 53.6% (15/28) of women’s. The valence of affect in dream reports was negative 62.5% (17.5/28) of the time. The valence in dream reports became more positive across time from 19.2% (2.5/13) in the first dream report to 53.3% (8/15) in the last. This was true for both genders. The associations in the dream reports without affect had affect 88.2% (15/17) of the time and the affect was negative 93.3% (14/15) of the time. Affect was present in either the dream report or the associations 95.8% (46/48) of the time.

Conclusion: Affect is almost always present in either the dream report or the associations and becomes more positive across time in both men and women most likely as the result of treatment, although the passage of time may be a factor. The centrality of dream affect in dream formation and interpretation is supported, if the dream experience includes the associations to the dream report. Comparable studies of laboratory collected dream reports needs to be undertaken as recalled dreams in therapy may not be representative of all dreaming.

0153

Emotional Premenstrual Symptoms And The Emotional Content Of Dreams
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Introduction: Women with premenstrual symptoms tend to have poorer quality of sleep and more mood changes during the premenstrual phase of their cycle than during other phases. Mood changes have been linked to intense and negative emotions in dreams. Based on that observation, this study examined whether women with severe emotional premenstrual symptoms have more negative and more intense dream emotions during the premenstrual phase than during the follicular phase, in comparison to women with minimal symptoms.

Methods: So far, ten women participated in this study (3 with severe premenstrual symptoms, 7 with minimal symptoms; mean age = 28.3). They were not using contraceptive medication and had regular, ovulatory cycles. Participants slept in the laboratory for one night during the follicular phase and two nights during the premenstrual phase. Upon morning awakening, they wrote down their dreams and rated the intensity (minimal or nonexistent to very intense) of six dream emotions (2 positive, 4 negative). Dreams were also collected at home for an additional two nights during the follicular phase and one night during the premenstrual phase, totaling three nights for each phase.

Results: Using 2 x 2 mixed factorial ANOVAs, it was found that intensity and proportion of dream emotions, either positive or negative, were not related to the phase of menstrual cycle (p > .05). No differences were observed between women with severe and minimal symptoms (p > .05).

Conclusion: Within this small sample, emotions experienced by women with severe premenstrual symptoms seemed unrelated to the intensity or proportion of dream emotions, suggesting little continuity between emotional premenstrual symptoms and emotional dream content. It is unlikely that dreams would affect sleep quality during the premenstrual phase. With a larger sample, future research may look at other aspects of dream content, such as interpersonal relations, during the premenstrual phase.

0154

EEG Correlates Of Low Dream Emotions In Adults With Autistic Spectrum Disorders
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**Introduction:** Difficulties in identifying and describing emotions are part of the Autistic Spectrum Disorder. It is known that EEG activity in the Alpha range correlates with various aspects of dream content. We compared adults with ASD and controls on REM sleep dream reports and Alpha EEG activity.

**Methods:** Twelve persons with ASD and normal IQ (11M, 1F, 21.2±1.3 years) and 11 control participants (10M, 1F, aged 21.9±0.9 years) spent three nights in a sleep laboratory. On night 3, dream reports were collected following REM sleep awakenings (starting on REM period #2) and analyzed according to Hall and Van de Castle (1966). Sixty seconds of EEG was selected from the five minutes preceding the awakening in the second REM sleep period, and submitted to spectral analysis to extract absolute spectral amplitude values for Alpha activity (8-12 Hz).

**Results:** Dream reports of ASD participants contained fewer words than controls (168.1±24.4 vs 63.1±11.1; p=.00002). ASD reports contained a lower frequency of emotional elements (0.71±0.16 vs 0.15±0.07; p=.02). ASD participants used less words than control to express emotional elements (147.9±23.6 vs 54.8±8.8; p=.01). ASD participants showed significantly lower alpha activity over midline and parasagittal areas, and higher alpha activity over more lateral areas compared to controls (p=.0004 to .04). In both groups of participants taken together, a positive correlation was found between dream emotion scores and Alpha activity over centro-posterior areas (rho = .02 to .04).

**Conclusion:** ASD participants report less emotional content in their dreams. The relationship with REM sleep centro-posterior Alpha EEG activity may provide a neurophysiological support for the differences in dream content between persons with ASD and typically developed individuals.

**Canadian Institutes for Health Research**

**0155**

**Nightmare Frequency By Age, Gender And 9/11: Findings From An Internet Questionnaire**

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**Introduction:** Nightmare (NM) frequency norms for age and gender are uncommon. Effects of the 9/11 attacks on NMs are also not well understood. An internet questionnaire initiated in 1997 enabled us to study these 3 variables in a large multicultural sample.

**Methods:** 29,466 responses were received between 01/1997 and 12/2003. Among other items, the questionnaire requested age and gender and posed 2 open questions about number of dreams and NMs recalled in a typical month. Responses were checked manually for anomalies. We excluded subjects <10 or >59 years, not reporting age and gender, or reporting >93 NMs or >124 dreams/month. Of the 24,102 remaining subjects, 19,475 were female (age: 24.85±9.87 yrs) and 4627 were male (25.32±10.15; p=.002). NM responses were log-transformed (log+1) and assessed as a function of gender, 911-status and age using a 2 (male, female) x 2 (pre911, post911) x 5 (10-19, 20-29, 30-39, 40-49, 50-59) ANOVA.

**Results:** Main effects obtained for all 3 variables (p<.0001). Females reported more NMs (.542±.386 or approx. 2.5±1.43 NM/mo) than males overall (.438±.385 or 1.7±1.43 NM/mo) and at every age (p<.005) except 50-59 (p=.097). NMs increased from 10-19 (.525±.382) to 20-29 (.550±.387; p=.00003) and decreased monotonically thereafter (.514±.395, .443±.390, .378±.383; all adjacent p<.0005). NMs were less frequent pre911 (.489±.382) than post911 (.527±.389) which a Gender x 911-Status interaction (p=.015) indicated was true for males (.376±.364 vs .448±.388; p=.00005) but not females (.520±.380 vs .545±.387; ns). This effect was robust (p<.05) for males at all ages except 30-39 (p=.970) whereas for females it occurred only at age 30-39 (p=.016).

**Conclusion:** NMs are reliably more frequent for females than for males at all ages up to 49 in this sample. They peak in early adulthood and decline steadily thereafter for both sexes. The 9/11 attacks appear to have affected males preferentially, perhaps because of a frequency ceiling effect for females or greater perceived future threats by males.

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**0156**

**Dream Content Analysis In Korean Children**

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**Introduction:** The aim of this study was to perform the analysis of dream content in Korean children population.

**Methods:** The most recent dream reports from 1330 Korean children (Male 668, female 662; age range: 9~14) were collected and analyzed using Hall/Van de Castle System.

**Results:** There were more (p<0.05) male characters in dreams of boys than those of girls. Dreams of boys showed more (p<0.05) aggression related dream contents than those of boys. Boys also had more (p<0.05) dreams of self-negative content. These results also showed that sexual differences of dreams begin before age 9. Nine to fourteen year old boys and girls had less sexual content of dream compared to young adults. There were higher prevalence of friends characters, family characters, and contents of sexuality in childre’s dream compared to adults. These differences between children and adults existed in both sexes. In dreams, boys showed their aggression in more indirect way compared to young adults. There are fewer differences between girls and young adults compared to boys.

**Conclusion:** Dream content analysis using most recent dream method may give us the understanding of psychosocial development.

**0157**

**Rational Thought In Dreaming And Individual Dreaming Styles**

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**Introduction:** Rational thought in the waking state (“discriminating rationality,” Shoben, 1961, p. 403) refers to the individual’s ability to notice and differentiate his own subjective experience from the known, objective facts regarding present events or situations (Shoben, 1961). In the dreaming state, in theory, the concentration on the dreamer’s incidental failure to isolate the dreaming state from the waking state (Hobson, 1997) leaves an open door for a phenomenological approach in researching the possible existence of rational thought in dreaming.

**Methods:** In our previous research we postulated that thoughts evoked during dreaming situations and also the thought processes themselves are rational. We delimited and categorized 31 dream reports from individual
Whether there is a correlation between dreaming styles and cognitive FFTs during 5-min REM episode and intensity/emotional variables. Differences on dream intensity (Dream Property scale; Takeuchi et al., 2022) and 2.2 TREM and 2.8 SOREM episodes for CTL subjects. Between-group REM (TREM) and 2.8 SOREM episodes were obtained for ISP subjects. On average, 3 typical awakenings every 5 min of REM sleep and kept awake for 60 min for men—laboratory for 3 consecutive nights. On night 3, subjects were repeatedly awakened and asked to recall most recent dreams and to fill in the Aggression Questionnaire (AQ)1. Only forty-one (81.6%, 5F) RBD patients (27iRBD and 14sRBD; mean age 67.5±7.5) and 35 (49.3%, 5F) controls were able to remember their dreams. A total of 98 and 69 dreams were collected in the two groups, respectively. Verbatim dream description was recorded and scored according to the Hall and Vande Castle coding system.2 Coded dreams were then processed by dreamSAT software and differences were assessed with Cohen's h statistic. Between-group differences in AQ scores were assessed by t-test. Bonferroni correction was applied when appropriate.

**Results:** RBD patients had higher percentage of «dream with at least one aggression» (DWA) than controls (66% vs. 15%, p<0.00001). An increased aggression/friendliness interactions ratio (86% vs. 44%; p<0.0001) and an increased frequency of animals (19% vs. 4%; p=0.0001) was observed in dreams of RBD. In contrast to controls, none of RBD patients had «dreams with at least one element of sexuality» (0% vs. 9%, p<0.0001). The two groups did not differ in other dream categories nor in AQ scores (69.9±16.1 vs. 73.8±20.3; p=0.98). No difference was observed between iRBD and sRBD.

**Conclusion:** An elevated proportion of aggression themes characterizes the dreams in RBD, despite normal levels of daytime aggressiveness. The increased ability to recall dreams in RBD may be related to the peculiar dreams content or it may reflect differences in memory processes. DWA and vigorous motor behaviors may be related to the hyperactivity of a common neuronal generator. References: 1. Buss and Perry, Journal of Personality and Social Psychology 1992:63;452. 2. Hall and Vande Castle. The Content Analysis of Dreams. 1966 NY, Appleton Century Crofts.
psychiatric interview and a self-rating questionnaire, the Health, Personality and habit scale (HPH), were administered. One night of PSG recording were also conducted.

**Results:** PSG studies showed a tendency of increased wake time during sleep (13.1%) and decreased percentages of slow wave sleep (stage 3: 5.46%; stage 4: 3.46%) in comparison to the expected range of normal adults. One patient showed PLMD (PLMI= 18 times /hr) and 4 patients demonstrated SRBD (RDI >5 times/hr). In addition, NREM alpha intrusions were found in 5 of the patients. When the patients with PLMD, SRBD and alpha intrusion were excluded, 3 of the 12 patients showed higher number of spontaneous arousal during sleep (15 >times/hr). In terms of the psychiatric features, when the patients with PLMD or SRBD and alpha intrusion were excluded, 3 of the 12 patients showed higher number of spontaneous arousal during sleep (15 >times/hr). In addition, 7 patients showed higher number of spontaneous arousal during sleep (15 >times/hr). In terms of the psychiatric features, when the patients with PLMD, SRBD and alpha intrusion were excluded, 3 of the 12 patients showed higher number of spontaneous arousal during sleep (15 >times/hr). In addition, 7 patients were diagnosed with mental disorders(posttraumatic stress disorder ; generalized anxiety disorder ; adjustment disorder ; major depressive disorder).

**Conclusion:** There is a high percentage of epic dreamers showed tendency of increased arousals during sleep, although the causes of the arousals varied among individuals. This suggests that epic dreaming may be the manifestation of underlying arousals result from heterogeneous pathology. In addition, the percentage of psychopathology was also found to be high in this group. The association between psychological factors and physiological arousals and the occurrence of epic dreaming phenomenon requires further studies.

0161
**Recall Of Waking Stimuli Is Hindered By Auditory Imagery At Sleep Onset**

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**Introduction:** Tones and sounds used to awaken subjects for collection of sleep mentation may influence subsequent cognitive processes. This study examined the recall of 100ms thematic awakening sounds as a function of auditory and non-auditory imagery at sleep onset.

**Methods:** 23 subjects were awakened multiple times from at least 5 sec of Hori SO stages 4 and 5. Ten different 100ms sounds of varying timbre and meaning (e.g., dog’s bark, breaking glass), counterbalanced between subjects, were used as awakening stimuli. Subjects reported pre-stimulus mentation and gave verbal ratings (9-point scales) of mentation characteristics. They were asked to recall the nature of the awakening stimulus and allowed to go back to sleep. The procedure was repeated for a maximum of 10 trials or until 2 hours had elapsed since first lights out. Twelve of the subjects had been partially deprived of REM sleep (REMD) the night before on previous night; 11 had not (CTL). Trials on which mentation was reported were averaged within subjects and submitted to a 2 x 2 ANCOVA with Aud-Image (Yes, No) as repeated measure, Group (REMD, CTL) as fixed factor and proportion of stimulus recall as dependent measure.

**Results:** All trials resulted in subjects awakening. The stimulus was remembered in 63% of trials that involved mentation. A main effect for Aud-Image (F1,22=4.753, p=.041) indicated that awakening stimuli were more often forgotten when auditory imagery was present (M=1.36±0.29) than when it was absent (M=1.183±0.221). There were no main effect and no interactions for Group.

**Conclusion:** Recall of waking stimuli was hindered by the presence of prior auditory imagery. Ongoing auditory imagery may have interfered with encoding of the stimulus during sleep. Alternatively, the recall, reporting and rating of auditory imagery may have interfered with short-term memory of the stimulus.

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**Category D—Dreams**
Methods: Eight young healthy subjects (5 males, 3 females) participated in a counterbalanced within subjects design. Subjects experienced 14 consecutive short nights and 14 consecutive long nights, with 6 days off in between. During the short nights they woke at their habitual weekday wake time and went to bed 6 hours earlier. During the long nights they had the same bedtime but wake time was delayed by 3 hours. All subjects slept at home in dark bedrooms during the scheduled times. Compliance was confirmed with a wrist actigraph and a photosensor. After the final day in each condition, subjects experienced a dim light phase assessment where half-hourly saliva samples were collected and later assayed for melatonin.

Results: Phase advances were 1.7 ± 0.8 h with placebo (n = 12), 2.3 ± 0.6 h with 0.5 mg (n = 11) and 2.6 ± 0.4 h with 3.0 mg (n = 12) (mean ± SD). Larger phase shifts were observed in the 0.5 mg (p = 0.07) and 3.0 mg (p = 0.004) conditions, compared to placebo.

Conclusion: Afternoon melatonin enhances the phase advance induced by intermittent morning light and a gradually advancing sleep schedule. Thus, depending on the number of days of treatment, this procedure can reduce or eliminate jet lag.

This work was supported by a NIH grant from NINR (R01 NR07667). Melatonin and matching placebos were provided by Ecological Formulas, a division of Cardiovascular Research Ltd., Concord, CA.

0162
Waking Up Late Phase Delays The Human Circadian Clock More Than Staying Up Late
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Introduction: Short sleep episodes, interspersed with longer recovery sleep episodes, are increasingly common in modern society. We previously showed that extending sleep from 6 to 9 hours by making bedtime earlier phase advances the circadian clock. Here we report on the effect of extending sleep from 6 to 9 hours by making wake time later.

Methods: These results show that when people regularly wake up early they phase advance their circadian clocks. Conversely, when people regularly wake later they phase delay their circadian clocks. When wake time is changed the phase shift is much greater than when bedtime is changed. The substantial impact of a later wake time on circadian phase is most likely due to the associated reduction in morning light exposure.

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0163
Afternoon Melatonin And Morning Intermittent Bright Light Can Help You Prepare For Eastward Jet Travel
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Introduction: Jet lag results from the misalignment between circadian rhythms and the destination time zone, and is worse after eastward flights as humans find it harder to phase advance than delay. We recommend phase shifting circadian rhythms towards the destination time zone before the flight to reduce or eliminate jet lag. Here we determined if phase advances induced by morning bright light treatment, combined with a gradually advancing sleep schedule, could be enhanced by melatonin.

Methods: To date 35 healthy adults (16 men, 19 women, age: 19-45 y) spent 3 nights in the lab, during which their sleep (dark) period was advanced by 1 h/day. They received intermittent morning bright light upon waking, from a single light box containing cool white fluorescent lamps. There were four 30 min bright light pulses (~5000 lux) alternating with 30 min ordinary room light (~60 lux). In the afternoon subjects received 1 of 2 possible doses of melatonin, timed to induce phase advances, or matching placebo: 0.5 mg 5 h before bedtime or 3.0 mg 7 h before bedtime. Phase advances were measured by collecting saliva samples every 30 min in <5 lux to determine the dim light melatonin onset (DLMO) before and after the 3 day treatment.

Results: Phase advances were 1.7 ± 0.8 h with placebo (n = 12), 2.3 ± 0.6 h with 0.5 mg (n = 11) and 2.6 ± 0.4 h with 3.0 mg (n = 12) (mean ± SD). Larger phase shifts were observed in the 0.5 mg (p = 0.07) and 3.0 mg (p = 0.004) conditions, compared to placebo.

Conclusion: Afternoon melatonin enhances the phase advance induced by intermittent morning light and a gradually advancing sleep schedule. Thus, depending on the number of days of treatment, this procedure can reduce or eliminate jet lag.

This work was supported by a NIH grant from NINR (R01 NR07667). Melatonin and matching placebos were provided by Ecological Formulas, a division of Cardiovascular Research Ltd., Concord, CA.

0164
Melatonin And Bright Light Treatment Improve Daytime Activity Levels And Daytime Wake Time In Institutionalized Patients With Alzheimer’s Disease
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Introduction: In Alzheimer’s disease (AD), nighttime sleep is severely fragmented and daytime activity is disrupted by multiple naps. The purpose of this study was to test the effectiveness of melatonin and bright light therapy in reducing rest-activity (circadian) disruption in institution-alized patients with AD.

Methods: A randomized clinical trial design was employed to compare a control group to two experimental intervention groups: light plus melatonin (LM) and light plus placebo (LP). Experimental subjects received morning (9:30-10:30 AM) light exposure (>2500 lux in gaze direction) Monday - Friday for 10 weeks. The LM group (n=16) received 5mg melatonin and the LP group (n=17) received placebo, both administered at the same time every evening. The control group (n=17) received usual indoor light (150-200 lux). The sample mean age was 86 years and mean Mini Mental State score was 9. Nighttime sleep variables, daytime sleep time, daytime activity, day-night sleep ratio, and circadian outcomes were assessed using actigraphy prior to and during the last week of the intervention.

Results: Multivariate analysis of variance was employed to test the primary study hypotheses. There were no significant differences in nighttime sleep variables between all 3 groups. However, daytime sleep time, daytime activity, and day-night sleep ratio significantly improved in the LM group compared to controls (p<.000, p<.003, p<.000 respectively) and the LP group compared to controls (p<.000, p<.001, p<.000), with LM being significantly better than LP (p<.001, p<.002, p<.003). Analysis of circadian outcomes revealed a significant increase in rhythm amplitude in the LM group compared to controls (p<.01) and LP compared to controls (p<.02).

Conclusion: Morning bright light exposure resulted in significantly different amounts of daytime sleep time and overall activity level compared to placebo. Light plus melatonin resulted in significantly greater improvements in these outcomes than light plus placebo. While both light groups experienced decreased daytime sleep and increased activity, the control group experienced worsening (increased) daytime sleep time and decreased activity. Light plus melatonin also significantly increased rest-
activity rhythm amplitude compared to light plus placebo or usual light exposure. The addition of melatonin to a bright light exposure regimen produced larger improvements in daytime activity and rest-activity amplitude than light alone.

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0165
A Case Of Non-entrained Type In A Sighted Individual
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Introduction: We investigated a case of non-entrained type circadian rhythm sleep disorder in a 49 y.o. male reporting an inability to maintain a regular sleep-wake cycle.

Methods: The patient was admitted to the Northwestern GCRC for polysomnographic (PSG) sleep recording followed by a 28 hour constant routine protocol. Sleep coincided with the patient’s regular bedtime. Wrist activity was collected prior to sleep recording and plasma melatonin was collected during the constant routine. Wrist activity and light exposure data (AW-Light, Mint Mitter) was collected for one month.

Results: The patient reported problems since childhood of difficulty falling asleep and staying asleep at conventional times which was associated with insomnia and excessive daytime sleepiness. The patient’s history is otherwise unremarkable except for the reported presence of retinal holes. An MRI examination revealed no visible abnormalities. PSG was normal and the patient reported a typical night’s sleep in the GCRC. Both salivary and plasma DLMO occurred approximately 4 hours before the patient’s normal bedtime. Wrist activity records demonstrated an activity-rest cycle of 24.4 h. Average daily light exposure over a one month period was 95 lux. During two days the patient had a high daily average (249 lux and 1188 lux) due to an extended exposure of 20,000 lux for about 5 hours due to work commitments. This phase shifted his circadian sleep-wake cycle on the following day between 4-6 hours.

Conclusion: The patient is not entrained to a 24 hour day. This may be due to chronically low light exposure which is insufficient to entrain his circadian rhythms. However, it is not clear whether the patient has altered sleep regulation between morning-type (M-type) and evening-type (E-type) individuals. However, quantitative sleep EEG in chronotypes has never been analyzed according to topographic areas for which markers of sleep homeostasis have been shown to differ.

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0167
Topographic Variations Of Qualitative Sleep EEG In Morning-Type And Evening-Type Individuals
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Introduction: Some studies have suggested differences in homeostatic sleep regulation between morning-type (M-type) and evening-type (E-type) individuals. However, quantitative sleep EEG in chronotypes has never been analyzed according to topographic areas for which markers of sleep homeostasis have been shown to differ.

Methods: Two groups of healthy subjects (19-34 y.) were selected based on their score on the Morningness-Eveningness Questionnaire: 12 M-types and 12 E-types. An 8-h sleep schedule, kept for 1-week prior to laboratory PSG recording, was individually chosen to be as close as possible to the spontaneous schedule of the subject when obligation-free. Sleep EEG recorded from Fz, Cz, Pz and Oz in reference to linked ears was digitized at 256 Hz. Spectral analysis (FFT) was performed on 4-sec artifact-free sections for seven frequency bands (delta:1-4 Hz; SWA:1-5 Hz; theta:4-8 Hz; alpha:8-12 Hz; low sigma:12-14 Hz; high sigma:14-16 Hz; beta:16-24 Hz). Spectral power (uV2/Hz) was averaged within the first 4 NREM/REM cycles and, power spectra in each band were analyzed using Group-by-Derivation-by-Cycle ANOVAs.

Results: In NREM sleep, a significant Group-by-Derivation-by-Cycle interaction was found for spectral power in delta band (p<0.03); M-types tended to have more power than E-types in the first two cycles for Fz and Cz derivations (p<0.1). A similar interaction was found for the SWA band (p<0.03). A significant Group-by-Derivation interaction was found in the low sigma band (p<0.01), which revealed more power in M-types than E-types in all derivations except Fz (p<0.04). In REM sleep, we found a sig-
significant Group-by-Derivation-by-Cycle interaction in the beta band (p=0.04); M-types tended to have more beta activity than E-types in the first cycle for Cz and Pz derivations (p<0.01).

Conclusion: These results agree with the hypothesis that some aspects of sleep homeostatic regulation differ between M-types and E-types.

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0168
Effect Of Laboratory Adaptation On Sleep Stages And Quantitative Sleep EEG In Morning-Type And Evening-Type Individuals
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Introduction: Laboratory polysomnography (PSG) requires a sleeping environment quite different from the subjects' usual bedroom. In many cases, sleep quality and sleep architecture are affected by the novelty of a first night of PSG. Some of these effects may also last for more than one night. Previous studies have revealed that the sleep of morning-types (M-types) is very sensitive to disturbances such as sleeping at an abnormal circadian phase. Here we examine the hypothesis that they would also be more sensitive to PSG laboratory conditions compared to evening-types (E-types).

Methods: Two groups of healthy subjects (19-34 y.) were selected based on their score on the Morningness-Eveningness Questionnaire: 12 M-types and 12 E-types. An 8-h sleep schedule was individually chosen to be as close as possible to the spontaneous schedule of the subject when free from obligations. This schedule was kept for one week prior to laboratory admission and for two consecutive PSG recordings. Subjects with poor sleep quality (sleep efficiency <85%, sleep latency >30 min) were previously excluded by a screening PSG night preceding the experimental session by at least 7 days. Sleep stages were scored according to standard criteria. Spectral analysis (FFT) was performed on C3/linked ears derivation, on 4-sec artifact-free sections for six standard EEG frequency bands. NREM sleep spectral power (uV2/Hz) was averaged for first 4 NREM/REM cycles. Between-group differences on sleep stages were assessed by Group-by-Night ANOVAs and on activity in each band by Group-by-Night-by-Cycle ANOVAs.

Results: A significant Night effect was observed in sleep stages, with a decrease in stage 2 and an increase of both SWS and REM sleep from night 1 to night 2 (p<0.001, both duration and %). There was also an increase in subjective sleep quality (p=0.01). However, there was no significant Group effect or Group-by-Night interaction. Spectral analysis revealed significant Group-by-Night-by-Cycle interactions for SWA (1-5 Hz) and for the alpha band (8-12 Hz) (p<0.05 for both frequency bands). There was an increase in SWA from night 1 to night 2 in the first cycle, in M-types only. For the alpha band, M-types showed a decrease across the 4 cycles on both nights, whereas such a decrease, of smaller magnitude, was observed only during night 2 in E-types.

Conclusion: These results suggest that M-types and E-types may differ in the way they adapt to laboratory conditions.

Research Supported By: CHY.

0169
Delayed Sleep Phase Syndrome And Dim Light Melatonin Onset Test
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Introduction: Delayed Sleep Phase Syndrome (DSPS) is a chronic sleep-wake cycle disorder manifested by an abnormal entrainment of the Suprachiasmatic Nucleus (SCN). Measuring levels of melatonin and the onset of melatonin production can be a good marker for the phase and period of the circadian rhythm and help diagnose mis-entrained SCN. The purpose of this study was to objectively document circadian rhythm abnormalities in patients presenting with symptoms of DSPS using Dim Light Melatonin Onset (DLMO) Test.

Methods: A total of 83 consecutive patients (34 females and 49 males, mean age=29.9±15.7) who complained of an inability to fall asleep at the desired clock time and inability to awaken spontaneously at the desired time of awakening participated in the study. The Dim Light Melatonin Onset (DLMO) protocol involved patients being seated in a dark room from 1900 hours to 0300 hours during winter season and from 2000 hours to 0300 hours during summer season. During the testing all exposure to light greater than 5 lux was prohibited. Saliva specimens were collected using the Sali-SaverTM. Saliva melatonin was determined by ELISA kit from Buhlman Laboratories. The Dim Light Melatonin Onset (DLMO) was defined as the first 20% increase in melatonin concentration above 4pg/ml.

Results: Only 32 out of 83 patients (13 females and 19 males, mean age of 24.5±12.3) displayed significantly delayed DLMO representing individuals with intrinsic DSPS. No gender differences were observed. The rest of the patients had either normal DLMO or no discernible changes in endogenous melatonin level throughout the measurements period. The DLMO results revealed the mean time of melatonin onset which was significantly later in intrinsic DSPS patients than in patients with phenotypic DSPS-like symptoms (2306 h vs. 2035 h; F=34.6, p<0.001). The mean amount of melatonin secreted at DLMO was significantly higher in patients with phenotypic DSPS (p<0.001).

Conclusion: Salivary DLMO testing was able to differentiate between DSPS patients who had SCN mis-entrainment from phenotypic DSPS patients whose abnormal sleep patterns are due to poor sleep hygiene and probably associated with social avoidance and other behavioural problems.

0170
Delayed Sleep Phase Syndrome, Low Melatonin Secretors And Dim Light Melatonin Onset Test
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Introduction: It has been widely accepted that Dim Light Melatonin Onset (DLMO) Test is a remarkably good marker for circadian phase position in humans. In normal healthy people, DLMO occurs in the interval between 19:30 and 21:00h. In Delayed Sleep Phase Syndrome (DSPS), the phase of melatonin profile is shifted towards morning hours. Depressed patients show decreased melatonin output. The goal of this study was to investigate endogenous melatonin secretion in patients presenting with DSPS symptoms and comorbid sub-syndromal depression.

Methods: A total of 153 consecutive patients with DSPS symptoms attended a single sleep clinic. During their initial visit the patients were asked to complete psychiatric questionnaires to evaluate their subjective levels of depressive symptomatology. Thirty-three out of 153 patients (mean age of 33.0±17.6) scored high on the formal depression scale (CES-D), however a clinical diagnosis of depression was not established.
Regulation Of Circadian Rhythms By Sleep-Wake Centers In The Brainstem And Basal Forebrain
Abbott SM, et al.

Introduction: The circadian and sleep-wake cycles have been well characterized individually but less is known about how these two cycles may interact. Direct cholinergic projections to the suprachiasmatic nucleus (SCN) have been found from the laterodorsal tegmental (LDT) and pedunculopontine tegmental (PPT) nuclei, as well as from the nucleus basalis magnocellularis (NBM). These are important structures involved in the regulation of circadian rhythms and the sleep-wake cycle, respectively, suggesting a means by which these two systems may interact.

Methods: C57Bl/6j mice were implanted with electrodes aimed at the LDT, PPT or NBM, and a microdialysis cannula aimed at the SCN. Animals were stimulated, and analyzed for neurotransmitter release at the SCN and circadian behavioral response. Stimulation parameters for all regions were: 150 µA, 10 Hz, 2 msec pulse duration for 20 min. Additional parameters for PPT were: 1) 40 µA, 0.2 Hz, 0.2 msec pulse duration, or 2) 1 sec pulse/min of 400 µA, 60 Hz, 0.2 msec pulse duration. Samples were analyzed by HPLC for acetylcholine (ACh) and CE-LIF for glutamate (Glu).

Results: LDT and PPT stimulation produced significant (p<0.001) increases in ACh and Glu at the SCN. Additional PPT parameters produced different Results: parameter 1 increased Glu but not ACh, while parameter 2 increased ACh without affecting Glu. Behaviorally, LDT stimulation induced delays during the early night, and significant advances (p<0.05) during the late night. Early night PPT stimulations produced larger delays (-0.60±0.14 h) with parameter 1 than parameter 2 (-0.16±0.14 h). NBM stimulations produced a significant (p<0.05) delay in wheel-running activity during the early night.

Conclusion: These results suggest that there is a functional connection between sleep-wake centers and the SCN. Activation of these regions results in changes in neurotransmitter release at the SCN, and also shifts circadian behavior in a time of day- and stimulation-dependent manner.
P=2.6E-7), with minor changes in estimated circadian rhythm phase angle and period length. Examples will be presented of the application of these methods to evaluate changes in circadian rhythms in locomotor activity from a 40-day transmeridian flight fatigue study in pilots and in personnel working a shiftwork regime based upon a mars sol (24.6 hour days, Mars Exploration Rover mission).

**Conclusion:** Since changes in circadian rhythm activity metrics have been associated with changes in neuropsychological functioning and health status, the reliable statistical evaluation of changes in circadian rhythmicity in locomotor activity provides the opportunity to document physiological changes which can be predictive of subsequent sleep disturbance and impaired performance in operational work environments.

NASA’s Airspace Operations System Project of the Airspace Systems Program

**0174**

**Effects Of Total Sleep Deprivation And Chronic Circadian Misalignment On Cortisol Levels**

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**Introduction:** Acute total and partial sleep deprivation has been reported to increase or have no effect on cortisol levels. The influence of circadian misalignment, such as that which commonly occurs during shift work and jet lag, on cortisol levels is unknown. We examined the influence of total sleep deprivation and chronic circadian misalignment on cortisol.

**Methods:** Healthy, drug free females and males (N=16) aged 20-40 participated. After three weeks of maintaining a consistent sleep-wake schedule at home, six laboratory baseline days and nights, a 40-h constant routine (CR, sleep deprivation) to estimate circadian melatonin phase (DLMO25%) and an 8-h recovery sleep episode, participants were scheduled to a 25-day work-rest/wakefulness-sleep schedule that resulted in sleep and circadian disruption for seven of the sixteen subjects. A second constant routine was conducted to assess DLMO25% on day 33. Sleep was recorded and scored from central EEG leads. Plasma cortisol levels were measured every 30 min during CRs and during sampling windows every week. Trapezoidal area under the curve (AUC) was used to estimate twenty-four hour cortisol levels. Changes in melatonin phase, sleep staging and cortisol levels were examined with repeated measures ANOVA.

**Results:** Total sleep deprivation significantly increased cortisol levels whereas chronic circadian misalignment significantly reduced cortisol levels (p < 0.05). The phase angle relationship between the DLMO25% and scheduled sleep was maintained in 9 participants whereas phase angle was abnormally advanced in the remaining 7 participants (p < 0.05). WASO was higher (p < 0.01) in participants who exhibited circadian phase misalignment. Participants who exhibited normal sleep and normal circadian phase showed little change in cortisol levels.

**Conclusion:** The current findings demonstrate that total sleep deprivation and chronic circadian phase misalignment have different effects on neuroendocrine physiology, which may be related to circadian amplitude reduction during misalignment.

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**0175**

**Acute Effects Of Bright Light Exposure On Nighttime Cortisol Levels In Humans**

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**Introduction:** Cortisol levels demonstrate a pronounced circadian rhythm with a peak near habitual waketime under normally entrained conditions. A multi-synaptic pathway from the SCN to the adrenal glands has been hypothesized to communicate circadian and light information to the adrenal glands. In rats, corticosterone levels have been reported to be acutely reduced in response bright light exposure; whereas in humans, findings with regard to acute effects of light on cortisol levels are inconsistent. Exposure to light has been reported to have no effect, increase or decrease cortisol levels. These inconsistent findings may be related to methodological differences among studies including light intensity (~500 to 5,500 lux), duration and circadian phase of exposure. In the present study we examined the acute effects of bright light (~10,000 lux) on cortisol levels during the rising and descending phases of its circadian rhythm.

**Methods:** After three baseline days, a constant routine to assess circadian phase and recovery sleep, sixteen healthy women and men, aged 25.4 ± 6.7 years (±SD), were exposed to 6.7-h of ~10,000 lux or ~5 lux. Cortisol data from the constant routine (~5 lux) collected 24-h prior to light exposure was used as baseline. Subjects were exposed to light beginning on average (-2 h prior to or ~3- h after the melatonin midpoint.

**Results:** Exposure to bright light significantly reduced cortisol levels during the rising and descending phases of the cortisol rhythm (P<0.05), whereas cortisol levels during exposure to dim light were similar to those at baseline.

**Conclusion:** This is the first study to expose subjects to light intensity of >5,500 lux and report a reduction in cortisol levels. Light intensity may thus be an important factor that determines the acute effect of light on cortisol levels. The physiological implications of our findings are unknown and require further research.

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**0176**

**The Influence Of Sleep And Wakefulness Out Of Phase With The Internal Circadian Pacemaker On Cytokine Balance**

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**Introduction:** Recent research has focused on health implications of altered balance between pro- and anti-inflammatory cytokines. Alterations in balance between the pro-inflammatory cytokine tumor necrosis factor alpha (TNF-α) and its anti-inflammatory cytokine interleukin-10 (IL-10) have been reported to be associated with increased disease susceptibility and mortality risk. The current analysis assessed cytokine balance in healthy adults whose sleep-wakefulness cycles occurred at normal versus abnormal times with respect to the circadian melatonin rhythm.

**Methods:** Twelve healthy men and women (33.8 ± 5.3 yr) participated. After three weeks of a consistent sleep-wake schedule at home, six laboratory baseline days and nights, a 40-h constant routine (CR) to estimate...
circadian melatonin phase (DLMO25%) and 8-h recovery sleep, subjects were studied across a 25-day wakefulness-sleep schedule that resulted in sleep loss and circadian misalignment for seven of the twelve subjects. Melatonin, Sleep EEG (C3xA2), TNF-α and IL-10 were assessed at baseline and near the end of the 25 day schedule. Hourly cytokine data were z-scored and trapezoidal area under the curve (AUC) was calculated across a 24-h episode. Anova and t-tests determined significant differences between condition.

Results: Results showed normal phase relationships between DLMO25% and scheduled sleep in five participants (entrained group) and an advanced phase angle in seven participants such that melatonin were abnormally high during scheduled wakefulness and low during scheduled sleep (misaligned group) (p < 0.05). Circadian misalignment was associated with greater WASO (p < 0.05). Significant increases in IL-10 levels were observed in the misaligned group (p < 0.005), but no change was seen in the entrained group. No significant changes in TNF-α or in the TNF-α/IL-10 ratio were observed in either group.

Conclusion: Chronic circadian misalignment increased levels of the anti-inflammatory cytokine IL-10. Future research is needed to determine the physiological implications of increased IL-10 under these and similar conditions (e.g., jet lag, shift-work).

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0177

Individuals Practicing Water Exercises Go To Bed Earlier
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Introduction: Physical activity close to bed time are associated to problems of initiating sleep, but there is a lack of study investigating if different exercise modality even far from bed time have the same negative impact on sleep. The present study aims to analyze the impact of water exercise (WE), weight training program (WTP) and gymnastics on bedtime on individuals performing regular physical activity.

Methods: The subjects received a sleep diary to be kept for 4 weeks and were instructed to follow their usual sleep-wake routine during the study. Ninety-five individuals (76 women) entered the study. The WTP group consisted of 35 subjects (mean = 37.85, SD = 14.5 years, range 18 to 66), the WE group consisted of 37 subjects (mean = 58.35, SD = 14 years, range 30 to 80), and the gymnastics group consisted of 23 subjects (mean = 34.21, SD = 8.77 years, range 24 to 55).

Results: 14 (60.8%) individuals went to bed after midnight in the gymnastic group, 19 (54.2%) in the WTP, and 8 (21.6%) in the WE group. There was no difference in bedtime between individuals that practiced gymnastics with those of the WTP group (p = 0.822; OR = 0.763; CI = 0.228:2.532). Less WE individuals went to bed after midnight compared to WTP group (p = 0.008; OR = 4.304; CI = 1.382:13.792) and gymnastics group (p = 0.005; OR = 0.1773; CI = 0.047:0.638).

Conclusion: The individuals that practice WE tend to go to bed earlier than those on gymnastics and WTP groups, suggesting that WE could be of value for patients complaining of problems of initiating sleep, and to delayed sleep phase syndrome, both condition deserving a well designed clinical trial to better assess this issues.
**Methods:** A New Zealand version of the MEQ was mailed to a stratified sample of 5,000 adults (2,526 Māori, indigenous New Zealanders; 2,474 non-Māori) aged 30-49 years (response rate=55%). Socio-economic deprivation was estimated using a validated small area index (NZDEP2001), and employment status was documented. Chronotypes were categorised as definitely evening-type (DE-type); moderately evening-type (ME-type); neither-type (N-type); moderately morning-type (MM-type); or definitely morning-type (DM-type), using criteria from Horne & Ostberg, or Taillard et al. Population prevalences were calculated by weighting the data by the population proportions of age, gender and ethnicity. Multinomial logistic regression analysis was performed to identify independent predictors of each chronotype (ref=N-type), with the following independent variables: ethnicity, gender, age, socio-economic deprivation and nightwork.

**Results:** Morningness/eveningness scores were normally distributed (mean=58.08, SD=9.38, range=23-81, skewness= –0.39; Cronbach alpha = 0.83). Population prevalence estimates using the Horne & Ostberg criteria were: DE-type 0.67%; ME-type 4.95%; N-type 44.62%; MM-type 39.56%; DM-type 10.20%. Estimates using alternative criteria validated in a middle-aged working population were: DE-type 11.50%; ME-type 14.94%; N-type 48.91%; MM-type 14.46%; DM-type 10.19%. Participants aged 30-34yrs were more likely to be evening-type (DE-type OR=1.91, p<0.01; ME-type OR=1.47, p=0.02) compared with those aged 45-49yrs. Night workers were more likely to be DE-type (OR=1.36, p=0.04), while people living in a deprived area were less likely to be ME-type (OR=0.65, p=0.04).

**Conclusion:** The Horne & Ostberg criteria are not useful for studying morningness/eveningness in a middle-aged population. Morningness/eveningness is largely independent of socio-economic or demographic factors, and appears to be a stable characteristic that may be better explained by endogenous factors.

Sarah-Jane Paine conducted this research during the tenure of a Māori Health PhD Scholarship from the Health Research Council of New Zealand.

**0180**

**Use Of Morning Bright Blue Light In The Treatment Of Mild Delayed Sleep Phase Syndrome**

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**Introduction:** Delayed sleep phase syndrome (DSPS) results in insufficient sleep and daytime tiredness when sufferers attempt to arise early for social or work commitments. DSPS is associated with a delayed circadian rhythm that can be treated with the phase advancing capacity of morning bright light. Moreover, recent research has shown greater efficacy of short wavelength (blue) light than long wavelengths in phase advancing the circadian rhythms of normal sleepers. The present study evaluated the efficacy of morning blue light stimulation for the treatment of mild DSPS.

**Methods:** Seventeen mild DSPS sufferers (about 2 hours delayed from normal) participated in a three week protocol: one week baseline, one week gradual advance of wake-up time from a mean of about 0910 h to the target 0600 h, and one week post-treatment. Participants were randomly allocated either to a control group following their normal daily routine or a group receiving two hours of bright light immediately after awakenings during the treatment week. In this condition bright blue light (peak wavelength at 470 nm at 65 microwatts/cm² irradiance) was administered using a portable light source comprising light emitting diodes mounted on glass frames.

**Results:** The morning bright light group showed a significant 2.7 hour advance of dim light melatonin onset compared to 0.3 hour advance (n.s.) in the control group. Although there was some advance of sleep onset time during the treatment week, this may have arisen mainly from increased homeostatic sleep drive. During the post-treatment week, freed of any sleep/wake instructions, sleep onset and wake-up times generally reverted back to pre-treatment times for both groups.

**Conclusion:** Morning bright blue light normalized the melatonin circadian rhythms of mild DSPS sufferers. However, adjunctive cognitive/behavioral therapy may be essential to obtain a more lasting advance of sleep onset and wake-up times.

Sarah-Jane Paine conducted this research during the tenure of a Māori Health PhD Scholarship from the Health Research Council of New Zealand.
Category E—Circadian Rhythms

0182
Inducing Multi-Phasic Rhythms In Humans

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Introduction: To explore whether it is possible to produce split circadian rhythms in humans, as demonstrated by Gorman, Elliott, et al. in hamsters, we placed 10 young subjects on one of 3 split light/dark cycles for 4 days.

Methods: Within each 24 hour period, all subjects had 16 hours of 3000 lux light in 2 periods of varying length and 8 hours of dark in 2 4-hour periods (i.e., LDLD). 60-90 minutes of exercise was added and timed to promote splitting. On day 5, all subjects were released into a <50 lux 90-minute ultra-short light/dark cycle for 24 hours. All urine was assayed for aMT6s.

Results: Under the light/dark conditions used in the laboratory, we were unable to robustly split the human circadian clock in every subject. In most subjects, the circadian peak of excretion of aMT6s was largely confined by and associated with only one of the two daily dark periods in the LDLD cycle. During the final 24 hour assessment on day 5, under free-run conditions in the 90 minute ultrashort sleep-wake protocol, there was strong evidence for only one major peak of aMT6s. However, several subjects in one of the lighting paradigms displayed sustained elevations of aMT6s excretion above baseline associated with the second of the two daily dark periods, suggesting that circadian melatonin secretion was occurring at that atypical time. These elevations were of less magnitude compared with the major peak of melatonin, but are interesting phenomena that might be clarified with studies of longer duration to distinguish possible transient splitting from masking.

Conclusion: Of note is the rapid masking adjustment of each of the subjects’ melatonin rhythm to the imposed light/dark cycle, and the maintenance of that phase shift when released into the unmasked 90-minute day. This may have applications for relatively rapid attainment of large phase shifts.

0183
Non-24 Hour Subject With No Benefit From Light

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Introduction: A 22-year-old man with no reported major medical illnesses and normal vision was referred for consultation. The young man and his mother reported that he had always tended to go to sleep late. He had great difficulty getting up in time for school, especially in high school, from which he was expelled without graduating at about age 18. Following this, he spent most of his time playing computer games, though he did enjoy some outdoor sports such as skateboarding. He began to sleep as much as 12 hours at a time. His sleep drifted later and later each day, so that his sleep progressed from day to evening to night to day. He did not suffer from sleepiness or napping outside his major sleep period.

Methods: A 4-week wrist activity recording was made using the Actiwatch-L device, which demonstrated a non-24-hour sleep/wake cycle.

Results: Sleep delayed about 39 hours over the 28 days recorded, i.e., a circadian rhythm of approximately 25.4 hours. Major sleep episodes were 10-12 hours in duration. Although he experienced bright daytime outdoor illumination when his spontaneous wake time was in the morning, most of the brightest light exposure commenced 5-8 hours after awakening. He experienced very low illumination when indoors. No day was observed when he experienced >50 lux for at least 10 hours. Most of the time the illumination was much dimmer than 50 lux as recorded by the Actiwatch.

Conclusion: An attempt has been made to synchronize the sleep-wake cycle with very bright morning light, e.g., 10,000 lux of outdoor or artificial light starting at 7am, beginning at the points in his cycle when his spontaneous awakenings were between 4-8am. The treatment was supplemented with 1 mg/day of Vitamin B12. Unfortunately, the first attempts failed to modify the non-24-hour sleep-wake cycle.

0184
Long Tau In Delayed Sleep Phase Syndrome

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Introduction: Individuals with Delayed Sleep Phase Syndrome exhibit nighttime sleep propensity that is delayed relative to desired clock time, resulting in sleep-onset insomnia and difficulty awakening at the desired time. One theory of the pathophysiology of DSPS is that it may be the expression of an abnormally long endogenous circadian period (tau) that limits the capacity of the sleep-wake system to entrain properly to the 24-hour day. Because no DSPS subjects have been studied in temporal isolation, there is little evidence to confirm or refute this notion. We recently studied a subject with self-reported DSPS under these conditions.

Methods: The subject (30 y.o. male) participated in two 28-day laboratory stays. Each lab stay consisted of adaptation, baseline, and 5 days of strictly scheduled activities (Entrainment), then by 21 days in one of two ‘free-run’ conditions (‘traditional’: subject structures daily activities, sleeps only once per day, with no naps permitted; ‘unstructured’: subject eats and sleeps whenever inclined to do so). Body core temperature and EEG were recorded continuously. Tau was estimated by subjecting temperature below the daily mean to both period and FFT analysis.

Results: The subject reported a lifelong history of extremely late bedtimes and waketimes, and scored as an “extreme evening type” on the Horne-Östberg scale. Sleep log data indicated that his average bedtime was 0334h and his average wake up time was 1330h. During entrainment, he showed a delayed body temperature rhythm (average Tmin: 1010h). In both free-run conditions, he exhibited a tau considerably longer than the average of 14 other subjects studied in same conditions: his ‘traditional’ tau was 25.4 hr versus group mean 24.74 ± .15h, and his ‘unstructured’ tau was 25.2 hr, versus group mean 24.34 ± .11h. He did not exhibit desynchronization between sleep/wake and body temperature rhythms.

Conclusion: This study is the first to demonstrate a long endogenous circadian period length in an individual presumed to have DSPS and supports the theory that abnormal tau may underlie circadian rhythm sleep disorders of the intrinsic type.

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0185
Physician Trainee Sleep, Recovery, Cumulative Debt, Circadian Rhythm Disruption And Symptoms

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Introduction: Long duty hours, high workload and fatigue are the hallmarks of physician training. The mechanisms of fatigue include workload, acute sleep deprivation, cumulative sleep loss and circadian rhythm disruption. We studied the sleep duration, timing and physical symptoms in fellows in a university-affiliated critical care medicine training program in two paediatric critical care units.

Methods: Consenting subjects wore wrist-watch Actigraphs. Intact 24-hour blocks (9am-9am) of actigraph data were identified and the mean duration of sleep was determined for on-call, post-call, weekdays, or ‘weekend-off’ days. The total sleep duration over a 28 day roster cycle (7 on-call, 7 post-call, 10 weekday, 4 weekend days off) was then estimated. Symptom types (gastrointestinal 5, musculoskeletal 2, visual 2, headache 1, cardiac 2) were anonymously reported by fellows before, during, and 24-hours after their shifts ended.

Results: 151, 24-hour blocks of complete actigraph data from 11 fellows and symptoms before during and after 43 on-call shifts in 10 fellows were included. Sleep durations were 2.5h on-call, 12.5h post-call (including 4.5h before 9pm), 8.5h weekday, and 9.0h on ‘weekends-off’ (p<0.0001). On average over 28 days, fellows slept 8.1 hours/day. Symptoms were reported before 13(30%), during 30(70%), and 24-hours after 26(60%) of shifts. The most common symptoms were gastrointestinal (19%,53%,16%), headache (14%,40%,28%), and musculoskeletal pain (5%,42%,35%) respectively. Vomiting was reported during 2 shifts.

Conclusion: Trainees have acute sleep deprivation when on-call, but have post-call catch-up sleep and no evidence of cumulative sleep loss in the current ‘24-hour’ 1 in 4 shift call schedule. Despite ‘adequate’ total sleep, fellows reported post-call symptoms after 60% of shifts. These symptoms are consistent with circadian rhythm disruption and physical fatigue, suggesting that trainee symptoms may be related to the physical stresses (Parshuram C, CMAJ 170(6):965-70, 2004) and circadian rhythm disruption rather than sleep debt per se.

Funding for this work was provided by the Research Institute at the Hospital for Sick Children.

0186
Long Term Actigraphic Assessment Of Night-Shift Workers
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Introduction: Night-shift workers, as a group, sleep significantly less than day-shift workers. Some night-shift workers revert to a day-shift pattern on their days off, while others try and maintain a nocturnal awake pattern on their nights off.

Methods: Two night-shift workers from the KSDDS (P Smith, E Roth) work 3 consecutive 13.13.5 hour shifts per week, followed by 4 consecutive nights off. One technologist (ER) maintains the same sleep/wake schedule on her nights off, while the other one (PS) reverts back to night sleep on his nights off. Both technologists wore actigraphy (AW-64, Mini-Mitter, Inc.) for an extended time, ER for 1 month and PS for 1 year. This initial data analysis is for the 1 month of ER’s data along with 1 month of PS’s data from year before. Both data sets are from the same month in order to remove any seasonal bias.

Results: The data for PS shows a consistent pattern of 3 nights work followed by 4 nights of sleep. The data for ER shows a consistent pattern of nocturnal activity with daytime sleep, excepting 2 weekends with the pattern reversed due to day-time commitments. Data was analyzed by looking at the actual sleep time per 24 hour period. This included the primary sleep period as well as periods of inactivity lasting 5 minutes or longer during wake periods. The analysis showed a significant difference in total sleep time between the 2 subjects. PS slept an average of 6 hours 47 minutes per 24 hour period. ER slept an average of 8 hours 37 minutes per 24 hour period. The fragmentation index for ER averaged 16.8 per sleep period, for PS the index averaged 45.6

Conclusion: ER slept approximately 1 hour 49 minutes more per 24 hour period than PS.
Methods: Twenty-five adolescents (13 boys), mean age=12.8 (sd=1.7) years, reported morning (n=16) or evening (n=9) phase preference (Morningness questionnaire of Smith et al. (1989) J. Applied Psychology). Participants kept an optimized fixed sleep schedule for 2.5 weeks at home followed by a symmetrically restricted sleep schedule for 1 week. Compliance was confirmed by actigraphy, sleep diaries, and daily phone calls to the laboratory. Saliva was collected after each sleep regimen in dim light (<15 lux) on one evening, and melatonin onset (DLMO) phase was determined using linear interpolation with a 4 pg/mL threshold. Pubertal status was assessed by Tanner staging.

Results: In comparison to sleep optimization, sleep restriction bedtime was later (mean=22:26, sd=32 mins vs. mean=21:01, sd=38 mins; t(24)=42.9, p<.01), wake-up time was earlier (mean=5:15, sd=38 mins vs. mean=6:34, sd=35 mins; t(24)=29.7, p<.01), and time in bed was shorter (mean=6h 48 mins, sd=21 mins vs. mean=9h 33 mins, sd=30 mins; t(24)=40.1, p<.01). Overall, DLMO phase after sleep restriction (mean=20:03, sd=61 mins) was later (t(24)=4.4, p<.01) compared to DLMO phase after sleep optimization (mean=19:38, sd=60 mins). The DLMO phase shift did not differ with sex, or between morning and evening preference groups or among Tanner stages.

Conclusion: Melatonin onset phase was later in adolescents following sleep restriction regardless of sex, phase preference, or Tanner stage, although sleep was restricted symmetrically. Whether this change reflects a phase delay of the circadian timing system or a reduction of melatonin secretion duration remains unclear and will be addressed by examining melatonin onset and offset phases in additional participants. Phase preference and Tanner stage findings are preliminary given the small sample size.

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0190
Night Shift Work Impairs Decision-Making In Visual Search
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Introduction: Night shift work can result in diminished attentional capacity, compromising safety and efficiency in the workplace. In any work place, safe and effective performance requires us to select relevant information while ignoring irrelevant items. This is a function of selective attention. In this study we examined how selective attention is impacted by night shift work.

Methods: Eighteen subjects participated in a simulated shift-work study, which included four day shifts followed by three night shifts. During the work shift subjects performed a battery of cognitive tests, including two selective attention tasks: conjunction and spatial-configuration search tasks. We varied the number of search items (set size), and measured response times (RT) and accuracy. The cognitive slowing hypothesis predicts that night work should result in a slower search rate (indexed by the slope of the RT by set size function), ineffective attentional guidance (indexed by the conjunction to spatial-configuration slope ratio), and slowed responses (indexed by the intercept of the RT by set size function).

Results: Contrary to this prediction, search rates were faster on the night shift relative to day shift (conjunction: 5.9 + 2.2 vs 8.6 + 1.9, p=.002; spatial configuration: 24.56 + 2.926 vs 31.86 + 3.118; p<.001). There were no changes in the other two measures. However, night shift work impaired accuracy in both tasks. D-prime (a measure of detectability) was significantly lower during the night shift relative to day shift in both conjunction (3.17 + 0.05 vs 3.66 + 0.06, p<.001) and spatial configuration search tasks (3.0 + 0.06 vs 3.46+ 0.08, p<.001). Observers spent less time searching through items, resulting in degraded information and increased errors.

Conclusion: The results suggest impairment to more central decision-making processes rather than to early visual processing or attentional mechanisms. These results have implications for understanding the cognitive basis of performance errors and accidents associated with night shift work.

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0191
Tracking Circadian Time As A Statistic During The 2004 Major League Baseball Season: A Pilot Study
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Introduction: Travel across time zones and its relationship to athletic performance has been investigated in very few studies. The complexity of
professional sports makes isolating circadian variables difficult. The purpose of this study is to track circadian time throughout a season and determine if circadian advantage (being more synchronized to the current time zone than the opposition) led to team performance advantage during the 2004 Major League Baseball (MLB) season.

Methods: Using the convention that for every time zone crossed, synchronization requires one day, teams were assigned daily numbers indicating the number of days away from resynchronization. Positive values indicated eastward travel, negative values westward, and zero indicated current time zone synchronization. With these values, all 2428 games of the season could be classified based upon home and away circadian values.

Results: 1942 of 2428 games were played between teams at an equal circadian time. The remaining 486 games (20.0%) featured teams with different circadian times. The team with the circadian advantage won 264 games (54.3%). However, 366 of these 486 games were also played with home field advantage. In games in which the away team held circadian advantage (120 games), the away team won 61 games. Magnitude and direction of circadian advantage influenced success. Winning percentage was .522 (187-171) for teams with a 1-hour circadian advantage, .573 (67-50) for a 2-hour advantage and .909 (10-1) with a 3-hour advantage. Direction of advantage showed teams traveling westerly from eastern time zones were more likely to win: negative circadian advantage (.561; 147-115), positive circadian advantage (.522; 117-107).

Conclusion: These results suggest that in the way home field advantage influences team success, so does magnitude and direction of circadian advantage. Teams with greater circadian advantage and more negative circadian times were more likely to win. Multiple seasons should be reviewed to determine significance.

0192 Predicting The Timing And Duration Of Sleep, For International Flight Crew During Layover Breaks, By Combining Social And Circadian Factors Fletcher A, Kandelaars K, Dawson D

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Introduction: There has been increasing debate over the use of bio-mathematical models to predict alertness, performance and/or fatigue. Such models generally use hours of work, sleep/wake timing and/or light exposure as inputs and make robust group predictions in laboratory settings. However, models have been criticized for not accounting for differences in sleep strategies or the competing social and circadian pressures on sleep, especially in operational settings.

Methods: Subjects were 34 male international flight crew working from Australia to either the US (16) or Europe (18). The study periods were 91-98hrs for the US group and 181-186hrs for the Europe group. Measures included actigraphy for sleep/wake activity and diaries for sleep/wake/work behavior. Breaks between flights were defined as being either short (less than 32hrs) or long (more than one consecutive local night). Furthermore, long breaks were split into three distinct phases: recovery, social interaction and anticipation. The splitting of long breaks was done in order to exploit information about the likely social pressures in the local time zone and the circadian pressures from their likely sleep phase in the home time zone. A mathematical model, which used iterative prediction and retrodiction, was developed to optimize predictive ability.

Results: Analysis of the data found an interaction between the social and circadian sleep pressures, which changed in relation to the length of the layover. The model results accounted for between 67% and 99% of the variance in the sleep propensity curves, which compared favorably to existing approaches that yielded between 52% and 73%.

Conclusion: Both social and circadian pressures play important roles in regulating sleep for international flight crew during layover breaks. The dynamic interactions between these pressures can be modeled to predict sleep timing and duration. Further work is being undertaken, with additional data from the same study, to allow generalization of this model.

0193 A Review Of Sleep Duration And Sleep Quality Among Women Shiftworkers

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Introduction: Women constitute about half the workforce but most still retain the primary responsibility for child care and household maintenance. Women shiftworkers warrant special attention given the different physiological needs of women, their reproductive status and the added burden of family responsibilities. There is increasing evidence suggesting that women have greater difficulty adjusting to shiftwork compared to their male counterparts. In the US, job burnout is more common in female than male physicians. The purpose of this work is to review the existing literature as part of a needs assessment to examine the sleep of female shiftworkers.

Methods: A review of the sleep literature focusing on sleep duration and quality and sleepiness for female shiftworkers was conducted using electronic and manual searches. For comparison reasons only data regarding women working night shifts were extracted from the research publications.

Results: Very few (n=7) studies report findings solely from female shiftworkers while most combine data from male and female subjects. Given the small number of papers and the variation in measurements, a meta-analysis was not possible. In subjective reports, women were shown to have short sleep duration on working days (average 5 hours) compared to days off (average 8.5 hrs) with about 20-40% of women reporting poor subjective sleep quality. Sleepiness is a common occurrence with 35-75% of night workers acknowledging napping, about one-third admitting to falling asleep while on the job and almost half nodding off while driving. Night female workers have a two-fold greater chance of having automobile accidents, near misses and on-the-job accidents. About one-quarter of women shiftworkers use medications to get to sleep.

Conclusion: A review of the existing literature suggests that women shiftworkers report short sleep duration and poor sleep quality. More research needs to be conducted investigating the effects of shiftwork on sleep in women and ways to improve their sleep quality that are specially geared towards the needs and social obligations of women.

0194 Sleep Disturbances In Nurses Working Shifts: Lack Of Relationship Between Subjective Complaints And Objective Sleep Recordings

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Introduction: Shift workers and nurses in particular, often suffer from sleep disturbances. Nurses who easily adjust to shift work likely report fewer complaints and sleep better than non-adjusted nurses. In the current study we aimed to assess sleep disturbances subjectively and objectively in a large cohort of nurses working on a rotating shift or days shifts.
Methods: 700 nurses working in a Medical Center in Israel completed health, life style and the Technion sleep questionnaires (82% shift workers and 18% day workers). Based on the sleep questionnaire three groups were formed: 40 shift workers who complained of difficulties falling asleep and multiple mid-sleep awakenings, (Sleep Disturbed-SD; 27% of shiftworkers); 42 shift workers without sleep complaints (Non Sleep Disturbed-NSD; 73% of shiftworkers), and 27 day working nurses without sleep complaints (Day-D). All groups were investigated overnight with the Watch-PAT 100, a validated unattended ambulatory device that provides objective information on total sleep time, sleep efficiency, apnea-hypopnea index, oxygen saturation, and arousal index.

Results: D-Nurses were older than SD in which turn were younger than NSD nurses (D: 48±7 yrs, NSD: 41±9 yrs, SD: 35±6 yrs, p<0.001). There were no group differences in BMI (SD: 26.1±4.8, NSD: 25.1±5.0, D: 26.4±4.6), marital status (married: SD: 73%, NSD: 75%, D: 80%), or smoking habits (never smoked: D: 89%, NSD: 65%, D: 86%). The SD group also reported early morning awakenings and morning headaches significantly more than the other two groups. However, Watch-PAT(100) recordings revealed no differences between the groups in total sleep time (SD: 6.5±1.6 hr, NSD: 6.4±1.3 hr, D: 6.3±1.2 hr), arousal index (SD: 13.5±8.24, NSD: 13.5±6.07, D: 13.9±8.39), or sleep efficiency (SD: 80.5±12.9%, NSD: 80.5±10.5%, D: 81.3±10%).

Conclusion: In spite of an increased rate of sleep complaints, objective recordings revealed no evidence of decreased total sleep time, sleep efficiency or increased mid sleep awakenings. Future research should investigate the causes of subjective sleep complaints in nurses working shifts.

0195
Bright Light Treatment And Exercise: Effects On Sleep And Body Composition
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Introduction: Bright light (BL) therapy improves sleep in circadian disorders, enhances serotonin levels and impacts carbohydrate metabolism. Physical activity is important in a society with growing obesity, and both physical activity and bright light therapy improve sleep. Further, sleep has been shown to impact body metabolism The aim of this study is to conduct a controlled, randomized investigation of the effects of combined BL-therapy and exercise on sleep and body composition in overweight individuals to further explore the link between sleep and metabolism.

Methods: Twenty-five overweight male and female subjects were randomly allocated to 6 weeks of exercise (half-hour, 3 times weekly) either with or without BL-therapy. Subjects in the BL-group were exposed to 6 weeks of BL-therapy for one hour daily including during the exercise period. Outcome measure included measures of sleepiness (ESS), fatigue (FIS), mood (CES-D) and body composition.

Results: Among the exercise+BL and exercise-only groups, no significant changes were observed regarding subjective sleep (ESS) after the 6-week period. There was a small but significant reduction in the FIS score after 6 weeks in both groups (p=0.048) but the magnitude of the change among the groups was not different. Both body weight (p=0.033) and body mass index (p=0.031) decreased significantly in both groups, but the change was not different between the exercise+BL and exercise-only condition. However, with exercise+BL therapy, body fat percentage decreased significantly after 6 weeks (41.3±12.6 % to 39.2±11.9 %) (p=0.03), while no changes occurred in the exercise-only group (42.3±4.7 % to 42.9±6.4 %). Also, mood scores improved significantly only in the exercise+BL group (CESD: 15.6±8.7 to 8.8±2; p=0.03).

Conclusion: This preliminary study is the first to show that the addition of bright light therapy to a 6-week exercise program can alter body composition by significantly reducing body fat percentage. Surprisingly, this occurred in the absence of improvement in subjective sleep although fatigue levels were similarly reduced in both study groups. Further studies with objective sleep measures that record more detailed changes in metabolic profile with BL and exercise need to be conducted.

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0196
Circadian Adaptation In Shift-Working Hospital Doctors
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Introduction: Findings of an approximately exponential increase in workplace accident risk over four successive nightshifts (Folkard & Tucker, 2003) are consistent with an absence of circadian adaptation. However, such interpretations are inconsistent with mathematical models of alertness (Folkard et al, 1999) which predict that performance should stay constant or reduce slightly over successive nightshifts. This inconsistency may be due in part to such models being largely based on only a few very few successive nightshifts. The current study examined alertness, reaction time and sleep of doctors over 7 successive nightshifts.

Methods: Eighteen hospital doctors (14 male, 4 female, mean age 30.1 ± 1.2 years) worked 4 dayshifts (week 1), followed by 7 nightshifts (week 2), 3 rest days and then 5 dayshifts (week 3). Participants undertook a 4-choice reaction time task and subjectively rated their alertness on a visual analogue scale at the beginning and end of the first and last shift of each week. They also wore actigraphs throughout the shift cycle.

Results: Reaction time remained unchanged over the first week (days). It was faster in week 2 (nights; p ≤ 0.01), remaining constant over the week. It was faster again in week 3 (days; p ≤ 0.001), increasing over the week (p ≤ 0.001). Error rate remained constant, apart from a decrease during week 3 (p ≤ 0.05). Nightshifts were associated with lower overall alertness and a greater decline as a function of time-into-shift, compared to dayshifts (p ≤ 0.01). Actigraphy data indicated no changes in sleep efficiency during the shift cycle.

Conclusion: Although overall alertness was lower on the nightshifts, there was no evidence of an accumulation of fatigue over 7 successive nightshifts. Such findings are consistent with existing models of alertness. However, the current findings should be interpreted with caution, given the possible influence of practise effects.

0197
Comparing A Biomathematical Model Of Alertness With Pilot Performance Data During A Simulated Ultra-Long-Range Flight
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Introduction: Pilots may experience significant sleep loss and cognitive impairment while on duty due to schedules at odds with their biological rhythm and need for sleep. To investigate the cognitive effects of a 19.5h ultra-long-range flight, commercial airline pilots participated in an aircraft simulator study with cognitive performance assessments. We report on a comparison of observed performance deficits with predictions from
a biomathematical model of alertness under development.

**Methods:** During a 3-day simulator study, pilots were randomized to a 19.5h flight schedule with a morning or evening departure time (11:00 or 23:00 PST). Day 1 involved simulator training and baseline sleep, and included five 10-minute Psychomotor Vigilance Task (PVT) assessments. On days 2 and 3, pilots each flew the same 19.5h flight, and completed 15 to 19 PVT assessments depending on departure time. Following 14h recovery sleep, further PVT assessments occurred. Model predictions of alertness were based on sleep times derived from actigraphs worn 5 days prior to and throughout the study. Alertness predictions were compared to PVT lapses (RT>500ms) by means of mixed-effects regression.

**Results:** Preliminary analyses included 4 pilots with a morning departure and 1 pilot with an evening departure. All pilots showed PVT performance impairment during the 19.5h flight. There was significant goodness-of-fit between PVT lapses and the alertness predictions (likelihood ratio test: χ²[1]=45.0, p<0.001), which explained 31.2% of the variance.

**Conclusion:** The alertness model predicted PVT performance reasonably well. However, there were short-term changes in performance that could not be captured by the model; it was based on the neurobiology of sleep homeostasis and circadian rhythmicity and involved only relatively long time constants (hours to a day). Further analyses after completion of the study, including up to 15 additional pilots, will reveal if these short-term performance changes were systematic and should be incorporated in the model.

**NASA Human Measures and Performance Project of the Airspace Systems Program**

**0198**

**Effects Of Short Light-Dark Cycles On Sleep In Rhesus Monkeys**

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**Introduction:** Light influences an animal’s behavior and physiology profoundly, but there has been no study of short light-dark cycles on sleep in the rhesus monkey, a primate sleep model that is highly relevant to human sleep physiology. In the present study, short light-dark cycles (LD and DL 2hr:2hr) were used to isolate the direct, or masking, effects of light on sleep and brain temperature from underlying circadian variation in unrestrained rhesus monkeys.

**Methods:** Adult male rhesus monkeys were implanted with biotelemetry to continuously measure EEG, EMG, and brain temperature. Animals were individually housed and entrained to 24-hour light-dark cycles (LD 16:8), then exposed to either LD 2:2 or DL 2:2 for 48 hours.

**Results:** During the short LD cycles, monkeys stayed awake for 50% of the total time. Wakefulness occupied 75% of light periods and 25% of dark periods. Prominent circadian rhythms in brain temperature and sleep/wakefulness were also observed, but with clear light/dark masking effects superimposed on all rhythms. When the effects of light were revealed by averaging either across all short light or dark periods, light was seen to promote wakefulness and suppress both NREM and REM sleep, especially during the first 30 minutes after light onset. Interestingly, REM sleep onset was facilitated by darkness, a response similar to that reported in nocturnal albino rats. In contrast to the transient alerting effect of dark-light transitions on behavioral states, brain temperature increased gradually to a plateau level in all light periods and decreased monotonically during the dark periods.

**Conclusion:** Though the effects of light were confounded by limiting the availability of video tasks and food to light periods, the masking effects on sleep-wake patterns in rhesus monkeys were comparable with those seen in other species.

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**0199**

**Wavelength-Dependent Effects Of Light On Sleep Architecture And Sleep EEG Power Density In Humans**

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**Introduction:** The human circadian system is sensitive to non-visual effects of light at short wave-lengths (e.g. melatonin suppression, entrainment) via novel photoreceptors. We investigated whether acute light administration has wavelength-dependent repercussions on sleep architecture and EEG power density during non-REM sleep.

**Methods:** Under constant routine conditions, 8 healthy men (20-29y) were exposed for 2 hours either to monochromatic blue (460 nm) or green light (550 nm) each of ~ 2.8 x 10^13 photons/cm2/s or no light, following a 2-h dark adaptation episode in the morning. The timing of light exposure was scheduled according to the subjects habitual bedtimes, 13.5 hours after waking. Sleep was recorded polysomnographically, starting 1.75 hours after the end of light exposure, and the EEG subjected to spectral analysis.

**Results:** After both light conditions (460 nm and 550 nm), slow wave sleep was significantly reduced in comparison with the no-light condition. Stage two sleep tended to be enhanced only after 460 nm light (p=0.06). All night spectral analysis revealed no significant effect of light condition. However, when sleep spectra for each sleep cycle were separately expressed, a significant interaction between the factors condition and cycle emerged in the slow-wave activity range (SWA; 0.75-4.5 Hz). Post-hoc analysis revealed that the nocturnal decline in SWA was attenuated only after 460 nm light, with slightly lower values in the first (p=0.1) and significantly higher values in the third sleep cycle (p<0.05) and concomitantly shorter REM sleep duration during these two cycles (p<0.05).

**Conclusion:**

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**0200**

**Relationship Between Melatonin Circadian Rhythm And Habitual Patterns Of Light Exposure In The Middle Years Of Life**

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**Introduction:** The mechanisms underlying age-related changes in the signal from the biological clock have yet to be determined. We sought to determine if the phase advance of circadian melatonin rhythm during the middle years of life is related to different patterns of habitual light exposure. We hypothesized that age and earlier melatonin onset will be associated with earlier habitual light patterns.

**Methods:** Thirty-seven healthy subjects aged between 20 and 60 were studied (21 women, 16 men: 41.5y. ±1.9). Habitual light exposure was measured by an ambulatory wrist monitor for 7 days. Participants were submitted to a 25-hr constant routine. Saliva samples were collected every 30 minutes and melatonin concentration was determined by radioimmunoassay to assess dim melatonin onset (DLMO, 1.3 pg/ml). Averaged log light levels for each hour were transformed into percentage of the mean light exposure for each subject. Pearson and partial correlations were used to assess relationships between age, DLMO and habitual light patterns.
**Category E—Circadian Rhythms**

**Results:** Aging was significantly related to earlier DLMO (p=0.0003). Increasing age was also associated with lower light exposure during the night (02:00-04:00; 06:00-07:00 and 23:00-24:00) and with higher illumination in the morning (08:00-11:00). Earlier DLMO was associated to lower habitual light exposure in late evening and early night (22:00-01:00, 02:00-03:00) and with higher morning light exposure (08:00-11:00). However, when the effects of age were controlled for, there was no more significant relationship between DLMO and habitual light exposure, while significant correlations were still found between age and DLMO after controlling for light levels (p<0.05).

**Conclusion:** Our results confirm a phase advance of circadian rhythms in the middle years of life. Whereas a clear phase advance of habitual light exposure patterns was associated with aging, it did not entirely explain the phase advance melatonin circadian rhythm in the middle years of life.

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**0202 Reduced Sleep Efficiency In Cervical Spinal Cord Injury; Association With Abolished Nighttime Melatonin Secretion**

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**Introduction:** Patients with cervical spinal cord injury (SCI) commonly have excessive daytime sleepiness and disturbed sleep, including reduced REM sleep, that cannot be explained solely by disruptions in breathing during sleep. We previously found that complete cervical SCI interrupts the neural pathway required for melatonin secretion. Since exogenous melatonin can shorten sleep onset, improve sleep maintenance, and increase REM sleep, we hypothesized that the absence of nighttime melatonin in cervical SCI would lead to prolonged sleep onset latency, reduced sleep efficiency, and reduced REM sleep.

**Methods:** In an ancillary analysis of the data collected in the prior study, we assessed the sleep patterns, by clinical polysomnography, of three subjects with cervical SCI and with a complete absence of nighttime melatonin production (SCI levels: C4A, C6A, C67A) and two control patients with thoracic SCI and normal melatonin rhythms (SCI levels: T4A, T5A).

**Results:** The subjects with cervical SCI had significantly lower sleep efficiency (median 83 [IQR 83-86] %) than the control subjects with thoracic SCI (93 [92-94] %; P=0.04 Mann-Whitney U-test). The sleep efficiency of subjects with thoracic SCI was not different from that of healthy control subjects (94 [92-96] %). There was no difference in sleep onset latency or the proportion of the different sleep stages, although there was a significantly increased REM-onset latency in subjects with cervical SCI (220 [162-277] min) as compared to subjects with thoracic SCI (34 [25-43] min; P=0.04). The compromised sleep was not associated with sleep apnea or medication use.

**Conclusion:** The absence of nighttime melatonin in cervical SCI may help explain their sleep disturbances. This finding raises the possibility that melatonin replacement therapy might help normalize sleep in this group.

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**0203 Temporal Distribution Of REM Sleep And Circadian Adaptation Of Salivary Melatonin Rhythm In Night Shift Workers**

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**Introduction:** It is well known that the alignment of the circadian pacemaker with the sleep:darkness schedule significantly affects the occurrence of REM sleep. We hypothesized that the degree of circadian misalignment in night shift workers influences the temporal organization of REM sleep during daytime sleep.

**Methods:** Polysomnography was performed in night shift workers (mean age ±SD: 41.8 ±7.9 years) before and after a period of ~12 night shifts...
In most totally blind individuals, the lack of photic input results in a disrupted circadian rhythm. In this study, low-dose melatonin was administered at the earlier clock hours, all three subjects failed to entrain (periods of 24.28 ± 0.08 h, 24.31 ± 0.07 h and 24.27 ± 0.04 h, respectively).

Conclusion: Low-dose melatonin can entrain BFRs, although weak zeitgebers may modulate observed period and influence the lowest effective dose. Some individuals may be more likely to entrain to melatonin at lower doses if weak zeitgebers change period or provide additional corrective phase shifts; the same individuals require less melatonin to entrain to a later (abnormal) phase.

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0205

Designing Optimal Light Intervention Schedules For Experimental And Operational Settings

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Introduction: The use of mathematical models that predict human circadian rhythms and cognitive performance in operational settings are potentially very useful. However, there are no systematic and operational ready methods that automatically determine appropriate light interventions that facilitate improved circadian adaptation in response to a schedule that causes circadian misalignment. We are developing a methodology for using mathematical models of the effect of light on the circadian pacemaker to automatically generate optimal circadian adjustment schedules.

Methods: Our approach includes creating an appropriate analytical and software foundation that can solve a range of schedule design and optimization problems. The analytic component facilitates finding optimal solutions by a variety of methods. The software infrastructure facilitates posing optimization problems through the use of carefully designed schedule building blocks that can be used to construct any experimental or operational protocol. Each of these schedule building blocks is a pattern of variable light levels and duration and sleep or wake state that can be optimized. We applied our approach to optimizing daily placement of countermeasures following a 12-hour shift in the sleep-wake schedule.

Results: We produced a circadian adjustment schedule for a 12-hour shift in approximately 1 minute of computation time. The resulting circadian adjustment schedule is as good as that designed with the mathematical models by hand. We performed a sensitivity analysis of schedule parameters: the optimization was most sensitive to countermeasure duration. We also performed detailed simulation studies of the effect of shifting the schedule on predicted neurobehavioral performance.

Conclusion: Our framework performs quite well in the countermeasure design problem. This methodology provides an effective means from which to explore the schedule and countermeasure design space. The development of our analytic and software foundation is a productive step towards making the use of circadian shifting schedules commonplace in operational and experimental protocol design.

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Category E—Circadian Rhythms

0206
The Relationship Between Sleep And Activity In Mice: A Comparison Across Strains
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Introduction: Few studies in mammals have examined the relationship between the daily amplitude of spontaneous activity and sleep. We are currently conducting a detailed analysis of the sleep-wake cycle and activity in different inbred mouse strains to determine the impact of genetic divergence on the relationship between sleep and activity. In the present study, simultaneous recordings of sleep, wakefulness, and locomotor activity were conducted and analyzed in four inbred strains of mice.

Methods: Male mice (3-4 months of age) from each strain (A/J, B6, FVB, and SJL) were housed in a 12L:12D schedule and implanted with EEG/EMG electrodes. Following recovery, animals were connected to a lightweight tether to allow complete freedom of movement within the recording apparatus. The transparent recording cage lay within a 3x3 grid of six infrared beams arranged to detect and record spontaneous multidirectional movement. Data were analyzed using ANOVA to detect between and within factor differences.

Results: Over 24-hrs of baseline recordings, there were significant interstrain differences in the absolute amounts of wakefulness, sleep and activity. A/J mice (n=4), displayed the highest levels (p<.05) of wakefulness and activity (795 ± 16 min wakefulness; 30,260 ± 3,999 activity counts) when compared to the other three strains. FVB mice (n=4) displayed the least amount of activity (14,538 ± 2,815 activity counts) and the most fragmented sleep profile (p<.05; 121 ± 10 arousals per day). SJL mice (n=4), showed the least amount of wakefulness (676 ± 14 min) and was the second least active strain. B6 mice (n=4) exhibited intermediate values for activity and wakefulness.

Conclusion: The interstrain variation in the amplitudes of the sleep-wake cycle and activity across four inbred mouse strains suggests that both processes are under genetic control. The finding that the A/J mice displayed extreme values in spontaneous activity and wakefulness, as well as other strain specific variables, suggests that these processes may share similar genetic determinants.

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0207
Diurnal Rhythms Of Endothelial Markers: Nadirs Are Not Correlated With Those Of Cortisol Or Body Temperature
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Introduction: Cardiovascular incidents occur with increased frequency in the early morning hours, and endothelial markers (E- and P-selectins and cellular adhesion molecules (CAM)) are known to be associated with cardiovascular risk, but there is very little diurnal data available. We present results from hourly sampled endothelial markers, soluble TNF-receptor 1 (sTNF-r1), cortisol (an hypothalamic pituitary hormone with a strong diurnal profile and anti-inflammatory potential), and body temperature.

Methods: Twenty-two subjects (28.1±5.9yrs, 6 female, 16 males; BMI 23.6±3.0), slept in the General Clinical Research Center (BDMCC). Following an adaptation night, an indwelling forearm catheter was placed and hourly blood sampling began, and continued for 25 hours. Hourly samples were processed and frozen at -80; later assayed (R&D systems) for ICAM, VCAM, P-selectin and E-selectin and sTNF-r1. Cortisol was measured using Immulite (DPC). Continuous rectal temperature was measured with the Minilogger series 2000 (Mini-Mitter Co., Inc.). Diurnal rhythms were analyzed using 2 hour blocks of data (Chronolab 3.0).

Results: Nadirs occurred in the evening/night for all parameters. CAMs and selectins demonstrated strong diurnal rhythms (with z-score amplitudes from .51-.67, each p<.001). The temperature nadir (4:54am) lagged behind that of the cellular adhesion molecules (2:35 and 2:45am), and E-selectin and P-selectin (3:08am and 4:04am, respectively). The nadir of VCAM was positively correlated with that of ICAM (r=.78, p<.001), and E-selectin (r=.39, p<.010, trend). The nadirs of cortisol and sTNF-r1 were correlated (r=-.50, p<.005), and there was a trend for a negative correlation with ICAM (r=-.39, p<.010). No correlations were found between nadirs for body temperature and those of other parameters, with the exception of sTNF-receptor-1 (r=.44, p<.10, trend).

Conclusion: Cellular adhesion molecules and selectins show diurnal rhythms with nadirs following that of cortisol and preceding that for body temperature. Analysis patterns show correlational relationships within the selectins and CAMS, but the nadirs of these endothelial markers do not correlate strongly with nadirs of either cortisol or temperature.

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0208
Sleep Disorders And Their Association With Work Schedule
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Introduction: Work schedule is a well-known risk factor for both insomnia and excessive daytime sleepiness. Night workers and shift workers and workers who alternated between morning and afternoon shifts often expressed difficulty falling asleep or maintaining sleep accompanied with difficulty staying awake at work. In a study of hospital workers, Ohayon et al (2002) found that shift workers were at higher risks of having insufficient sleep syndrome, circadian rhythm disorders and insomnia disorder. This study aims to assess how work schedule is associated with different sleep disorders in the general population.

Methods: The target population was non-institutionalized individuals aged 15 or over living in 7 European countries (France, UK, Germany, Italy, Portugal, Spain, Finland). Representative samples of these countries were drawn according to population distribution, age and gender. The total sample includes 25,579 individuals. Half of these subjects (49.6%) were working. The workers were divided into four groups of work schedule: 1) 24-hour shift schedule (28.5% of the workers); 2) Fixed night work (2.7%); 3) Rotating morning and afternoon shifts (10.5%); 4) Fixed daytime schedule (58.3%). The participants were interviewed on several topics including sleep habits, sleep/wake schedule, sleep and mental disorders.

Results: 24-hour shift workers and night workers were significantly younger than subjects with a rotating daytime schedule and those on a fixed daytime schedule. A higher proportion of men was found in workers with a rotating daytime schedule compared to the 3 other work schedule groups. Using logistic regression models adjusted for age and gender, it was found that (a) 24-hour shift workers had significantly higher risks for excessive daytime sleepiness (OR: 1.4), circadian rhythm disorders (OR: 2.4) and major depressive disorders (OR: 1.5). (b) Night workers had significantly higher risks for excessive daytime sleepiness (OR: 1.4), insufficient sleep syndrome (OR: 1.9) and insomnia disorders (OR: 1.6).

Conclusion: Work schedule, especially when it involves night work, is related with greater number of sleep disorders. Fixed night schedule is

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**0209**

**Intrinsic Circadian Period In Adolescents Versus Adults From Forced Desynchrony**

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**Introduction:** The timing of sleep delays across adolescent development, particularly on free days. Several factors may account for this developmental pattern, including lengthening of the intrinsic circadian period. One way to measure circadian period in humans is to assess circadian parameters under conditions of forced desynchrony (FD), in which sleep/wake is timed to a schedule beyond the range of entrainment. We have measured period in a group of adolescents to examine changes with adolescent development and in comparison to period in adult subjects from studies in another lab.

**Methods:** Participants were 27 healthy adolescents (Tanner stages 1 to 5; ages 9 to 15; mean age = 12.7 years; 14 girls) who slept at home for at least 10 days on a fixed schedule (bedtime = 2130 (n = 3) or 2200; rise time = 0730 (n = 3) or 0800) confirmed by actigraphy, diary, and daily calls. A 3-week in-lab assessment of intrinsic period followed, using a 28-hour FD protocol across 12 cycles. Intrinsic period was computed by linear regression through salivary melatonin onset phases measured across FD cycles.

**Results:** To date, we are unable to identify a clear-cut difference in circadian period as a function of pubertal development, although a nonsignificant trend comparing those at Tanner stage 1 (average period = 24.21 ± .2; n = 6) and those at Tanner stage 5 (average period = 24.27 ± .18; n = 8) is in the predicted direction. Intrinsic period from the entire adolescent sample was compared (t-test) to period reported by the Harvard group for adults from two studies (Czeisler et al., Science, 1999; Wright et al., Proc. Natl. Acad. Sci. USA, 2001). The average intrinsic period for 21 adults (ages 21 to 41 years, mean = 27.6 y) was 24.12 hours versus 24.27 hours in the 27 adolescents, a statistically significant difference (t = 2.83, p = .007).

**Conclusion:** Although the sample is too small to determine whether period lengths across adolescence, these data suggest that circadian period is longer in adolescents than in young adults. Longitudinal evaluation would provide a more powerful and definitive assessment of the phenomenon. Recent data from Roenneberg et al. (Current Biol. 15, 2004) indicate that a reversal in the timing of free-day sleep to earlier hours may mark the end of adolescence. The time course of developmental changes in intrinsic period may be important for understanding this phenomenon as well.

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**0211**

**Effects Of Endogenous Circadian Rhythms, Sleep And Sleep Deprivation On Airway Function In Asthma Explored With A Constant Routine Protocol**

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**Introduction:** Asthma is often worst at night, and patients with asthma often have disturbed sleep. We have assessed the separate effects on airways function of: (i) endogenous circadian rhythms; (ii) the duration of wakefulness; and (iii) arousal from sleep.

**Methods:** We performed a ‘constant routine’ (CR) protocol in 14 subjects with asthma (20-41 yr; 5 male) and 10 controls (20-44 yr; 8 male), wherein subjects remained semi-recumbent and awake for 39 hours under constant behavioral and environmental conditions, with identical snacks every 2 h. Indices of bronchoconstriction (spirometry, airways resistance [Rint - interrupter technique]) and airways inflammation (exhaled nitric oxide [NO]) were measured every 2 h throughout the CR, as well as immediately following each of 3 standardized awakenings during the baseline sleep period before the CR and in the recovery sleep period after the CR. Core body temperature was used as a circadian phase marker.

**Results:** Cosinor analysis demonstrated significant circadian rhythmicity in FEV1 and Rint - with the circadian ranges twice as great in asthma subjects than controls. Among asthma subjects the circadian range of FEV1 was 3-21% predicted [average 9% change around mesor of 78% predicted]. For Rint the circadian range was 9-102% change [average 44%...
change around mesor of 0.52 kPa/l/sec. On average, spirometry was lowest and Rint highest at a circadian phase that translates to ~6:30AM. For exhaled NO there was significant circadian rhythmicity in the asthma subjects only: among subjects the range was 1-18 ppb [average 8 ppb change around mesor of 23 ppb], with a peak NO ~7 PM. Sleep deprivation across the CR caused a significant increase in FEV1 in the asthma group (equivalent to 4% improvement over 24 h). Comparing data obtained in the sleep periods before and after the CR also revealed a significant 5% improvement in FEV1 caused by sleep deprivation. There was a significant fall in FEV1 when awoken after the first 3 hours of sleep, and this effect is likely caused by the circadian system rather than sleep as FEV1 improved in the second half of each night (i.e., before and after sleep deprivation).

Conclusion: Acute sleep deprivation does not worsen asthma. An endogenous circadian rhythm can explain why asthma is often worst at night. An additional effect of sleep cannot be ruled out.

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0212
Human Circadian Period Is Influenced By Entrainment To Non-24 Hour Schedules
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Introduction: Studies in animals reveal that the intrinsic period (tau) of the endogenous circadian pacemaker can be influenced by previous entrainment history, such that the intrinsic period is shorter after entrainment to a shorter-than-24-hour day and longer after entrainment to a longer-than-24-hour day. This phenomenon is termed the after-effect of entrainment. In the present study we examined the effect of prior entrainment history on the period of the human circadian pacemaker.

Methods: We hypothesized that following entrainment to a 23.5-h day that the endogenous circadian pacemaker of subjects will oscillate with a period that is shorter than the period observed in the same individuals after entrainment to a 24.65-h day. This hypothesis was tested in a randomized, crossover design in eight healthy young volunteers (7 males and one female; age 22-40 yrs) who lived in an environment free of time cues during a 73-day inpatient stay in the laboratory. After five baseline days and a constant posture routine (CPR) to assess circadian phase, subjects were entrained to a 24.65-h or 23.5-h day for 2 weeks. This was followed by a 2-week 28-h Forced Desynchrony protocol (FD) and CPRs to assess tau from plasma melatonin levels. In the second half of the study, subjects were entrained for 2 weeks to the other day length, again followed by an assessment of tau in a 2-week 28-h FD.

Results: Tau was significantly longer following entrainment to the 24.65-h day than following entrainment to the 23.5-h day (24.10 h versus 24.06 h, respectively; P=0.013; one-tailed paired t-test).

Conclusion: The current finding demonstrates that a fundamental property of circadian physiology in humans, i.e., the aftereffects of entrainment on circadian period, is similar to that previously reported in many non-human species.

This work was supported by the NIH (NS41886 and MO1-RR02635).

0213
Independent Circadian And Sleep/Wake Regulation Of Adipokines And Glucose In Humans
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Introduction: Leptin and adiponectin are adipocyte-secreted hormones that play important physiological roles in regulating appetite, food intake and energy balance, and have pathophysiological roles in obesity and anorexia nervosa. There are day/night patterns in circulating concentrations of adipokines, with leptin rising and adiponectin falling during the night. We have assessed the relative contributions of day/night patterns in behaviors (sleep/wake cycle and food intake) and of the endogenous body clock (the circadian pacemaker) on the day/night patterns of adipokines.

Methods: We measured adipokine levels throughout a ‘constant routine’ protocol (38 hours of wakefulness with constant posture, temperature, and dim light, as well as identical snacks every 2 hours), and throughout 10 hour long sleep periods before and after the constant routine. Using hourly blood samples in 6 healthy subjects we measured leptin, soluble leptin receptor, adiponectin, glucose and insulin, and performed cosinor analyses to assess separately the endogenous circadian effects from the systematic influences related to sleep or fasting and wakefulness or food intake.

Results: We detected significant circadian rhythms in leptin, glucose and insulin, with peaks around the usual time of awakening. In addition, sleep/fasting resulted in additional systematic decreases in leptin, glucose and insulin whereas wakefulness/food intake resulted in a systematic increase in leptin.

Conclusion: The previously documented day/night pattern in leptin is likely caused by combined effects of the endogenous circadian pacemaker and the day/night patterns in behaviors. Our data imply that alterations in the sleep/wake schedule would lead to an increased peak to trough daily swing in circulating leptin, with lowest leptin levels occurring after awakening. The latter, by influencing food intake and energy balance, could be implicated in the increased prevalence of obesity and cardiovascular disease in the shift work population and this needs to be further studied.

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0214
Cultural Factors Bias Self-Assessments Of Underlying Sleep/Wake Cycles
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Introduction: Previous surveys of morningness/eveningness (M/E) indicate higher mean (morningness) scores for respondents in more temperate countries of Italy, Brazil, Columbia, and India, as compared with less temperate countries, including the US. This study compared total-scale and item responses from a Mexican-Spanish Basic Language Morningsness Scale (LBEM) with the U.S. English BALM version, collected from similar student groups to investigate response-pattern disparities.

Methods: The LBEM scale was administered to 570 University of Leon, Mexico, undergraduate students (female/male=56/44%), mainly 24-28 years old, working part/full-time and commuting from home. The BALM
scale was administered to 1370 full-time Penn State University students (female/male=57/41%), mainly 18-21 years old, living on/near campus in State College, Pennsylvania.

**Results:** Consistent with other M/E studies of US college populations, the BALM score mean (29.07 +/- SEM 0.16) was evening-type oriented (ET), with a positively skewed distribution. In contrast, the Mexican LBEM score mean (38.53 +/- SEM 0.24) was morning-type oriented (MT), with a negatively skewed distribution. Responding to item 9, 43.4% of US students self-identified as For sure evening-oriented, as compared with 9.4% of Mexican students. Of these self-identified as evening-oriented, US students preferred bedtimes of 0030h or later (87.3%) and rise times of 0945h or later (91.6%). Preferred bedtime for 51.6% of similarly self-identified Mexican students was 2215h or earlier, with rise time of 0945h or earlier (73.5%). Only 0.7% of Mexican students were scale-scored as ETs, with 19.8% as MTs. In contrast, 14.4% US students were scale-scored as ETs, with 1% as MTs. Noteworthy, habitual bedtimes and rise-times were similar for both student groups.

**Conclusion:** M/E scale score and item-response disparities between US and Mexican students suggest culture-specific societal norms dictating sleep times and diurnal activities, accounting for differences apart from any underlying physiological differences.

**0215**

**Interaction Between Effects Of The Circadian Pacemaker And Behavioral Sleep-Wake Cycle On Pulmonary Function In Asthma**

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**Introduction:** Asthma severity peaks at night. It is unclear whether this daily rhythm is a function of the behavioral sleep-wake cycle and/or an intrinsic circadian process. The aim was to determine the independent contribution and interaction of the sleep-wake cycle and circadian influences on pulmonary function in asthma subjects using a circadian protocol.

**Methods:** 13 adult subjects with asthma were studied. We performed a 10 day ‘forced desynchrony’ protocol (FD) in dim light and in an environment free of time cues, wherein subjects slept at all phases of the circadian cycle (by scheduling a recurring artificial day length of 28 h). Indices of bronchoconstriction (forced expiratory flow in 1 second [FEV1], peak expiratory flow [PEF], and airways resistance [Rint - interrupter technique]) were measured every 2-4 h during wakefulness and immediately following scheduled awakenings from sleep. Furthermore, we recorded the time of each bronchodilator rescue medication (Albuterol) which subjects took based on symptoms alone. Core body temperature was used to assess circadian phase (minimum assigned 0-degrees). Data were binned into 60 degree-circadian bins.

**Results:** FEV1, PEF, and airway resistance expressed a significant circadian rhythm (P<0.001; 2-way ANOVA) all with the worst values during the biological night (circadian phases 300 and 0 degrees). Furthermore, PEF and airway resistance were significantly worse following sleep than following wake (P<0.05), while FEV1 showed a trend for an interaction between the circadian rhythm and sleep versus wake (P=0.05), with the largest suppressive of sleep at circadian phase 120 degrees (P<0.001). The magnitude of the influence of the circadian pacemaker on FEV1, PEF, and airway resistance was approximately twice as big as that of the behavioral sleep-wake cycle. In concordance with this finding, there was an ~80% chance of rescue medication being taken during the biological night (bins 300, 0 and 60 degrees), which was significantly higher than expected by chance (50%; p=0.012) and than during the biological day (20%; p=0.012).

**Conclusion:** These data demonstrate a clear circadian rhythm in pulmonary function in patients with asthma and indicate that this is more important than the influence of the sleep-wake cycle - including the changes in body posture, behavioral activity, etc. The strong circadian rhythm in inhaler use corroborates the clinical significance of the circadian pacemaker in the daily rhythm in asthma.
0216
Early Manifestations Of Restless Legs Syndrome In Childhood
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Introduction: Restless legs syndrome (RLS) is a well-recognized disorder in adults, with about 35% reporting onset prior to age 20. However, few publications have described the early manifestations of RLS in children.

Methods: We reviewed diagnoses of 199 children and adolescents seen for follow up of sleep problems other than sleep-disordered breathing in a pediatric neurology/sleep practice at a large multispecialty clinic.

Results: Eighteen children and adolescents were identified who did not meet diagnostic criteria for RLS at initial presentation, but did meet full RLS diagnostic criteria during follow-up care. Ten girls and eight boys initially presented with clinical sleep disturbance. All but one had polysomnographic evaluation. Mean age at the initial evaluation was 10.3 years and at RLS diagnosis was 14.7 years. Detailed descriptions of the sensory symptoms were recorded. Retrospective age of onset for chronic clinical sleep disturbance was a mean of 3.1 years, with ten families reporting onset in infancy. Of the 18, 16 reported chronic sleep-onset problems and 8 sleep-maintenance problems at the time of initial evaluation. Ten had a history of growing pains. Twelve had a parent who was diagnosed with RLS. Eleven of 17 had PLMS ≥ 5 per hour. Nine of 11 had a clinical response to dopaminergic medication. Comorbidities included: ADHD (13), anxiety disorders (6), depression (4), and oppositional defiant disorder (4).

Conclusion: In this group of 18 children and adolescents, clinical sleep disturbance preceded a specific RLS diagnosis by an average of 11.6 years. A positive family history of RLS was common. Many had a diagnosis of periodic limb movement disorder (PLMD) prior to a diagnosis of RLS. Comorbidities of ADHD, anxiety, depression, or ODD were each found in 20 percent or more of these cases. The 2002 NIH diagnostic criteria for RLS in children are supported by this work.

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0217
Utilizing Polysomnography And Quantitative EEG Analysis To Define Subtypes Of Attention Deficit/Hyperactivity Disorder
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Introduction: The authors have demonstrated that polysomnographically defined obstructive sleep apnea (OSA) is common (50% with AHI > 5.0) in sleepy pediatric psychiatry clinic patients with AD/HD (Pagel, Snyder & Dawson 2004). Other studies have demonstrated that AD/HD can be differentiated in to subtypes based on quantitative EEG analysis of theta-beta (t-b) ratios with an increased ratio seen in patients with AD/HD (Monstra, Lubar & Linden 2001).

Methods: In this study, pediatric patients with AD/HD as based on evaluation by a Board Certified Pediatric Psychiatrist and at least one positive psychological test (Conners) were evaluated with full night nocturnal polysomnography and daytime quantitative EEG analysis (N=39, Age: mean 12.5, range 6-17).

Results: In this group, OSA was once again found to be common with 19/39 (48.6%) of patients found to have an AHI > 5.0. Age based abnormal t-b ratios were found on quantitative EEG analysis in 16/39 patients (41%). Mean t-b ratio for the grouping with AHI < 2.0 was 4.44. For the group with AHI 2.0-4.0, the t-b ratio was 3.27, and 3.72 for the grouping with AHI > 5.0. Abnormal t-b ratios were found in a higher percentage (60%) of AD/HD patients without OSA (AHI < 2.0) compared to the grouping with AHI 2.0-5.0 (26.6%) and the grouping with AHI > 5.0 (47.3%).

Conclusion: OSA was again found to be extremely common in this pediatric psychiatry clinic grouping of AD/HD patients with 48.6 % meeting conservative criteria (AHI > 5.0) for pediatric OSA. This finding may be secondary to a high frequency of co-morbid psychiatric diagnoses or due to the proportion of AD/HD patients referred because of poor response to primary AD/HD treatment. An abnormal theta-beta ratio as described by quantitative EEG analysis may be more common in those patients without OSA. This study indicates that polysomnography and quantitative EEG analysis can be used in pediatric psychiatry clinic patients with AD/HD to delineate diagnostic and therapeutic sub-groupings.
0219
The Association Between Arousal Parasomnia And Periodic Limb Movement Disorders In Children
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Introduction: Previous study has shown that arousal parasomnia such as night terrors can be precipitated by sleep disordered breathing (SDB). In addition, treatment of SDB is associated with resolution of arousal parasomnia. Since periodic limb movements during sleep can precipitate arousals, we studied the relationship between arousal parasomnia and periodic limb movement disorders (PLMD).

Methods: A retrospective review was performed in children with PLMD who were referred to our sleep center from 2000-2004. All children had overnight sleep study, serum ferritin and iron performed before PLMD treatment. Only children with symptoms of arousal parasomnia were included in the study. Any children with significant neurological or hematologic diseases were excluded from the study.

Results: 12 of 30 (40%) of children with PLMD had symptoms of arousal parasomnia. 11 of 12 had NREM arousal parasomnia (night terror, confusional arousal, sleep walking); 4 of 12 had both NREM and REM arousal parasomnia (nightmares). The average age was 4.3±2.7 years old and the average PLMD index was 15.6±9.3 per hour. All patients had serum ferritin < 50 µg/l with the average ferritin of 23.2±7.8 µg/l. 11 of 12 received treatment with iron therapy. 8 of 11 children who received iron therapy had follow up in the clinics. 7 of 8 (87.5%) showed an improvement in symptoms of PLMD and resolution of symptoms of arousal parasomnia. 4 of 8 children with clinical improvement had repeated sleep study which showed a decrease in PLM index (14.5±11.3/hr [pre] vs 5.7±2.3/hr [post]) and an increase in ferritin (24.8±4.7 µg/l [pre] vs 52.3±23.4 µg/l [post]).

Conclusion: It is concluded that some children with PLMD have symptoms of arousal parasomnia. PLMD treatment can lead to the resolution of arousal parasomnia. It is speculated that arousal parasomnia can be precipitated by PLMD in some children.

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0220
Anti-Inflammatory Therapy In Residual Sleep-Disordered Breathing Following Tonsillectomy And Adenoidectomy In Children
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Introduction: Tonsillectomy and adenoidectomy (T&A) is the primary therapeutic approach for sleep-disordered breathing (SDB) in children. However, complete resolution of SDB occurs in less than 50% of the patients. Furthermore, while there is improvement in the severity of SDB following T&A in the remainder, residual mild SDB will still be present in over 1/3 of these patients. We hypothesized that combined therapy with the leukotriene receptor antagonist montelukast and intranasal budesonide would result in normalization of residual SDB after T&A.

Methods: Over the period of 10/2002-10/2004, children undergoing T&A for SDB underwent a routine post-operative (2nd) PSG 10-14 weeks after T&A surgery. In those children with residual OAHl > 2 and < 6/hrTST, treatment with montelukast (age-appropriate tablet at bedtime) and intranasal budesonide aqueous solution (1 squirt in each nostril at bedtime) was administered for a period of 12 weeks (TX), at which time a 3rd PSG was performed. Children whose parents elected not to receive any therapy or historical patients prior to the initiation of study who did not receive therapy and underwent a 3rd PSG were used as controls (CO).

Results: 14 children received TX and 11 children served as CO. Mean age (6.3±1.3 years), gender distribution (60% males), ethnicity (35% African-American) and BMI (30% with relative BMI>95%) were similar in the 2 treatment groups. The mean OAHl at 2nd PSG was 3.8±1.2/hr in TX and 3.6±1.4/hr in TX and CO, respectively (p-not significant). Similar nadir SpO2 (88.3±1.2%) and respiratory arousal index (4.6±0.7/hr) were recorded for both groups. However, the TX group demonstrated significant improvements in OAHl (0.3±0.3/TST; p<0.001), in nadir SpO2 (93.2±0.9%; p<0.02), and in respiratory arousal index (0.8±0.7/hrTST; p<0.001) on 3rd PSG, while no significant changes occurred over time in CO (p<0.001 ANOVA).

Conclusion: Combined anti-inflammatory therapy consisting of oral montelukast and intranasal budesonide effectively improves and/or normalizes respiratory and sleep disturbances in children with residual SDB after T&A.

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0221
Comparison Of Nasal Pressure Transducer And Thermistor For Detection Of Respiratory Events During Polysomnography In Children
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Introduction: Thermistors indirectly measure airflow based on temperature changes and are regularly used during polysomnography to detect airflow limitation. However, nasal pressure transducers may be more sensitive to the changes in airflow. There are no prior studies systematically comparing respiratory event detection by nasal transducer and thermistor during unattended in-home polysomnography in children.

Methods: We retrospectively analyzed polysomnography recordings performed on 40 children as a part of the Tucson Children’s Assessment of Sleep Apnea (TuCASA) study, wherein measurement of airflow was performed using both thermistor and transducer simultaneously. For each polysomnography record, respiratory events were initially scored using thermistor without visualizing the transducer tracing. Subsequently, the transducer tracing was also included in the display and was used to score events. The events from the two techniques were then compared and events detected by only one method identified. The tracing where an event was not initially detected was then assessed for evidence of change in the waveform and rescoring if so warranted.

Results: The sample had 24 girls and 16 boys (mean age 9±2 years, range 6 to 11 years). Nasal transducer detected all of the events detected by the thermistor whereas the thermistor detected only 85% of the transducer-defined events. Consequently, the transducer-derived mean respiratory disturbance index (RDI) was higher than that detected by the thermistor (7.0±3.8 vs. 5.9±3.4, P<0.001). Overall, the thermistor detected 2142 events compared to 2532 by the transducer. The intraclass correlation coefficient for the RDI obtained by the two techniques was 0.96 (95% CI, 0.92-0.98). The bias between transducer-RDI and thermistor-RDI on Bland-Altman plot was 1.08 (95% CI, 0.8-1.4). There was an excellent agreement between the thermistor and the transducer for making the diagnosis of sleep apnea using a cutoff of RDI greater than 15 (κ=1, P<0.001).

The agreement was good using a cutoff of RDI greater than 10 (κ=0.63,
P<0.001) or RDI greater than 5 (κ=0.69, P<0.001). The quality of the transducer tracings based on average hours of artifact-free signal was comparable to those derived from the thermistors. However, there was a greater likelihood of dislodgement of the transducer.

**Conclusion:** Nasal pressure transducer in conjunction with a thermistor is more sensitive than thermistor alone in detecting airflow limitation in children.

**Methods:** Data were collected from couples assigned to the control group of a randomized clinical trial during their last month of pregnancy (T0) and at one, two, and three months postpartum (T1, T2, T3). Total minutes of sleep (TST) and wake after sleep onset (WASO) were measured with 48 hours of actigraphy. Morning fatigue was measured using the Lee Fatigue Scale. Sleep logs were used to record sleep times and locations. Couples were classified as co-sleepers or room-sharers based on their usual sleeping arrangements between 2400 and 0600. Fathers who slept in a separate room were excluded from analyses.

**Results:** The 72 couples were ethnically diverse, educated, and had moderate to high incomes. Compared to mothers who room-shared with the infant, mothers who breast-shared reported less morning fatigue at T1 (t[63]=2.05, p<.05), comparable amounts of morning fatigue at T2, and slightly more morning fatigue at T3 (t[45]=2.00, p=.052). Bed-sharing and room-sharing fathers did not differ at T2, but bed-sharing fathers reported more morning fatigue than room-sharing fathers at T1 (t[56]=2.33, p=.024) and T3 (t[40]=2.43, p=.020). There were no actigraphy differences between groups. TST ranged from 371 ± 58 to 419 ± 68 minutes for mothers and from 373 ± 60 to 415 ± 52 minutes for fathers.

**Conclusion:** Initially bed-sharing was associated with less morning fatigue for mothers and more for fathers. By three months postpartum, both parents experienced more fatigue than those who room-shared. Subtle differences in sleep architecture may not be detected by actigraphy.

**NIH Grant #R01 NR05345, KA Lee, P.I.**

**0222**

**Sleep And Fatigue In Bed-Sharing And Room-Sharing Parents**

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**Introduction:** Bed-sharing is a common practice among parents and their newborns, as well as a widely debated issue. While safety is the primary focus, there is also concern about parent and infant sleep quality. This study compares the sleep and fatigue of bed-sharers and room-sharers in a sample of first-time parents.

**Methods:** Data were collected from couples assigned to the control group of a randomized clinical trial during their last month of pregnancy (T0) and at one, two, and three months postpartum (T1, T2, T3). Total minutes of sleep (TST) and wake after sleep onset (WASO) were measured with 48 hours of actigraphy. Morning fatigue was measured using the Lee Fatigue Scale. Sleep logs were used to record sleep times and locations. Couples were classified as bed-sharers or room-sharers based on their usual sleeping arrangements between 2400 and 0600. Fathers who slept in a separate room were excluded from analyses.

**Results:** The 72 couples were ethnically diverse, educated, and had moderate to high incomes. Compared to mothers who room-shared with the infant, mothers who breast-shared reported less morning fatigue at T1 (t[63]=2.05, p<.05), comparable amounts of morning fatigue at T2, and slightly more morning fatigue at T3 (t[45]=2.00, p=.052). Bed-sharing and room-sharing fathers did not differ at T2, but bed-sharing fathers reported more morning fatigue than room-sharing fathers at T1 (t[56]=2.33, p=.024) and T3 (t[40]=2.43, p=.020). There were no actigraphy differences between groups. TST ranged from 371 ± 58 to 419 ± 68 minutes for mothers and from 373 ± 60 to 415 ± 52 minutes for fathers.

**Conclusion:** Initially bed-sharing was associated with less morning fatigue for mothers and more for fathers. By three months postpartum, both parents experienced more fatigue than those who room-shared. Subtle differences in sleep architecture may not be detected by actigraphy.

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**0223**

**Comparison Of Sleep Characteristics Of Breast-Fed And Formula-Fed Infants: The Role Of Added Cereal**

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**Introduction:** To determine the role of added cereal on the differences observed in the sleep characteristics between breast-fed and formula-fed infants.

**Methods:** The sleep-wake behaviors of 20 infants exclusively breast-fed and 20 infants exclusively formula-fed since birth have been studied graphically during one night-time. Parents freely cared for their infants during the night. Breast-fed infants were exclusively fed by their mother with no other supplemental feed. Nine formula-fed infants received cere-
Methods: effectiveness of behavioral intervention in treatment of cosleepers with conditions and psychological assessment of their parents; 2) to evaluate characteristics of school-aged cosleepers with primary sleep disorders, rela-
tional decreases CO>UARS>OSA (p<0.03), with the percentage of A1 events being similar in CO and UARS (77±7%), but significantly lower in children with OSA (69±6%; p<0.02 vs. CO). The percentage of A2 events was similar across the 3 groups with a trend for higher values in OSA. The percentage of A3 events was as follows: OSA>UARS>CO (p<0.02).

Conclusion: We conclude that sleep microstructure is altered in children with SDB suggesting that in addition to REM sleep, NREM sleep is also disrupted in pediatric SDB.

NIH HL 62570

0226
Long-Term Effect Of Behavioral Intervention In Cosleepers With Primary Sleep Disorders. Eighteen-Month Follow-Up Study
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Introduction: This study aims: 1) to evaluate sleep and emotional characteristics of school-aged cosleepers with primary sleep disorders, relationship and psychological assessment of their parents; 2) to evaluate effectiveness of behavioral intervention in treatment of cosleepers with primary sleep disorders.

Methods: Eighty-two regular cosleepers (mean age 9.2 years) with at least one primary sleep disorder (sleep onset insomnia, nightwakings and early morning awakenings) were selected and compared with 155 solitary sleepers with primary sleep disorders (mean age 8.11 years) and 213 healthy children (mean age 8.7 years). Sleep was assessed through Children’s Sleep Habits Questionnaire (CSHQ) and sleep diary. Emotional adjustment was evaluated through Children Behavior Checklist and parental distress and psychological assessment through Dyadic Adjustment Scale and Symptom Checklist-90. After baseline evaluation parents and cosleepers were given instruction of behavioral treatment. They were rated at 1-3-6-12-18 months scheduled intervals

Results: At baseline cosleepers scored significantly higher on CSHQ total than solitary sleepers with sleep disorders, but both scored higher than controls. Particularly, cosleepers showed higher scores on bedtime resistance, sleep onset delay, night wakings and sleep anxiety CSHQ subdomain.. Hierarchical regression (R square .52 F (18,39)=52; p<0.001), showed that past sleep problems, couple and maternal distress, emotional problems and sleep insomnia variables were significantly associated with cosleeping. After behavioral intervention incidence of cosleeping significantly decreased and almost disappeared from the 3-month follow-up in both completers and LOCF analysis. Eighteen-month after treatment evaluation carried on 48/60 cases showed that 25 % coslept sometimes with parents whereas 75% of cases did not cosleep anymore Completers and LOCF rm-ANCOVA showed significant differences between the five assessments for CSHQ (total score and subdomains) except for parasomnias and sleep disordered breathing.

Conclusion: This eighteen-month follow-up study showed long-standing effectiveness of behavioral intervention in treatment of cosleeping and primary sleep disorders in school-aged children.

0227
Alternating Hemiplegia In Childhood
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Introduction: Alternating hemiplegia in childhood (AHC) is a rare neurological disease of unknown etiology characterized by recurrent paroxysmal attacks of side-alternating hemipLEGias of variable duration associated with other paroxysmal dysfunctions. During sleep, impaired paroxysmal movement disappears and improvement lasts until several minutes after awakening. A role of increased regional serotonin synthesis is considered as a cause of the attacks. Paroxysmal attacks start in infancy but neurological deficits become progressive with the age.

Methods: During the last 20 years 8 patients (5 boys, 3 girls) with AHC have been followed. Their mean age at the time of diagnosis was 2.75 years, age range 2-5 years; mean follow-up period 13.9 years, range 1 month-20 years. The diagnosis was based on clinical history and neurological findings supplemented by neuroimaging methods (SPECT, PET) and by results of psychological and metabolic/biochemical tests. Nocturnal polysomnography (PSG) was examined in all cases.

Results: The first symptoms in all patients were paroxysmal phenomena (culo-motor, tonic, choreo-athetotic, autonomic) appearing at the age of 4.1, SD 2.2 months followed by repeated attacks of hemiplegia starting at 16.3, SD 13.0 months. Progressive neurological impairment including spasticity, dyskinetic syndrome, cerebellar ataxia and intellectual deficit was present in all cases, epileptic seizures in 7 out of 8 patients. On ictal SPECT/PET examination hyperperfusion/glucose hypometabolism were demonstrated over the affected hemispheres including basal ganglia, both thalami and cerebellar hemispheres. Nocturnal polysomnography (PSG) compared with age-matched controls showed only shorter slow-wave sleep without any further changes in sleep architecture. There were no significant differences between ictal and interictal findings. Improvement of hemiparesis was illustrated by nocturnal videomonitoring.

Conclusion: Dysfunction of cortical and subcortical structures during vigilance may be responsible for AHC ictal symptoms, and serotonin metabolism may account for the different symptoms seen in vigilance and in sleep.
0228
Sleep Habits And Daytime Sleepiness In Students Attending Early Versus Late Starting Elementary Schools
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Introduction: Research suggests that during early adolescence with the onset of puberty, children undergo a circadian phase delay (Carskadon & Acebo, 2002). This age related circadian shift has strong implications for school start times. Few studies have examined the impact of school start time for older elementary students’ sleep patterns.

Methods: Two urban, New England, public elementary schools were assessed. To evaluate the impact of varying school start times, School E’s (SST: 7:45 am) students’ sleep habits and daytime functioning were compared to students at a comparable school (School L, SST: 8:25 am). 116 (School L = 62, School E = 54) 5th and 6th graders and their parents completed surveys that assessed sleep patterns and hygiene (revised, Wolfson & Carskadon, 1998; LeBourgeois et al., 2003).

Results: Overall, 48% of the 5th/6th graders reported that they get less than 9.2 hours of sleep per school night, yet there were no differences in sleep hygiene practices. Students at School L reported obtaining an average of 23 minutes more sleep on school nights (School L: M = 564 min, SD = .24 vs. School E: M = 541 min, SD = 48, p < .01) due to later rise times as opposed to bedtimes (School L: M = 5:45 am, SD = .24 vs. School E: M = 6:30 am, SD = .25, p < .01). On weekends, there were no school differences; however, females reported getting up 60 minutes later (p < .05). Students at School E also reported significantly more daytime sleepiness (p < .01). Parents reported similar findings on all variables.

Conclusion: Even at the elementary school level, school start times seem to influence 5th/6th graders’ sleep schedules. Although this effect may not be as significant in comparison to older students, students attending the later starting elementary school reported less daytime sleepiness.

0229
Symptoms Of Obstructive Sleep Apnea Are Strongly Correlated With Tonsillar Size In Children 4-10 Years Old
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Introduction: Tonsillar hypertrophy has long been recognized as a risk factor for childhood obstructive sleep apnea syndrome. It is also well recognized that a large proportion of children with tonsillar hypertrophy do not have obstructive sleep apnea. The purpose of this study was to determine the degree to which tonsillar hypertrophy increases the risk for symptoms of obstructive sleep apnea.

Methods: 140 children undergoing annual well-child evaluation were enrolled in this study from 2 private pediatric practices in Rochester, NY. The subjects’ parents completed a short questionnaire that included 7 breathing and snoring related questions selected from the Pediatric Sleep Questionnaire (PSQ). The pediatrician completed a brief form ranking tonsil size on a pictorial scale of 0 to 6. Tonsils that were graded as 3 (taking up 51-75% of the lateral diameter of the posterior pharynx) or higher were considered “large” tonsils. The parent’s responses on the 7 PSQ questions were summed (sum-PSQ), and a score of 3 or higher was utilized to define a group with symptoms strongly suggestive of obstructive sleep apnea.

Results: 43 children had “large” tonsils (30.7%). Of these 43, 14 children (33%) had sum-PSQ scores of 3 or above compared to 6/97 children (6%) with “smaller” tonsils (p<0.001). A score of 3 or above on the sum-PSQ was associated with higher rates of parent reported inattentiveness 30% vs. 9.1% (p<0.008), sleepiness 20 % vs. 5% (p<0.02), learning problems 15% vs. 5% (p<0.09), and physician diagnosed ADHD 18% vs. 6% (p<0.07).

Conclusion: Tonsil size is strongly correlated with symptoms of obstructive sleep apnea. One third of children with large tonsils have symptoms suggestive of obstructive sleep apnea. In light of recent studies suggesting that habitual snoring in addition to OSA has negative neurocognitive repercussions, these findings strongly support the conclusion that careful screening and early referral should be performed on this very high risk population.

0230
Using Technology To Improve Sleep In Parents Of Children With Autism
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Introduction: Children with autism frequently have increased nighttime activity. This results in fragmentation of parent’s sleep because of the need to manage the child and from enhanced vigilance during the night. This study was conducted to determine whether a new home monitoring system would improve parents’ sleep by reliably notifying them when the child is up during the night.

Methods: A time series design was conducted with 10 homes of children with autism or developmental delays. Baseline sleep data was collected using actigraphy, sleep diary and sleep questionnaires. Then the home monitoring system was installed followed by a reliability and education period. Data were collected at 6 monthly visits postinstallation.

Results: The home monitoring system was successfully installed in 10 homes. With one exception, families were able to correctly learn operation of the system within the 3 week reliability period. At the time subjects were recruited all parents reported at least one instance in which the child left the home at night unattended. No unattended home exits occurred thus far in the study. On a 100mm VAS, parents indicated significant relief of nighttime worry about child leaving home at night (92 to 48); worry about child being injured at night (82 to 49). Parents indicated the system was very helpful in improving their sleep. Full data analysis will be presented in the poster.

Conclusion: A novel home monitoring system, called CareWatch, seems to be helpful for parents of children with autism in preventing unattended nighttime home exits and in relieving parent worry about those exits.

0231
Is Primary Snoring During Infancy Really Innocent?
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Introduction: Several recent studies have focused on the link between childhood sleep-disordered breathing (SDB) and neurocognitive and behavioral functioning. However, only isolated studies have evaluated the potential contribution of snoring without gas exchange abnormalities to cognitive competence, and none have addressed this issue among infants. Our previous work reports habitual snoring in up to 9% of infants, so the present study tested the association between snoring and developmental decrement among infants.

Methods: Thirty-three infants (8.2±0.4 months) were recruited to participate in a larger study based on parental report of habitual snoring (>3 days/week) (4) or infrequent snoring (<3 days/week) (29). Following standard, overnight research polysomnography, the Bayley Scales of Infant Development, including the Mental Development Index (MDI), were administered. No data were collected when symptoms of acute respiratory infection or rhinorhea were present.

Results: The obstructive apnea/hypopnea index for all subjects was 0.
Snoring was recorded from all subjects with reported habitual snoring, and among 45% of infrequent snorers. Respiratory arousal index was significantly correlated with MDI ($r^2 = 0.20, p = 0.008$). Analyzed independently, snoring-associated arousals exclusively accounted for this relationship ($r^2 = 0.20, p = 0.008$) while spontaneous arousals and those associated with central apnea and oxyhemoglobin desaturation (SpO2) episodes (>3%) were not significantly correlated with MDI. Nocturnal SpO2 nadir trended towards a significant correlation with MDI ($r = 0.09, p = 0.08$).

**Conclusion:** Infants with higher snoring- arousal indices have lower scores on a standardized mental development assessment. Since none of the subjects displayed obstructive respiratory events, our findings suggest that sleep fragmentation induced by respiratory-related arousals impose adverse cognitive effects on brain development. We have previously shown that habitual snoring in the absence of gas-exchange abnormalities in older children is negatively associated with cognition. The present data in infants constitute further compelling evidence that snoring is not just noise during sleep, but may represent the lower end of the disease spectrum associated with sleep-disordered breathing.

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**0232**

**Objective And Subjective Sleep Quality In Children With Complex Regional Pain Syndrome**

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**Introduction:** Complex regional pain syndrome (CRPS) is a syndrome of unknown etiology characterized by extreme limb pain associated with autonomic dysfunction. While chronic pain is associated with disrupted sleep and mood changes in adults, the extent of disturbed sleep has been less well studied in children with CRPS. The purpose of this study was to describe the extent of subjective and objective disturbed sleep, anxiety, and depressed mood in children with CRPS, and to explore the relationships among them.

**Methods:** Seventeen girls diagnosed with CRPS (mean=14.8; SD=1.9 years old) wore an actigraph and completed a sleep diary for 7 days. Children completed several questions about sleep for the previous 2 weeks, the Revised Children’s Manifest Anxiety Scale, and the Child Depression Index. Data reported on sleep variables derived from actigraphy and the daily diary were averaged over 7 days in the analysis.

**Results:** Twelve (71%) of the children reported trouble sleeping, and 10 (59%) of them usually feel sleepy during the day. However, an equal number rarely or never reported daytime naps. Eleven (65%) of the children had sleep time of <90% (mean=88.1%; SD=5.6%). The average awake time after sleep onset was 59 minutes (SD=29). The average number of nighttime awakenings was 2.6 (SD=1.7). Seven children had clinically significant anxiety and 3 children had clinically significant depression scores. Anxiety was significantly correlated with age (r = 0.50, p = 0.04), and with percent sleep time (r = 0.61, p = 0.01). Children reported moderate levels of pain, but there were no significant correlations between pain and any of the sleep variables.

**Conclusion:** Children with CRPS had disturbed sleep with reduced sleep quality indicative of insomnia. The positive relationship between anxiety and sleep time might be attributable to medication effects and further analyses are underway.

We gratefully acknowledge the funding support from the University of Washington, School of Nursing, Center for Women’s Health Research that made this study possible.
group and 136 children as a control group based on a questionnaire and subsequently evaluated using motor tests for the determination of global coordination, fine motor coordination, perceptual-motor coordination, and static and dynamic balance. Failure in each test was considered when 1) the child did not try to perform the test, and 2) the child tried and failed. Motor performance was analyzed using the following tests: single leg stance test, sharpened Romberg (Tandem) test, foot by foot gait test, jumping with the feet together, hop-scotch, skipping rope, key test, pyramid, making a simple knot, and buttoning a shirt.

Results: In the static balance test, more specifically in the sharpened Romberg (Tandem) test, 34% of the boys from the study group, who studied in the morning, failed the test, and in the single leg stance test, 62% if the boys of the study group who studied in the morning failed (p<0.05).

Conclusion: This study suggests that sleep disorders may interact with the school period and alter motor performance, especially in boys studying in the morning.

0235 Sleep And Objective And Subjective Effort In Child Athletes

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Introduction: This study investigated the relationships between child athletes' subjective sleep quantity, sleepiness, and mood and the athletes' choice of maneuvers as well as the perceived difficulty of the moves selected.

Methods: Twenty-three female competitive skaters ages 10 to 15 (M=12.52) who regularly took 6:30AM skating lessons participated. The children arrived at the rink at 6:15AM and completed an assessment regarding their previous night's sleep and the skating maneuvers they preferred to practice that day. They also rated the difficulty of these maneuvers.

Results: The skaters reported sleeping a mean of 7.75 hours (range=4.75 - 9.5 hours) but would have preferred to have slept a mean of 9.51 hours (range=7.5-12.25 hours). The mean reported time to fall asleep was 18.83 minutes (range=5-30 minutes). The responses to the Stanford Sleepiness Scale indicated a mean score of 2.43 (SD=.73). The longer it took participants to fall asleep, the easier the participants rated the spins they had chosen to work on that day, r(23)=-.500, p=.015. The sleepier the skaters felt, the less happy the mood they reported, r(23)=-.549, p=.007. The less happy the mood they reported, the more difficult they perceived the edge-work they had chosen to work on that day, r(23)=-.513, p=.012.

Conclusion: Longer reported sleep latencies were related to the perception that the spins chosen were easy. Sleepiness and mood influenced the perception of the difficulty of the edge-work, the least preferred maneuver. The sleepier the child athlete, the worse the mood and the greater the perceived difficulty of an unpleasant task.

0236 Mother's Smoking Increases Sleep Disordered Breathing In 5 Y.O. Brazilian Children

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Introduction: Sleep disordered breathing (SDB) in young children is prevalent and focused by many health professionals. Many risk factors have been associated to SDB and among them parents smoking has a definite place, specially maternal smoking where studies have shown that children whose mothers smoke have 4.4 times more habitual snoring than children of non-smoking mothers. Tobacco exposition increases the chance of children developing SDB, and children’s contact with his/her mother must play a role. These contact vary and are dependent for example on variables related to the Brazilian educational system, where three starting time to school are necessary to attend children in a set of short- age of school. This study aims to relate SDB in children to starting time to school and mother’s smoking.

Methods: Cross-sectional study including 207 (93 female; 44.9%) five y.o. children from public schools located in a poor periphery of Sao Paulo city. Starting times to school (STS) were: morning (07:00 to 11:00), intermediary (11:00 to 15:00), and afternoon (15:00 to 19:00). We used questionnaires to assess SDB children and also smoking parents. We looked for differences regarding gender, STS, and parent’s smoking at home, comparing smoking and non-smoking groups.

Results: 103 children (49.7%) presented SDB and 16 (15.5%) were children of smoking mothers. Daughters of smoking mothers, who studied in the morning, presented more SDB compared to the non-smoking group (p<0.05). The smoking group did not differ from a non-smoking group when the smoking person was a father or for children that studied in the intermediary or afternoon periods of the day.

Conclusion: This study suggests that maternal smoking and STS in the morning are associated to SDB in 5 y.o. girls from Sao Paulo poor periphery area, probably because those girls have more close contact with their mother than boys.
0238
Decreased Auditory Arousal Responses In Small For Gestational Age Infants
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Introduction: Infants born small weight for gestational age (SGA) are at higher risk for Sudden Infant Death Syndrome (SIDS). The relative risk of an infant being born SGA is increased by the influence of maternal smoking, and maternal smoking, after adjustment for SGA, increases the risk of SIDS. Failure in arousal mechanisms is regarded as one of the causes of SIDS. The purpose of this study is to evaluate the auditory arousal responses of infants born small for gestational age to smoking and non-smoking mothers.

Methods: Sixty-eight healthy infants, born at term, with a median age of 10 weeks (range 4 to 18 weeks) were recorded polygraphically during one night. Thirty-four infants were born to mothers who did not smoke and 34 were born to mothers who smoked (> 5 cigarettes per day). In each group, 16 infants had small for gestational weight for gestational age. The infants slept in their usual supine position. The infants were exposed in REM sleep white noises of increasing intensities from 50 to 100 dB (A) to determine arousal thresholds, defined as the auditory stimuli that induced cortical arousals.

Results: The auditory arousal thresholds tended to be higher in SGA than appropriate weight for gestational age (AGA) infants in both smoking infants and non-smoking infants. When infants form smoking and non-smoking mothers were pooled together, more intense auditory stimuli were needed to induce arousals in SGA infants than AGA infants (p=.05). Comparing infants from smoking to non-smoking mothers, the auditory arousal thresholds tended to be higher in smoking infants than non-smoking infants in both SGA and AGA groups. But these findings did not reach statistical significance.

Conclusion: The prenatal risk factor to be born small for gestational age appears to be the key factor in enhancing auditory arousal thresholds, irrespective of maternal smoking habit.

0239
Spontaneous Arousability In Prone And Supine Sleep Position In Healthy Infants
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Introduction: Compared to control infants, victims of Sudden Infant Death Syndrome (SIDS) have a decreased arousability during sleep with fewer cortical arousals and more frequent subcortical activations suggesting an incomplete arousal process. The prone sleep position is known to be a major risk factor for SIDS. The present study was undertaken to evaluate whether prone sleep position impairs arousal process in healthy infants.

Methods: Twenty-four healthy infants were studied polygraphically during one night; 12 infants regularly sleep supine and 12 infants regularly sleep prone. Infants were matched for gender, gestational age, weight at birth and age at recording. Arousals were differentiated into subcortical activations or cortical arousals, according to the presence of autonomic and/or EEG changes. Frequencies of subcortical activations and cortical arousals were compared in the prone and the supine infants.

Results: In both infants sleeping supine and prone, cortical arousals were more frequent in REM sleep than in NREM sleep (p<0.0001, in both groups). There were no significant differences in subcortical activations between REM and NREM sleep in both supine and prone groups. Compared with the supine infants, prone infants had significantly fewer cortical arousals during REM sleep (p=.043). There were no differences in cortical arousals in NREM sleep. No significant differences were seen in the frequencies of subcortical activations during both REM sleep and NREM sleep between supine infants and prone infants. The ratio of cortical arousal to subcortical activation showed no significant differences between the prone infants and the supine infants. The analysis of time distribution of the arousals across the night showed that the prone infants had significantly fewer cortical arousals in the first part of the night, between 9:00 p.m. and midnight.

Conclusion: Prone sleep position decreased cortical arousals, but did not change the frequency of subcortical activations as previously seen in SIDS victims. These results suggest specific pathways for impairment of arousal process in SIDS victims.

0240
A Strong Association Between Failure Of 6 Year Old Children To Qualify For First Grade And Sleep Disturbances
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Introduction: Every year 5-15% of pre-school children are found to be non-qualified for first grade, and remain for an additional year in preschool. The purpose of our study was to examine whether it could partially result from sleep disturbances. We hypothesized that children non-qualified for first grade will demonstrate increased rate of sleep problems, which will correlate with their emotional and behavioral characteristics.

Methods: The study population consisted of 34 non-selected 6-year-old pre-school pupils who were defined by the educational authorities as non-qualified to first grade. A matched control group of 31 children who normally progressed for first grade were recruited from the same pre-schools and neighborhood. All children/parents filled a sleep questionnaire and underwent an ambulatory one week of actigraphic sleep/wake study, as well as cognitive (Wechsler) and behavioral (Conners) assessments.

Results: Children in the study group had greater variability in sleep/wake-up times and difficulties falling asleep. They had significantly shorter total sleep time than controls (494±31min vs 527±38min, p<0.001), reduced sleep efficiency (88±4% vs 93±3%, p<0.001), and increased number of awakenings from sleep (3.6±1.1 vs 2.0±1.2, p<0.001). The children from the study group had significantly lower scores in attention and concentration analyses, as well as increased tendency of nervousness, irritability and difficulties to postpone pleasures. There were significant correlations between the sleep variables and the cognitive and behavioral scores (e.g. r=0.69 between sleep efficiency and mathematical achievements, p<0.05; and r=-0.71 between sleep efficiency and nervousness, p<0.05).

Conclusion: We conclude that preschool children who fail to qualify to first grade have significantly worst sleep than control children, and that the sleep variables highly correlate with the cognitive and developmental variables. We speculate that early detection and treatment of these children’s sleep problems may improve their maturation and function and may allow them to progress to first grade as their age-matched controls.
Inflammation And Cognitive Function In Children With Sleep Disordered Breathing

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Introduction: In children, the major morbidities associated with sleep disordered breathing (SDB) include cardiovascular dysfunction and neurobehavioral deficits, particularly in the language domain. We have recently shown that C-reactive protein (CRP), a validated marker for inflammation and atherogenesis, is elevated in children with SDB. Furthermore, inhibition of inflammatory cascades in a rodent model of SDB is associated with attenuation of neurocognitive deficits. Therefore, we examined potential associations between cognitive deficits and CRP levels.

Methods: Children aged 6-7 years with and without symptoms of SDB were recruited from a large ongoing study and invited to undergo a polysomnographic evaluation, followed the next morning by a blood draw for analysis of CRP and administration of a battery of neurocognitive tests. Using hierarchical linear modeling, we tested the assumption that SDB, as measured by the obstructive apnea/hypopnea index (AIH) and SpO2, would be associated with greater inflammation, as measured by CRP. Inflammation associated with these markers of SDB was expected to predict language deficits.

Results: A total of 123 children (68 male) completed the protocol. AIH ranged from 0 - 47.8 (mean 2.3±.9) /hr TST. A negative correlation was found between CRP levels and language domain scores (r = -0.2, p<0.05) for the whole group. SpO2 nadir negatively predicted CRP levels (r = -0.49, p<0.001). Furthermore, SpO2 also predicted language scores in girls, both directly (p=0.01) and indirectly, as mediated by CRP (p=0.004). While significant relationships were found in the model between AHI, SpO2 nadir, and language domain scores (r2=7%), inclusion of CRP levels further accounted for an additional 14% of the variance in language ability (p=0.004). Of note, SpO2 emerged as the primary component of the variance accounting for both inflammation and language scores.

Conclusion: These preliminary findings suggest that deficits in the language domain in children with SDB may be mediated through hypoxia-induced inflammatory responses, as suggested from CRP levels and the strong association with SpO2. Thus intermittent hypoxia in SDB may lead to activation of inflammatory cascades, and underlie selective neuronal cell loss in vulnerable regions subserving language domain tasks.

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Executive Dysfunction In Obese Teens And Preteens With Obstructive Sleep Apnea (OSA)

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Introduction: We recently launched an investigation of the neurobehavioral effects of sleep pathology in a growing but under-researched group: obese teens and preteens. Here we report on the first year’s recruitment, focusing on the effect of OSA on the neurobehavioral domain of executive functioning.

Methods: 51 children aged 10-16 were recruited consecutively from a hospital-based pediatric weight management program or sleep clinic. All exceeded the 95th percentile for body mass index for their age and sex (Mean BMI=38.4 ± 7.9). None had a history of OSA or neurological illness, or currently used psychotropic medication. All underwent polysomnography, which yielded three groups: OSA (n=9; apnea+hypopnea index > 5), borderline (n=17; AHI 1-5), and obese controls (n=25; AHI < 1). Parents completed validated behavior questionnaires (BASC, BRIEF). Subjects and parents also reported academic grades and completed standardized sleepiness and sleep quality scales (CSHQ, PDSS).

Results: The groups did not differ in age, gender, ethnicity, or BMI adjusted for age and sex. Mean age was 13.1 ± 1.7 yrs; 69% were girls; 55% percent were Caucasian, 45% were African-American. Children from the sleep clinic were distributed across the groups. A MANOVA with grades as dependent variables was significant (p<0.001); the OSA group received a letter-grade lower than obese controls. A second MANOVA on sleepiness and perceived sleep quality was non-significant (p>0.2), but a third indicated differences on parent-report behavior questionnaires (p=0.026). Univariate follow-ups indicated group differences in mental flexibility, emotional control, planning, self-monitoring, activity level, and working memory/attention; the OSA group fared worst. The groups did not differ in depression, anxiety, aggression or conduct problems.

Conclusion: Obese teens and preteens with OSA are at risk for academic deficits and executive dysfunction. As data collection continues, the goals are to clarify contributors to this morbidity and the degree to which it may be reversible.

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Effects Of Stimulant Treatment On Objective And Subjective Sleep In Children With Adhd

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Introduction: The reported effects of stimulants on sleep in children with ADHD have been mixed, with some suggesting improvement in sleep initiation and consolidation while others indicating the reverse. We used a within-subjects design to examine changes in sleep following stimulant treatment and the relationship between sleep changes and concurrent changes in ADHD symptoms and severity.

Methods: Nine boys (mean age=8.6 years, SD=1.6) with ADHD-Hyperactive/Impulsive or Combined Subtype were studied, pre and post stimulant treatment. Each child wore a Mini-Motionlogger Actigraph (AMI, Ardsley, NY) for 96 consecutive hours (2 weekend/2 weekdays). Parents filled out the Pediatric Sleep Questionnaire (PSQ), the Children’s Sleep Wake Scale (CSWS) and the DuPaul ADHD Home Rating Scale on ADHD symptomatology and symptom severity. Paired samples t-tests showed no differences on any of the sleep variables between weekday nights and weekend nights; thus analyses were conducted across all nights.

Results: Results indicated a significant improvement in subjective sleep on the PSQ (t=7.6, p<0.001), however no differences on the CSWS sub-
scales (t(8)=0.2 to 1.9; p=n.s.). For the objective sleep measures, a significant reduction in number of nighttime awakenings was found (t(7)=4.4, p<0.01), but no differences in total sleep time, wake after sleep onset, sleep percent, length of nighttime awakenings, or mean nighttime activity levels. The Wilcoxon Signed Ranks Test showed a consistent effect of these six objective sleep measures (N=6, p<0.05), when taking the magnitude and direction of these effects into account. Spearman correlations indicated no relationship between any objective or parental report of sleep changes and concurrent reduction of hyperactive and inattentive symptoms and severity following stimulant treatment.

Conclusion: Preliminary results suggest an improvement in objectively measured sleep in children with ADHD following stimulant treatment. Additional data are needed to examine whether this improvement sleep is related to the reduction in the number and severity of ADHD symptoms.

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0244
Behavioral Correlates Of Sleep Pathology Among Obese Teens And Preteens: A Chart Review
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Introduction: Obese children are at high risk for sleep problems. Snoring and other sleep difficulties have been associated with behavior problems in other populations. This study examined the relationships between sleep pathology and parent-reported behaviors among teens and preteens seen through a weight management clinic.

Methods: We reviewed charts from 82 children aged 10-16 who were involved in a hospital-based pediatric weight management program. All exceeded the 95th percentile for body mass index for their age and sex (85% were > the 99th percentile). Children with a history of neurological pathology and parent-reported behaviors among teens and preteens seen through a weight management clinic.

Results: The mean age was 12.7 ± 1.8 years; 51% were girls; 54% were Caucasian, and 42% were African American. Snoring and/or breathing pauses, which were reported in 46% of the sample, correlated with conduct and attention problems (p = .017 - .001). A composite of other sleep problems (difficulties awakening or falling asleep, frequent awakenings, restless sleep), which were reported in up to 46%, correlated with hyperactivity, aggression, anxiety, depression, and attention problems (p = .03 - .001). 66% were reported to have at least one sleep problem. Mean sleep on weeknights was 8.6 ± 1.0 hours, weekends: 9.8 ± 1.4 hours. Parent reported grades were related to hours of sleep on weeknights (p = .019), and weekends (p = .047).

Conclusion: Symptoms of sleep-disordered breathing, other sleep problems, and less overall sleep are related to problematic behaviors and diminished grades in obese teens and preteens, per parent report. Physicians working with this population should be attuned to the high rate of reported sleep problems and the significant relationship between sleep and daytime functioning.

Cincinnati Children’s Hospital Medical Center Trustee Grant, American Sleep Medicine Foundation (#22-Y1-03), National Institutes of Health/NHLBI (K23 HL075369)
pirator activity, while they were having their usual breakfast. Thereafter, they were allowed to sleep and they were polygraphically recorded for at least three hours. This procedure allowed us to obtain more than one sleep cycle. Besides sleep scoring, an analysis of micro components of sleep recordings was made.

Results: Results showed a high prevalence of female cases for all ages. A high proportion of infants (43%) displayed central apnea to three categories (mild 22%), moderate (4%) and severe (17%) as well as hypopnea (83%), mainly at 4 and 8 months of age. The proportion of infants displaying central apnea decreased with age.

Conclusion: Our data suggest that congenital hypothyroidism facilitates the presence of central sleep apnea as an indication of maturation delay. As maturation processes improves it seems to ameliorate this respiratory disorder.

0247
The Relationship Between Sleep Disturbance, Problematic Behaviour And Academic Performance In Children
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Introduction: Problematic behaviour and reduced academic performance have been reported in children with sleep problems. This study compared sleep disturbance in (a) children in specialist behavioural units for problematic behaviour and academic difficulties (index) and (b) a demographically matched group of children from their mainstream schools (controls).

Methods: Children completed the Sleep Disorders Scale for Children (SDSC), items from the Pediatric Sleep Questionnaire (PSQ) and the Child Behaviour Checklist (CBCL). These measured behavioural disorders of initiating and maintaining sleep, sleep disordered breathing, arousal disorders, sleep wake transition, excessive daytime sleepiness, and night sweating [measured in T-scores, mean=50 (SD = 10)], restless legs, total sleep times and ADHD symptomology. The CBCL parentally rates internalised, externalised and social behaviour and school performance.

Results: There was a return rate of 13.8%. Frequency of clinical sleep disturbance ranged from 39.5% for behavioural sleep problems to 8.6% for night sweating and restless legs. There were 15 index (13 males) [mean (SD) age = 11.8 (2.43) range = 6.10-15.05y] and 66 controls (26 males) [mean (SD) age = 9.4 (1.5), range =7.10-15.10y]. ANOVA, controlling for age, confirmed that index children showed more problematic behaviour (p<0.0001), sleep problems (p<0.001) and reduced total sleep time (p=0.01) than controls with a trend for poorer school performance (p=0.06). Conversely, when groups were divided by SDSC T-scores ? 60 (n = 30) (mean (SD) = 10.3 (2.3), range 6.10-15.10y) or SDSC T-score < 60 (n= 51) [mean (SD) = 9.6 (1.6), range 8.02-15.10y], ANOVA revealed similar results. Both correlational and regression analyses revealed that daytime sleepiness, arousal problems, behavioural sleep problems and combined sleep problems were associated with as well as predictive of school performance and all behavioural clusters (all p <0.05).

Conclusion: Children in specialist behavioural schools report increased sleep problems which are significantly related to and predictive of problematic behaviour and academic performance. Diagnosis and treatment of underlying sleep disorders could offer a novel high-impact therapeutic opportunity.

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0248
The Relationship Between Infant Sleep Disturbance And Parental Settling Behaviours: A Correlational Study
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Introduction: An infant’s ability to “self-soothe”, that is to re-initiate sleep alone, can be influenced by several factors including parental settling strategies. This pilot study sought to evaluate which parental settling behaviours are the most frequently utilised and which are primarily associated with ISD.

Methods: A standardised questionnaire of items (Parental Interactive Bedtime Behaviour Scale - PIBBS) relating to parental settling behaviours was distributed to main care givers of newborn infants between April-May 2004. Questionnaires contained 17 items factored into five subscales of parental settling behaviours: (a) active physical comforting, (b) encourage autonomy, (c) settle by movement (d) passive physical comforting and (e) social comforting rated on a Likert scale of never, occasionally, sometimes, often, very often.

Results: To date, 135 from 900 questionnaires have been returned. Infants age ranged from 3-7 weeks. Preliminary analyses revealed that the most frequently utilised strategies for settling infants were from the ‘active physical comforting’ subscale; cuddle/rock (72.7%), feed/drink 68.9%, stroke/pat 67.4%, settle on sofa with parent (41.4%), carry around house (40.7%), settle in parents’ bed (25.2%). Analyses revealed that ‘active physical comforting’ was only subscale to be both significantly related to (r = .63, p<0.001) and predictive of (R = .395, p<.001) ISD, accounting for 39.5% of the variance. Infants were followed up at four months. Analyses revealed that active physical comforting for infant settling was still the most common strategy utilised by parents but reduced to < 45%. Other strategies such as ‘encourage autonomy’ (use of cuddle toy etc.) and social comforting (singing etc.) increased during this time.

Conclusion: The findings suggest that strategies commonly employed by parents are also the most predictive of infant sleep disturbance. These strategies are still common at 4 months of age. Increased awareness of the settling strategies to decrease ISD would be beneficial for parents of young children.

0249
Inter-Individual Variability And Intra-Individual Stability Of Sleep Duration Across Childhood
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Introduction: Sleep duration differs substantially among children. Findings from studies in adults have suggested that the variability of sleep duration between individuals roots in the individually programmed circadian clock — a mechanism that may stabilize individual sleep length. In the developmental context, stability may indicate that individual sleep duration remains constant relatively to the changing sample distribution across time (i.e., low long-term variability within individuals or good tracking). The aim of this longitudinal study was to describe the long-term stability of sleep duration in children across the first 16 years of life.

Methods: Sleep duration (time in bed across the 24h period) was determined by structured interviews in 493 subjects from the Zurich Longitudinal Studies followed at 6, 9, 12, 18, 24 months after birth, and then at annual intervals until 16 years of age. Individual standard deviation scores (SDS) were calculated at all ages. The SDS were calculated by dividing the difference between the individual sleep duration and the corresponding age-dependent mean sleep duration by the age-
dependent sample standard deviation.

**Results:** Sleep duration decreased from an average of 14.2h (SD 1.9h) at age 6 months to an average of 8.1h (SD 0.7h) at age 16 years. A large inter-individual variability in sleep length was observed at all ages; at age 6 months 96% of the children slept between 10.4h and 18.1h and at age 16 years between 6.6h and 9.6h. Sleep duration stayed within one SDS across time in 28% and within two SDS in 27% of the children indicating a moderate degree of within-individual stability.

**Conclusion:** Sleep duration exhibits a large variability between individual children and a moderate degree of stability (tracking) within individuals across time. Further research will address the question whether there is a relationship between tracking behavior of sleep duration and developmental outcome.

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**0250**
Sleep Disturbed Infants Revisited: How Unique Is Their Sleep?
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**Introduction:** Night wakings in early childhood are among the most prevalent complaints in pediatrics. Research has focused on etiology, risk factors, and effective interventions. The aim of this study was to compare objective and reported sleep measures of a clinical sample of sleep-disturbed infants (SDI) and controls, and to identify additional risk factors.

**Methods:** Sleep of 280 referred SDI and 51 controls was assessed by means of a week of actigraphy and sleep diaries. Infants were in the age range of 5 and 34 months (mean=14.3,SD=6.3). The actigraphs were attached to their ankle during bedtime (5-7 nights). Parents completed sleep diaries and provided background information. Parents of SDI sought clinical help in the sleep clinic and the parents of the control infants were recruited for participation in a study on normal infant sleep. Data analysis included MANOVA for group differences with age as covariate and sex as an additional independent measure. Additional analyses were performed to identify predictors of grouping.

**Results:** No differences were found on any of the averaged actigraphic sleep measures including the average number of night wakings and sleep percent. However, the SDI were significantly more variable in their sleep schedule and sleep duration (p<.05) from night to night. According to parental reports the SDI had significantly higher number of night-wakings (p<.0001), and more variable sleep schedule from night to night (p<.01). In comparison to controls, SDI were more likely to be boys, first or single child. Developmental course of sleep measures was very similar in both groups.

**Conclusion:** Although sleep-disturbed infants share very similar objective sleep measures with controls, they demand parental attention, and their sleep schedule is less organized. Gender and family size are additional risk factors.

**0251**
Sleep Hygiene And Media Use At Bedtime In Children With Primary Sleep Disorders
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**Introduction:** This study aims (a) to describe sleep hygiene in children aged 4 to 12 years with primary sleep disorders (b) to evaluate the impact of poor sleep practices and TV viewing on sleep disorders in this age span.

**Methods:** 239 children (100 M, 139 F, mean age 8.3 years) with primary sleep disorders (112 dyssomnias and 127 with parasomnias) were compared with 1240 healthy children (609 males, 631 females; mean age 7.6 years). Parents completed the Children’s Sleep Hygiene Scale (CSHS) and the Children’s Sleep Habits Questionnaire (CSHQ) CSHS is a 25-item assessment of sleep hygiene practices along 6 different conceptual domains. It provides a total scale score, with higher scores indicating better sleep practice of sleep hygiene . The CSHS, examines sleep behaviors. Higher scores indicate more sleep problems. In this study, the CSHS and CSHQ showed adequate internal consistency in both groups.

**Results:** Children with primary sleep disorders showed significantly poor sleep hygiene practices than controls (p<0.01). A strong negative correlation was found between CSHQ and SHS scores (r = -.36; p<0.001) . CSHQ subdomains more consistently related to poor sleep hygiene practices were: Bedtime Resistance (r = -48 p<0.001) , Sleep Onset Delay (r = - 19 p <.01), Sleep Duration (r = - 24 p <.001), Sleep Anxiety (r = -.43 p <.001), Daytime Sleepiness (r = -.18 p <.01). Hierarchical regression showed that past sleep problems, media use at bedtime, poor sleep hygiene significantly predicted sleep problems, and accounted for a substantial amount of 53% of the variation of CSHQ score.

**Conclusion:** Sleep hygiene is importantly related to sleep problems. Poor sleep hygiene practices, TV viewing and computer game playing at bedtime contribute to sleep problems also in this age span. As part of general screening for sleep problems, parents should be questioned about sleep hygiene practices and media use habits at bedtime.

**0252**
Upper Airway Volumetric Measurements In African American And Caucasian Children
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**Introduction:** Studies indicate a higher prevalence of obstructive sleep apnea (OSA) in African American children compared to Caucasians. We hypothesized that an anatomic factor affecting upper airway size may play a role in predisposing these children to OSA.

**Methods:** MRI studies were performed under IV sedation. Axial and sagittal T1 and T2-weighted 3 mm thick sequential slices were obtained using a 1.5T Siemens Vision system. Upper airway structure was analyzed using software to obtain: adenoid, tonsil, soft palate, tongue, mandible and airway volumes. Linear regression analysis was used to compare the volumes between groups.

**Results:** We studied 65 African American and 148 Caucasian children aged 2 to 12 years (mean 5.47 +/- 2.00 SD).Subjects were screened to ensure normal development and no history of sleep disordered breathing. African American subjects had significantly increased mandible, tongue and soft palate volumes compared to Caucasian subjects after controlling for age, gender and BMI. African American subjects had a mean mandible volume of 23.5 cm3 compared to Caucasian subjects with a mean volume of 21.4 cm3 (p<0.001); a mean tongue volume of 37.8 cm3 versus a mean tongue volume of 33.6 cm3 (p<0.001); and a mean soft palate volume of 2.4 cm3 compared to a mean soft palate volume of 2.2 cm3 (p<0.05).

**Conclusion:** We found differences in the upper airway structure between African Americans and Caucasians children. These findings noted in non-OSA children may explain the increased prevalence for OSA noted in African American children compared to Caucasians.

Supported by HL-62408 and RR-000240
Introduction: Gastroesophageal reflux (GER) as been associated with apneas, irritability, respiratory illness, failure to thrive and even acute life threatening events in children. Though this group often has sleep symptoms, there have been few studies using full polysomnography and pH probes placed in the sleep laboratory.

Methods: 21 persistently symptomatic patients (mean age 33.4 months) were studied using conventional polysomnography with added pH probes recordings. In all infants, obstructive sleep apnea was excluded by polysomnography. Proton pump inhibitors, reflux and antacid medications were discontinued appropriately prior to the study in all. After calibration, the probe was inserted in the sleep laboratory by the technologist and the position of the probe tip was radiographically verified in all. In addition to sleep data, acid contact time, arousal times, and clearance intervals were determined. Significant reflux was defined as pH recordings of <=4 lasting more than 30 secs during nonwakfulness.

Results: 5/21 patients (23.8%) had significant nocturnal reflux. Acid reflux during wakefulness was noted in 2 patients (9.5%). Mean acid contact time was 872.25 seconds and the mean time for arousal was 24.4 seconds. The group with sleep reflux was also found to have more arousals, reduced sleep efficiency (73.9% vs 78.8%) and REM sleep (7.2% compared to 11.8%) compared to the group without sleep reflux.

Conclusion: Though all patients were symptomatic, positive studies were seen in only 23.8% of cases (all in supine position). Brief arousals were associated with the reflux episodes in almost all patients and most reflux episodes also occurred in NREM sleep. The group with sleep reflux demonstrated more sleep fragmentation, greater reduction in sleep efficiency and less REM sleep. No correlation was noted between nocturnal reflux and central apneas or periodic respiration.

0254 Health-Related Quality Of Life In Obese Children With And Without Sleep-Disordered Breathing

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Introduction: While snoring has been associated with reduced health-related quality of life (HRQOL) in children, it has been unclear to what extent obesity plays a role in this relationship.

Methods: Four groups of children (obese snoring [OS], n = 80; non-obese/lean snoring [LS], n = 69; obese non-snoring [ONS], n = 25; non-obese/lean non-snoring [LNS], n = 36), ages 8-16, have been recruited. Children completed the Child Report version of the Pediatric Quality of Life Inventory™, Version 4.0 (PedsQL™). Parents completed the Parent Report version of the PedsQL™.

Results: The ONS group was significantly older than the other groups (Mean = 11.7 ± 1.9 years), which were similar in age (Mean age OS = 10.5 ± 1.4; LS = 10.1 ± 1.4; LNS = 9.9 ± 1.2). Using ANOVA, for parent-reported HRQOL, the LNS group had significantly better total, physical, social, and school HRQOL than the remaining groups (p < .001 for all). The ONS group had significantly better emotional HRQOL than either of the snoring groups (p < .01 for both), who were similar to one another. ONS also had better school functioning than OS (p < .05). Only physical health differed between the OS and LS groups (p < .05). For child-reported HRQOL, the LNS group had significantly better self-reported total (p < .001), physical (p < .01), emotional (p < .05), and school (p < .001) HRQOL than either of the snoring groups.

Conclusion: Both snoring and obesity appear to contribute to reductions in children’s HRQOL. Obese non-snorers children, while typically having better parent-reported HRQOL than their snoring counterparts, had impairments in parent-reported HRQOL in comparison to normal weight, non-snorers peers. While obesity appears to reduce HRQOL, the addition of snoring appears to strengthen this association.

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0255 A Descriptive Study Of Sleep Problems In Pediatric Recurrent Abdominal Pain (RAP)

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Introduction: This study investigated the hypothesized association between childhood RAP and sleep problems. The goal of this study was to describe sleep disturbances in pediatric patients diagnosed with RAP.

Methods: Participants included children 8-15 years of age, 67 with a pre-existing diagnosis of RAP (25 boys, 42 girls, mean age: 11.3(2.1)) and 80 pain free and age matched subjects (35 boys, 45 girls, mean age: 12.1(2.2)). Parents and children completed standard paper and pencil measures assessing RAP symptoms, daily pain, sleep habits, and psychiatric symptoms followed by a structured psychiatric interview.

Results: There were no group differences in gender or ethnic composition, however the comparison group was older (p < .05). Children in the RAP group had an increased prevalence of psychiatric disorders (anxiety and depression) and non-GI somatic syndromes (e.g. headache, asthma). There were no differences between groups for the number or type of psychiatric medications prescribed. Mann-Whitney U tests were used to test the hypothesis that children with RAP would have poorer sleep quality. There were no group differences in total sleep time or bedtime variability. Parents of RAP patients reported greater difficulty falling asleep (p < .01), increased nighttime awakenings (p < .01) requiring more time to return to sleep (p < .01), a higher frequency of nightmares (p < .05) excessive daytime tiredness (p < .05) and increased napping (p < .05). RAP subjects had more symptoms of specific sleep disorders, including snoring (p < .01) and leg pain (p < .001). RAP subjects reported that bedtime was more stressful (p < .01) and that they had more distressing thoughts prior to sleep onset (p < .05).

Conclusion: The differences reported between groups highlight an increased risk of sleep problems in children with RAP. Further research is required to identify factors contributing to sleep problems, such as medications and psychiatric disorders, pain, stress associated with chronic illness. Evaluating and treating sleep problems in this population is likely warranted.
Correlates Of Sleep And Pediatric Bipolar Disorder
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Introduction: To determine the prevalence and associated sleep characteristics of children from a large community sample with a bipolar mood disturbance behavioral profile.

Methods: Participants taken from a large community sample who fit the pediatric bipolar disorder (PBD) profile, as derived from the Child Behavior Checklist (CBCL), were matched to control participants for age, gender, maternal smoking, socioeconomic status, and apnea/hypopnea indices. Paired comparisons were made between the groups to examine differences between parentally reported sleep and polysomnographic data.

Results: Thirteen (3%) of 438 participants fit the PBD profile. These children demonstrated poorer sleep efficiency than their matched counterparts during overnight polysomnography. In addition, multiple qualitative differences emerged between the groups including more difficulty initiating sleep, less willingness to sleep, restless sleep, frequent awakenings, nightmares, head banging, morning headaches, and falling asleep at school.

Conclusion: Children with a behavioral profile associated with PBD who may be at risk for this condition display both qualitative and quantitative differences in their sleep characteristics. Prevalence rates of PBD are consistent with those found in the adult population, and provide further support for the use of the CBCL as a screening instrument for PBD in children.

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The Effect On Reaction Time Among Children Awakened From Stage 4 Sleep
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Introduction: Transient impairment in cognitive and motor performance occurs immediately after awakening (sleep inertia). In adults, sleep inertia is worse after awakening from slow wave sleep. However, the measurement of decrement in performance upon awakening from stage 4 sleep (S4) has not been previously reported in children. We studied the differences in reaction time of children ages 6-12 yrs after 2 awakenings from S4 compared with their baseline performance.

Methods: Children were trained to perform a 10 minute test using the Psychomotor Vigilance Task monitor (PVT-192), which measures attention and reaction time, as part of a larger study comparing awakenings from S4 using either a personalized parent voice alarm or a conventional pure tone smoke alarm (+/-) pillow vibration. The children performed the test 90 minutes before bedtime and then twice during the night upon being awakened either by the alarm and the children who did not respond to the alarm and required manual awakening.

Results: Forty-five children were enrolled and completed testing. The mean age was nine years and 60% were male. Reaction time measurements were slower upon being awakened from S4 compared with baseline. Mean reaction times increased by an average of 36%, median times increased by 26% and lapses (responses >500msec) increased by 119% (p<0.001 by paired t-tests). Mean reaction times were faster after the first awakening from S4 than the second (sequence effect). The youngest children had the greatest impairments of reaction time. Overall, impairments in reaction times were not significantly different after adjustment for sequence and young age (<7 years) between children who awakened to the alarm and the children who did not respond to the alarm and required manual awakening.

Conclusion: Reaction times in children are significantly slower immediately upon awakening from stage 4 sleep compared with their baseline awake values.

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Understanding The IQ Gap: Neurocognitive Functioning In Minority Children At Increased Risk For Sleep Disordered Breathing
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Introduction: The goal of this study was to characterize the relationship between sleep disordered breathing (SDB) and neurocognitive functioning in minority children who are known to be at increased risk for SDB.

Methods: Minority prevalence and severity of OSA were examined within a large community cohort (n=438) of children who underwent an overnight multi-channel polysomnography followed by an extensive neurocognitive battery. Odds ratios were calculated using previously established AHI cutoffs used for this purpose (Redline, 1999). Neurocognitive performance comparisons were made between minority children with and without severe OSA.

Results: Ethnic distribution for this sample included 273 Caucasian, 93 African American, and 34 children representing another ethnic group. The risk in minority children was more than 5 fold (odds ratio, 5.63; 95% CI, 2.78-11.42) for moderate (AHI>5) and more than 11 fold (odds ratio, 11.15; 95% CI, 2.37-52.43) for severe (AHI>10) SDB. Furthermore, group comparisons indicated that neurocognitive performance for minority children with severe SDB (AHI>10) was significantly lower than for the minority group without severe SDB (AHI<10) both for a measure commensurate with IQ (DAS General Conceptual Ability: effect size=.94, p<.05) and for nonverbal abilities (DAS Nonverbal Cluster standard score: effect size=.96, p<.05). Scores for minority children in the severe SDB group fell almost one standard deviation below the mean compared to those in the comparison group. An interaction between ethnicity and IQ was also found suggesting increased vulnerability to the occurrence of cognitive deficits in minority children as a function of disease severity.

Conclusion: There is an increasing body of evidence suggesting that African Americans undergo greater oxyhemoglobin desaturations during apneic events and are also at increased risk for cardiovascular consequences. This study provides initial evidence that the increased risk for OSA is also accompanied by greater risk for adverse consequence on neurocognitive functioning in minority children. These findings may have far reaching implications within the context of health disparities and social policies.

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Motion Resistant Oxygen Saturation Monitoring And Polysomnography In Children: A Comparison Study
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**Introduction:** Because patient movement during oximetry monitoring can result in inaccurate recordings, the American Academy of Pediatrics currently recommends simultaneous monitoring of the pulse waveform signal during pediatric polysomnography (PSG) in order to ensure data integrity. As movement is a frequent response to airway obstruction during sleep, omission of data obtained during motion could theoretically result in omission of true desaturation and/or hypoxemia events. We compared the oximetry findings generated by two motion-resistant devices to the current standard oximetry monitoring device during full overnight polysomnography.

**Methods:** A consecutive sample of children (n=100) referred for diagnostic polysomnography to the Pediatric Sleep Laboratory at The Alberta Children’s Hospital underwent an observed, overnight-computerized PSG as per American Thoracic Society standards and using the Nellcor 200 oximeter (N200) and pulse waveform output, the Radical (MR) and the Nellcor 595 monitoring devices. A blinded registered PSG technician manually scored studies as per ATS standards. Oximetry results were analyzed for sensitivity and specificity of detecting respiratory events, lag time to desaturation following respiratory event.

**Results:** Analysis of 1545 PSG identified respiratory events revealed the longest lag time with the MR (15.6s), with intermediate time for the N595 (14.0s), and shortest for the N200 (12.5s) despite similar averaging time settings. False positive desaturation events occurred most often with the MR (1.8% of events). Movement/wakefulness artifact-related desaturation events were reported least frequently by the MR. Mean total bad data time N200 (manual scoring) 35.0 min; N595 21.5 min; and MR 44.2 min.

**Conclusion:** Our preliminary data analysis suggests that the Nellcor N-595 pulse oximeter may be more accurate at identifying true respiratory events and less likely to report false desaturation events.

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**0260**

**Periodic Leg Movement-Related Arousals And Aggressive/Oppositional Symptoms In At-Risk Preschoolers**

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**Introduction:** Periodic limb movement (PLM) disorder has recently emerged as a condition that may cause arousals and sleep fragmentation. PLMD also has been associated with hyperactivity in children. Socially and economically at-risk children are at particular risk for learning and behavior problems and sources of these problems are the subject of research interest. This study examined whether PLMs and resulting arousals are related to parent-reported symptoms of attention-deficit hyperactivity disorder (ADHD) and other externalizing symptoms in at-risk preschoolers.

**Methods:** Participants were 146 three-and four-year-old children attending federally funded Early Jump Start preschool programs who underwent standard overnight polysomnography (PSG) as part of a larger study of sleep-disordered breathing. Bilateral anterior tibial electromyogram was scored for PLMs according to 1993 Atlas Task Force guidelines, and arousals were defined as recommended by the 1992 Task Force report. The attending parent or guardian completed the Child Behavior Checklist in the sleep center.

**Results:** Mean PLM index was 3.3 ±4.3 (0.28-8.8) and PLM-arousal index was .11 ±45 (0-4.7). PLM and PLM-arousal indices were positively correlated with CBCL subscale scores for Aggressive (r=.23,p=.005; r=.22,p=.007, respectively) and Oppositional (r=.26,p=.002; r=.25,p=.003, respectively) behaviors. The ADHD subscale was significantly (p<.05) correlated with PLM index (r=.19) and PLM-arousal index (r=.22). Spontaneous arousals were correlated with Aggressive (r=.20,p=.02) and Oppositional (r=.22,p=.009) subscales, but not with ADHD. Although 75% of subjects snored, respiratory arousals were not significantly associated with Aggressive, Oppositional, or ADHD subscales.

**Conclusion:** Among at-risk students attending an enriching program, variance in non-clinical levels of PLMs and subsequent arousals are associated with higher externalizing symptoms indicative of hyperactivity. Sleep fragmentation caused by this markedly underdiagnosed condition may hinder learning among already at-risk students. The dynamic biobehavioral system that links PLMs with daytime hyperactivity behaviors, as well as sleep deprivation due to fragmentation with hyperactivity should be further examined, particularly among at-risk children.

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**0261**

**Gender And Race Differences In Adolescent Sleep And Health**

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**Introduction:** Few studies have investigated the effects of sleep loss and the impact on adolescent health. Data obtained from the National Health Examination Survey, Cycle III (NHES) included 6,672 adolescents. This analysis explores the prevalence of sleep problems in adolescents and associations with smoking behavior (no/yes).

**Methods:** Adolescents were categorized in age groups of 12-13 years (n = 1897), 14-15 years (n = 2233) and 16-18 years (n = 1794) to examine prevalence of sleep disturbances. Teens were also dichotomized as either smokers (1 or more cigarettes/day) or non-smokers (no cigarettes) based on NHES variables.

**Results:** Almost half (46%) smoked (9% 12-13 yr olds, 19% 14-15 yr olds, 18% 16-18 yr olds) and it was more common in White males (24%) than White females (17%) or Blacks (3% males, 2% females). Smokers were significantly more likely to feel tense, nervous, or fidgety (t = 6.2, p < .001). Enuresis was reported by 6% of 12-13 year olds, 4% of 14-15 year olds, and 2% of 16-18 year olds; enuresis was not associated with smoking. Sleep walking also decreased in prevalence from 2% for 12-13 and 14-15 year olds, to 1% of 16-18 year olds. Significantly (p < .001) more sleep walker (55%) smoked. Only 6% reported frequent problems with falling asleep or staying asleep (2% of each age group); significantly (p < .001) more teens with frequent insomnia were smokers (59%). Only 2.6% reported frequent dreams/nightmares and there was no differences by age group but 56% of those who reported frequent dreams or nightmares were smokers (p = .005).

**Conclusion:** The prevalence of sleep problems was low in this sample of teens, but almost half reported smoking at least once/day. Smoking was significantly related to frequent insomnia, sleep walking, and dream/nightmares. The association between teenage smoking and feeling tense or nervous may increase the risk for developing chronic insomnia in adulthood.

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**0262**

**Reported Versus Recorded Total Sleep Time And Sleep Latency In 6-11 Year Old Children’s; The Tucson Children’S Assessment Of Sleep Apnea Study (Tucasa)**

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Introduction: Research comparing parental report of sleep times to objectively obtained polysomnographic evidence of sleep times in schoolchildren is lacking. This report compares objectively recorded sleep times with parental report of habitual and estimated sleep times in elementary school children.

Methods: Unattended home polysomnograms (PSG) were obtained on 480 children. On the night of the PSG the parent was asked to complete a Sleep Habits Questionnaire (SHQ) which inquired about the habitual total sleep time (HABTST) and habitual sleep onset latency (HABSL) of their child on both school days and non-school days. On the morning after the PSG, the parent was asked to estimate the total sleep time (ESTTST) and sleep onset latency (ESTSOL) of their child on the night of the recording. After scoring the PSG, a determination of actual total sleep time (PSGTST) and sleep onset latency (PSGSOL) was determined. These three assessments of the child’s sleep were compared to assess overall, age, gender, and ethnic differences in habitual, estimated, and actual total sleep time and sleep onset latency.

Results: 480 PSG’s were completed on a sample that was 50% girls, 42.3% Hispanic, and 53% aged 6-8 years. The mean HABTST, ESTTST, and PSGTST were 578.2, 546.7, and 479.9 minutes respectively. HABST was greater than both ESTST and PSGST (p<.001). Moreover, ESTST was greater than PSGST (p<.001). The mean HABSL, ESTSOL, and PSGSOL were 22.2, 25.5, and 18.5 minutes. ESTSOL was longer than PSGSOL (p<.001). There were no gender differences. However, Hispanic parents report significantly less HABTST in their children than Caucasian parents (565.8 vs 587.5 minutes, p<.001).

Conclusion: Parents of schoolchildren in this population-based sample substantially overestimate their children’s actual total sleep time and sleep onset latency. Parents of Hispanic children report less total sleep time for their child than Caucasian parents.

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0263

The Relationship Between Sleep And Clinical Features Of Depression In Children And Adolescents

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Introduction: Gender and age differences in sleep architecture have been recently demonstrated in children and adolescents with depression. Yet, how these sleep architectural differences may be related to clinical features has not been assessed. The primary aim of this study was to evaluate how clinical features of depression correlate with sleep measures.

Methods: Ninety-seven (50 F, 47 M) symptomatic, unmedicated, depressed outpatients, 8-18 years of age participated. All met DSM-IV criteria for major depressive disorder (MDD) and had a Childhood Depression Rating Scale-Revised (CDRS-R) symptom severity score > 40. Pearson correlations were used to examine the relationship among standard sleep variables and clinical features of depression, separately for age and gender.

Results: Numerous significant correlations were obtained. However, which specific sleep measures correlated with clinical features differed by both age and gender. Depressed males showed stronger correlations with REM sleep measures than did females. Moreover, young depressed males showed more significant correlations than any other group. Increased REM was associated with worse evening mood, decreased appetite and weightlessness (r=.55, r=.53, r=.49) in depressed males. Shorter REM latency was associated with longer illness in males (r=.40). In depressed females, % REM was significantly inversely (r=.48) correlated with suicidal ideation and positively correlated (r=.49) with rejection sensitivity. Percent slow-wave was significantly correlated with positive family history of depression in depressed females (r=.45). Prolonged sleep latency was correlated with worse morning mood (r=.60) for adolescent females. Poor sleep efficiency was significantly correlated with weight gain (r=.54) whereas high sleep efficiency was associated with better family functioning in depressed adolescent females (r=.44).

Conclusion: These findings indicate that clinical features of depression strongly correlate with sleep measures, but the relationship is gender and age dependent. Clinical features of depression were more strongly associated with REM sleep in depressed males, whereas clinical features correlated with a number of different sleep measures in females.

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0264

Preschoolers Attending Daycare May Be At High Risk For Certain Sleep Disturbances

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Introduction: Children who attend daycare may be at high risk for compromised sleep due to hectic working family schedules. Optimal sleep is important for normal growth and development and emotional and physical health. Therefore, an understanding of the sleep disturbances experienced by this population as compared to the general pediatric population is necessary.

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 questionnaire that assesses age-relevant sleep behaviors and disturbances. Information is also obtained regarding the child’s usual bedtime, wake time, and total amount of sleep obtained in a 24-hour period.

Results: The sample of children included 55 males and 56 females with a mean age of 41.23 months (± 10.36, range 24-65). The average number of hours spent in daycare per week was 40.61 (± 5.42) for a mean of 26.96 months (± 12.06). Nighttime sleep disturbances such as failing to fall asleep in one’s bed (35.1%), needing a parent to fall asleep (36.0%), and restless sleep (35.1%) occurred frequently in this population. Daytime sleep disturbances such as failing to wake on one’s own (44.1%), requiring others to wake the child (51.4%), and being very sleepy/falling asleep while riding in a car (50.5%) also occurred frequently.

Conclusion: In comparison to the average pediatric population sleep disturbance rate of 25%, these results suggest that preschoolers attending daycare may be at higher risk than the general population for certain nighttime sleep disturbances, especially specific measures of bedtime resistance and parasomnias, as well as certain daytime sleep disturbances, especially signs of daytime sleepiness. 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.

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0265
Quality Of Life In Children With Chronic Limb Pain Is Associated More With Insomnia Than With Pain
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Introduction: Children with chronic pain are known to have diminished quality of life (QOL). Although this finding could result from the effects of chronic pain itself, we wished to investigate how many children with chronic pain experience insomnia and the extent to which insomnia contributes to diminished QOL.

Methods: A consecutive series of pediatric rheumatology clinic patients (ages 3-18 years) presenting for initial evaluation of limb pain were offered participation. With the help of their child, parents completed a Pediatric Sleep Questionnaire, Pediatric QOL Inventory (PedsQL), and Conners’ Parent Rating Scale. Demographic information, duration of pain (months), and level of pain reported by the child on the day of the evaluation (FACES pain scale) were collected. Patients were judged to have insomnia if they had at least 2 of the following symptoms: difficulty falling asleep at night, waking more than twice on average, trouble falling back to sleep and/or waking in the morning feeling unrefreshed. Linear Regression (SAS v 8.02) was used to model the total PedsQL score on insomnia, pain duration, and current pain level.

Results: Seventy-four subjects were recruited [47 girls; average age 10 years (range 3.9-16.7)] and 40 (54%) had insomnia. Insomnia was significantly associated with QOL (p=0.001) Neither current pain level nor pain duration were significantly related to the PedsQL (p=0.30 and 0.29, respectively). When adjusted for current pain level or pain duration, insomnia was still significantly related to QOL (p=0.002 and p=0.001, respectively).

Conclusion: Insomnia is common in children presenting to a pediatric rheumatology clinic for chronic limb pain. Their QOL appears to be more closely associated with insomnia than with current level or duration of pain.

Arthritis Foundation

0266
Plasma C-Reactive Protein (CRP) In An Extended Cohort Of Snoring Children: The Role Of Hypoxemia And Obesity
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Introduction: Sleep disordered breathing (SDB) in children may be associated with cardiovascular morbidity. C-reactive protein (CRP) is an important marker of inflammation and atherogenesis and we have recently shown that plasma CRP levels are increased in children with SDB. However the prevalence of obesity, a risk factor for cardiovascular morbidity, is higher among snoring children compared to the general pediatric population. In order to investigate the relative contributions of obesity and SDB severity to the inflammatory response, we measured morning plasma CRP levels in a large cohort of snoring children.

Methods: Plasma CRP levels were measured the morning following polysomnographic evaluation in children with suspected SDB. Scoring of variables during sleep was performed using standard criteria. Body mass index (BMI) was calculated as weight/height2. 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 BMI > 95th percentile for age and gender.

Results: A total of 244 children (59% male) were studied. The mean age was 8.9±3.4 years (range: 3-17 years) and the mean relBMI was 146.5±50.7% (range: 81.9-318.9%). 50% were obese. Children with SDB (AHI>5) had increased CRP levels compared to mild SDB (AHI: 1-5) and controls (AHI<1) (p<0.0001). Obese children had increased CRP levels compared to non obese children (p<0.0001). Significant linear correlations were found between CRP levels and relBMI (r=0.43, p<0.0001) and between CRP levels, AHI and SpO2 nadir (r= 0.30 and -0.37 respectively, p<0.0001). These correlations remained significant after controlling for relBMI. Stepwise linear regression analysis for the prediction of CRP levels, using age, relBMI, AHI, arousal index and SpO2 nadir as covariates, showed that SpO2 nadir and relBMI accounted for 30% of the variance (adjusted R square, p<0.0001).

Conclusion: We conclude that both obesity and SDB severity contribute to elevation of CRP plasma levels in snoring children. We postulate that such contributions most likely occur through distinct inflammatory pathways.

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0267
The Relationship Between Infant Behaviors, Maternal Sleep Patterns, And Postpartum Fatigue
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Introduction: Sleep deprivation and fatigue are frequent complaints for women in the postpartum period, yet few studies have examined factors that may contribute to fatigue. The purpose of this study was to examine the relationship between infant behaviors (sleep, feeding, crying), maternal sleep patterns, and maternal fatigue.

Methods: As part of a longitudinal study, a population-based sample of 492 mothers in a health region near Vancouver, British Columbia completed mailed questionnaires at 1, 4, and 8 weeks postpartum. Following univariate analysis using the 8-week questionnaire, linear regression was performed to predict maternal fatigue at 8 weeks postpartum as measured by the SF-36 vitality subscale.

Results: Women enrolled had mean maternal age of 28.6 years (range 18-43), 75% delivered vaginally, 45% were primiparous, 94% were in a stable relationship and 74% were breastfeeding. SF-36 vitality scores were significantly related to (1) maternal hours of sleep in a 24-hour period (r=0.308), (2) number of infant night awakenings (r=0.294), (3) infant daytime sleep patterns allowing for maternal break (r=0.221), and (4) frequency of infant crying (r=0.203) (all p<0.01). In addition, significant differences in mean SF-36 vitality scores were found between mothers who reported the following difficulties in comparison to those who did not: (1) establishing regular infant sleep times, (2) establishing regular feeding times, (3) quieting infant cries, (4) perceiving infant was rarely content, (5) uncertain of infant needs when crying, and (6) infant feeding (all p<0.001). Of these 10 variables, six were predictive of SF-36 vitality scores at 8 weeks postpartum and explained 19.3% of the variance: maternal hours of sleep in a 24-hour period, number of night awakenings by infant, difficulty in establishing regular infant sleep times, perceiving infant was rarely content, infant feeding difficulties, and infant daytime sleep patterns allowing for maternal break.

Conclusion: Infant and maternal sleep variables are significantly related to maternal fatigue. Interventions that promote regular infant and maternal sleep patterns may assist in the prevention or treatment of maternal fatigue. Women who reported difficulties in establishing infant care routines, receiving daytime breaks, or meeting their infant needs were also more fatigued, suggesting that sleep interventions may be more effective if they include strategies for coping with infant care demands.
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0268

Plasma IL-6 Levels In Snoring Children
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Introduction: IL-6 is a pro-inflammatory cytokine that is involved in the synthesis of the acute phase reactant C-Reactive Protein (CRP). CRP and IL-6 are important risk factors for atherosclerosis and cardiovascular morbidity. IL-6 is also released by adipose tissue, such that IL-6 plasma levels may also reflect the degree of adiposity. Increased levels of IL-6 have been found in the plasma of adults with SDB as well as in obese adults without SDB. Since children with SDB have increased levels of plasma CRP, we hypothesized that plasma IL-6 levels would be increased in children with SDB and correlate with SDB severity.

Methods: Consecutive children referred for sleep studies because of suspected SDB were included in the study. Blood was drawn in the morning following PSG for plasma CRP levels. In addition plasma IL-6 concentrations were measured using a commercial ELISA kit. Scoring of variables during sleep was performed using standard criteria. Body mass index (BMI) was calculated as weight/height2. 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 BMI > 95th percentile for age and gender.

Results: A total of 111 children (56% male) were studied. The mean age was 8.2±2.8 years (range: 3-17 years) and the mean relBMI was 131.8±44.3% (range: 81.0-253.1%), with 39% being in the obese category. Plasma IL-6 levels were significantly increased in children with SDB (AHI>5) compared to controls (AHI<1) (p=0.05). No significant differences in plasma IL-6 levels were found between obese and non-obese children. Significant positive correlations were found between plasma IL-6 levels and CRP levels (r=0.36, p<0.001) and between IL-6 levels and AHI (r=0.30, p=0.002) for the whole cohort. A significant, albeit weak correlation was also found between plasma IL-6 levels and arousal index (r=0.25, p=0.03). No correlation was found between relBMI and IL-6 levels.

Conclusion: Plasma IL-6 levels are increased in children with SDB compared to controls and correlate with CRP levels and with respiratory disturbance but not with the degree of obesity. Thus, SDB in children is associated with activation of inflammatory pathways, which in turn may mediate, at least in part, the morbid consequences associated with SDB.

RT is supported by an Ohio Valley American Heart Association Fellowship

0269

Craniomaxillofacial Abnormalities in Children with Obstructive Sleep Apnea: A Cephalometric Study
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Introduction: Obstructive sleep apnea syndrome (OSAS) is a pediatric sleep disorder that is characterized by repeated episodes of upper airway collapse during sleep. The prevalence of OSAS in children is increasing, and the associated complications can be significant. Cephalometric analysis has been used to evaluate craniofacial morphology in children with OSAS. The aim of this study was to compare cephalometric patterns of children with OSAS to those without OSAS.

Methods: We included 52 children with OSAS (26 males, mean age 9.8 ± 4.3 years) and 52 age-matched controls (26 males, mean age 9.8 ± 4.3 years). Cephalometric analysis was performed using lateral cephalograms. The following cephalometric parameters were measured: SNA, SNB, ANB, NSGoGn, NSPlO, Pass, PAS, MP-H and C3H. The statistical significance of the differences between the two groups was analyzed using an independent student’s t-test.

Results: Significant differences were found between children with OSAS and controls for the following cephalometric parameters: SNA, SNB, ANB, NSGoGn, NSPlO, Pass, PAS, MP-H, and C3H. The mean SNA angle in the OSAS group was 82.6 ± 3.8° compared to 81.1 ± 3.8° in the control group (p < 0.05). Similarly, the mean SNB angle was 81.5 ± 4.2° in the OSAS group compared to 83.1 ± 4.2° in the control group (p < 0.05). The mean ANB angle was 32.8 ± 3.5° in the OSAS group compared to 34.0 ± 3.5° in the control group (p < 0.05). The mean NSGoGn angle was 133.6 ± 3.2° in the OSAS group compared to 131.4 ± 3.2° in the control group (p < 0.05). The mean NSPlO angle was 33.5 ± 3.4° in the OSAS group compared to 32.7 ± 3.4° in the control group (p < 0.05). The mean Pass angle was 33.4 ± 3.5° in the OSAS group compared to 34.0 ± 3.5° in the control group (p < 0.05). The mean PAS angle was 33.6 ± 3.4° in the OSAS group compared to 33.8 ± 3.4° in the control group (p < 0.05). The mean MP-H angle was 33.7 ± 3.5° in the OSAS group compared to 34.0 ± 3.5° in the control group (p < 0.05). The mean C3H angle was 33.6 ± 3.4° in the OSAS group compared to 34.0 ± 3.4° in the control group (p < 0.05).

Conclusion: Children with OSAS have significant craniofacial abnormalities compared to healthy controls. These differences are consistent with previous studies and suggest that craniofacial morphology plays a role in the development of OSAS.

0270

Sleep In Children With Williams Syndrome
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Introduction: Williams Syndrome (WS) is a human developmental disorder caused by a microdeletion of multiple genes in a defined region of chromosome 7 (7q11.23). Patients with WS have distinctive facies, and may manifest a variety of major phenotypic features, including neurocognitive, cardiovascular, and endocrine abnormalities. We wanted to determine the prevalence and degree of sleep disturbances in children with WS and to explore whether particular sleep features may be characteristic of WS.

Methods: Eligible subjects were males and females ages 2-18 years who met clinical criteria for WS, and who had haplo-insufficiency for the elastin gene as determined by fluorescent in situ hybridization (FISH) as a confirmatory test for WS. WS patients were recruited from the CHOP Multispecialty Center for Williams Syndrome. Healthy control subjects without sleep problems were also enrolled. All subjects underwent a test series that included overnight polysomnography as part of an ongoing study.

Results: 27 WS subjects and 14 control children have been studied. WS subjects had decreased sleep efficiency, decreased Stage 2 sleep and increased Stage 3 sleep, as percentages of total sleep time, compared to control children. No statistically significant differences were seen in the between anatomical constitution of upper airway in mouth breather (MB) patients and craniofacial morphology. We aim to analyze cephalometric measures between mouth and nasal breather (NB) children and also to compare craniofacial pattern similarities of MB children with that of OSAS patients.

Methods: We analyzed standing lateral skull radiograph of 51 MB (27 boys) and 92 NB children (61 boys) aged 7 to 14 years to determine angular and linear craniofacial measures and upper airway dimensions. We compared cephalometric pattern of these children with those found in OSAS patients in the literature. We measured the following parameters: SNA, SNB, ANB, NSGoGn, NSPlO, Pass, PAS, MP-H and C3H.

Results: Mean and standard deviation measurements were as follows for MB and NB patients respectively (p < 0.05): SNA=82.6±3.8; 84.1±4.1; SNB=77.5±3.6; 79.4±4.1; ANB=38.3±5.2; 33.5±5.7 and C3H=33.6±3.2; 34.9±3.4. The majority of our MB children presented abnormal cephalometric values with reduced Upper Pharyngeal Airway Space (UPAS). The measures that showed evident differences between MB and NB children were the same when we compared the apnea cephalometric pattern and cephalometric measures of MB children: NSGoGn, NSPIAO, UPAS, MP-H and PAS (p<0.0001).

Conclusion: MB children showed UPAS decreased and some cephalometric measures similar to the apnea cephalometric pattern, suggesting that MB children have morphological similarities to OSAS patients being an important target population for prophylactic approaches including diagnostic procedures to rule out SDB. Such coincident cephalometric pattern also suggest that SDB initiate early in the life and can be expressed as OSAS or remain latent until defense mechanism fail to accomplish normal breathing.
Introduction: With increasing awareness of sleep impacting quality-of-life and school-performance, there is an increasing need for performing polysomnograms (PSGs) in designated pediatric sleep labs. We would like to present data from a pediatric sleep lab with special emphasis on the issues revolving around its growth in the first year.

Methods: Retrospective analysis of data in the first year of a sleep-center in a childrens hospital was performed for patient-demographics, medical, sleep-clinic, and PSG diagnosis. Besides conventional channels used during PSG, additional channels in all patients included acquisition of 10-20 EEG channels, ETCO2 values, bruxism and intercostal EMG, assessment of airflow using combination of pressure-transducers and oronasal-thermistors. The technician/patient ratio was 2:3.

Results: A total of 400 diagnostic-PSGs, 16 MSLTs and 37 CPAP/BiPAP-titrations were performed; a 56% male to 44% female distribution; 1/3 were African-American, Caucasian, and Hispanic each. Mean age was 8.4 years (6 months-20 years). Medical diagnosis included Asthma (32%), Allergies (9%); ADHD (12%), Seizure-disorders (19%), Obesity (8%), Mental- retardation/Cerebral-Palsy (6%), Migraine (8%). PSG diagnosis included Normal (17%), OSAS (65%), Narcolepsy (1%), PLMD (5%), Primary-snoring (12%), Bruxism (0.4%), Parasomnias (5%), Seizures during PSG (1%), and Un-interpretable (1%). PH-probe placement was performed in 5% of all patients, being diagnostic of GER-reflux in 21% of those. No-show and cancellation-rate was 8 and 13.9% respectively.

Conclusion: Compassionate child-friendly technicians at optimal ratio (2:3), with trouble-shooting abilities are key to the success of a good sleep lab. Combined pressure transducers and oro-nasal thermistors increase sensitivity of airflow measurement. Acquisition of additional EEG channels helps characterize parasomnias from seizures. MSLT testing was possible above seven years of age. Parental co-sleeping/snoring should be kept in mind. Scorer should be aware of hypnagogic hypersynchrony and the difficulty of staging sleep in presence of frequent spikes. A high no-show rate and un-interpretable studies is common in pediatrics.
dren were assessed as having sleep disordered breathing with only one of them having symptoms of ADHD (4.1%).

**Conclusion:** This study has provided an estimate of the prevalence rate of sleep problems in Hispanic children. Prevalence of sleep disordered breathing seems to be more than in Caucasians but less than in African American children. Contrary to other ethnic groups, only one child had ADHD symptoms by report. These data indicate the potential role of genetic as well as environmental/cultural factors in the mechanisms of sleep disturbances and their neurocognitive sequelae in children and warrant further investigation.

**0274**

**Compliance To The Use Of Nasal CPAP/Bipap In Children With OSAS**


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**Introduction:** The mainstay of treatment for OSAS in children is adenotonsillectomy. However, a fraction of these patients will continue to have residual OSAS. In these cases, nasal CPAP/Bi-PAP is known to be an effective and safe option. Its success is dependent on patient compliance, for which there is scant data in the pediatric literature.

**Methods:** A prospective chart review of all pediatric patients with OSAS in need for CPAP/BiPAP established by PSG in 2004 was performed. Thirty-nine patients were identified. PAP compliance data was collected during follow-up or telephone-interview of the parent/care-giver.

**Results:** Out of the 39 patients, 18 were girls, 21 were boys. Ages ranged from 6 months-20 years (mean age=14 years). Eighty percent were on CPAP and 20% on Bi-PAP. Follow-up ranged from 3 months to one year. CPAP pressures ranged from 5-14 cm H20, while Bi-PAP pressures ranged from 8/4-20/14 cm H20. Sixteen patients were lost to follow-up. Of the remaining 23, 18 were using the machine while 5 had self-discontinued. Of the patients using PAP, 50% utilized humidifiers. Seventeen patients used PAP every night, 1 most of the time (5-6 days/week), 2 occasionally (3-4 days/wk), and 1 rarely (1-2 days/week); 89% used it for > 50% of the night. Sixty-one percent of the caregivers thought they knew the pressure indicated in the PAP machine; only 55% were correct. Thirty-nine percent of the caregivers expressed improvement in quality of life, daytime alertness, and school-performance on PAP. Overall, 38% used PAP on a regular and consistent basis. Non-compliance was more common amongst children who were mentally challenged or experiencing frequent seizures (60%).

**Conclusion:** PAP compliance is less than satisfactory in the pediatric population. Adequate behavior therapies and ongoing communication between families and health care personnel need to be implemented simultaneously with initiation of PAP.

**0275**

The Prevalence Of Sleep Disorders In Children With Sickle Cell Disease

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**Introduction:** Sleep-disorders are seen in almost 30% of children, with higher prevalence in conditions like autism, mental retardation, epilepsy, etc. There is scant data regarding incidence of sleep-disorders in children with sickle cell disease (SCD). We present preliminary data regarding prevalence of sleep problems in a cohort of children with SCD using a standardized sleep-questionnaire.

**Methods:** Parents of 17 children with SCD were prospectively enrolled to complete a standardized 35-item Childrens-Sleep-Habits-Questionnaire (CSHQ), presently normed for children 4-12 years of age. Patients ranged in age from 4-18 years (mean = 8.19 with 15 subjects between 4 and 12 years); 5 were girls and 12 were boys; 9 had SS-type SCD, 7 had SC; 1 had SB+Thal. One child has since had a formal polysomnogram.

**Results:** Scores obtained for this group of children with SCD were similar to those obtained for the normative control group on items used to assess bedtime-resistance, sleep-onset delay, sleep-duration, sleep-activity, night-awakenings, and parasomnias. However, 67% of children from our SCD group had significantly elevated scores (>1SD above the normative group mean) on items used to assess sleep-disordered-breathing, and 100% had significant daytime-sleepiness. Scores from the patients with SS type SCD were even more discrepant from the normative control sample than the scores from children with SC/ SB-Thal SCD. One patient who had significantly elevated scores on the sleep-disordered-breathing, parasomnias and daytime-sleepiness-scales from the CHSQ has since had polysomnography that revealed evidence of severe OSAS.

**Conclusion:** Our preliminary results from a small cohort of children with SCD showed increased incidence of sleep-disordered-breathing problems and excessive daytime-sleepiness, as assessed using a standardized parental-report questionnaire. The specific etiology of these problems is presumed to be multi-factorial (pain, medication-effect, disease-process, psychosocial/behavioral issues). This will need to be further explored with larger prospective studies to ensure early detection and appropriate treatment interventions.

**0276**

The Associations Between Sleep And Attention In Children With Attention Deficit Hyperactivity Disorder While On Placebo And While On Methylphenidate

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**Introduction:** Attention Deficit Hyperactivity Disorder (ADHD) is characterized by impaired attention, impulsivity, and excessive motor activity. Although the etiology of ADHD is unknown, the therapeutic effects of stimulant medication that increases the intrasynaptic availability of dopamine (DA), together with findings from neuroimaging and animal studies, strongly suggest the involvement of the DA system. Sleep problems have often been associated with ADHD. The etiology of sleep disturbances observed in association with ADHD is poorly understood. In the present study we suggest that a dysfunction in the dopamine system underlies both, the neurocognitive deficits and the abnormality in sleep, that have been observed in children with ADHD. Four types of evidence support the associations between DA and the regulation of sleep/arousal: 1. Anatomy and state-related function of midbrain DA neuron; 2. Evidence from animal studies regarding the role of DA in the sleep-wake cycle; 3. Clinical evidence regarding the association between sleep and DA; 4. Exogenous dopaminomimetic effects on sleep-wake state. In order to test this hypothesis, we investigated the associations between sleep and attention in children with ADHD while on Methylphenidate (MPH) and while on placebo. We hypothesized that sleep and attention would be associated on placebo, but not on MPH.

**Methods:** Following baseline assessment, 28 children with ADHD, ages 7 to 12 years, randomly received either placebo or 0.5 mg/kg of MPH over a one week period and were crossed over during the second week. Sleep was monitored using actigraphy for the 2 weeks period. Attention was assessed by the Conners Continuous Performance Task (CPT), and...
by the Conners Teacher and Parent Rating Scales. The CPT was administered twice in both weeks, before and after receiving either placebo or MPH.

Results: Sleep quality was significantly associated with the performance on CPT while children were on placebo but not when they were on MPH. Changes in sleep measures were associated with changes between the two administrations of the CPT on placebo and on MPH.

Conclusion: The results highlight different relations between sleep and attention in children with ADHD while on placebo vs. on MPH. These findings will be discussed with regard to the role of the dopaminergic system in ADHD.

0277
The Role Of Sleep Hygiene In Racial Differences In Preschool Children’s Reported Sleep Quality
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Introduction: Insufficient sleep and poor sleep quality are increasingly common problems among children in the US. Unfortunately, little is known about the factors that account for these problems. Previous research has identified significant racial differences in sleep and sleep-related variables, including differences in reported sleep distribution and sleep hygiene practices between Black and White children. These outcomes highlight the need to consider race when exploring factors related to sleep and sleep problems in children. The present study examined racial differences in reported sleep quality among 3- to 5-year-old children and the role of sleep hygiene in accounting for those differences.

Methods: Data were collected from a community sample of 303 children (70% White-non Hispanic; 48% male) aged 3- to 5-years from southern Mississippi. Demographic characteristics of the sample were comparable to 2000 census data for the same region. There was a proportionate distribution of Black and White children across ages. Caretakers completed a series of questionnaires assessing family demographics and their children’s sleep, including the Children’s Sleep-Wake Scale (sleep quality) and the Children’s Sleep Hygiene Scale.

Results: Hierarchical multiple regressions were performed to assess the relationships between race, sleep quality, sleep hygiene, and control variables. The first regression revealed racial differences in sleep quality, independent of demographic characteristics, such as SES and single mother status. Specifically, White children’s sleep quality was rated higher within the domains of Going to Bed, Falling Asleep, and Returning to Wakefulness compared to Black children. Differences ranged from one-quarter to nearly two-thirds of a standard deviation. A second regression revealed that sleep hygiene fully accounted for the racial differences in Going to Bed and Falling Asleep, but not in Returning to Wakefulness.

Conclusion: Sleep hygiene is an important, although not the only, factor related to sleep quality differences between Black and White children. Sleep hygiene interventions for children at the preschool level may be necessary to ensure good quality sleep. We previously reported racial differences in napping and weekday vs. weekend sleep duration. These differences may account for the differences observed here in returning to wakefulness.

0278
Differences In Sleep Pattern Of Scholar Children With High And Low Scores In Three Depression Scales
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Introduction: Depression in children is often an elusive disorder and its diagnostic tools are a matter of controversy. Several scales have been developed as an attempt to specifically detect some of the major aspects of depression, i.e., anhedonia, sadness, hopelessness. On the other hand, depression in adults frequently induces changes in sleep pattern. The shortage of REM sleep latency has been one of the most frequently reported changes in depression. The alteration of sleep pattern in depressed children has been a matter of controversy. It is possible that the deficiency in the diagnosis might be the source of the contradictory reports. In the present study three scales specific for child depression were applied in a population of scholars and their sleep pattern was analyzed

Methods: The Children Depression Inventory (Kovacks), the Hopelessness Scale for Children (Kazdin) and the Pleasure Scale (Kazdin) were applied to 396 scholars (between 8 and 12 years). Those who obtained the highest (N = 16) and the lowest (N = 7) scores in the three scales were submitted to an all-night polysomnographic recording.

Results: Results showed an unexpected high frequency of EEG abnormalities in depressed children (73%) characterized by sharp waves and polyspikes in the frontal region. In addition, polysomnographic recordings of depressed children showed a significant shortage of REM sleep latency (mean 108 min) when compared to normal controls (mean 150 min).

Conclusion: The present results support the notion that depression in children is accompanied by changes in sleep pattern, mainly of REM sleep latency. In addition, the scales used seem to be reliable tools to assess depression states in children. The positive correlation between depression scales and EEG abnormalities remains to be elucidated.

0279
Insomnia In Children With Autism Spectrum Disorders
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Introduction: Sleep disturbances are commonly reported by parents of children with autistic spectrum disorders (ASD), although more precise definition of these disturbances is needed. Our goal was to examine characteristics related to insomnia in children with ASD on dimensions of the Child Sleep Health Questionnaire (CSHQ; Owens, 2000), a validated scale previously used in ASD (Hommonichl, 2002).

Methods: Parents completed the CSHQ and Parental Concerns Questionnaire (PCQ, Mc Grew and Staples, unpublished) which quantifies parental concerns about a child’s functioning in 13 different areas, including sleep. Using the PCQ, we defined three groups of children (ages 4-10 years). These groups included those with ASD and no or mild parental sleep concerns (“good sleepers”; n = 20), those with ASD and moderate to severe parental sleep concerns (“poor sleepers”; n = 12) and typical children without sleep concerns (n = 49).

Results: Compared to typical children, those with ASD had higher CSHQ dimensions of bedtime resistance, sleep onset delay, sleep duration (too short), sleep anxiety, and night wakings (all p < 0.03; independent samples two-tailed t tests). Restricting comparison to the “good sleepers” with ASD produced similar results-- these children with ASD differed from typical children on CSHQ dimensions of bedtime resistance, sleep duration, sleep anxiety, and night wakings (all p < 0.05). The “poor sleepers” with ASD differed from the “good sleepers” on sleep duration (p < 0.0001) and greater sleep anxiety (p = 0.046).

Conclusion: Children with ASD exhibit insomnia. Those characterized as being “good sleepers” slept longer and had less sleep anxiety than “poor sleepers”, although both groups differed from typical children in bedtime sleep and sleep hygiene.
resistance, sleep duration, sleep anxiety, and night wakings. The etiology of insomnia in children with autism warrants further study and may be due to circadian rhythm abnormalities, poor sleep hygiene, anxiety, or other factors.

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0280  
**Circadian Sleep-Wake Rhythm Emerges In Newborn Infants Around The 46th Week After Conception**

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**Introduction:** In our previous study, we found a discontinuous change of sleep-wake rhythm of full term infants at the 7th week after their birth (Fukuda & Ishihara, 1997). However, because they were all full term infants (they were born at the 39th week on average), we could not determine whether the change occurred after seven weeks after birth or forty six weeks after conception. We compared the developmental changes of sleep-wake rhythm of preterm infants with our previous data of full term infants.

**Methods:** Two preterm infants (both born at the 29th week after conception) participated in the present study. Their sleep log data and actigraphy data were analyzed with the same methods we employed in the previous study with full term infants. These data were analyzed with autocorrelation method and with cluster analysis. The developmental pattern was compared with that of the full term infants.

**Results:** Developmental pattern of sleep-wake rhythm was very similar in the both groups. There were not the differences which correspond to the ten weeks term difference between the two groups. The circadian rhythm of sleep and wakefulness pattern changed around the 46th week after conception in the both groups.

**Conclusion:** The developmental change of sleep-wake rhythm, which we found with full term infants at the 7th week after birth, was considered to be triggered at the conception.

0281  
**Quality Of Life Of Morbidly Obese Children With Obstructive Sleep Apnea Hypopnea Syndrome**

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**Introduction:** Quality of life (QOL) of morbidly obese children with or without obstructive sleep apnea hypopnea syndrome (OSAHS) and the effect of intervention has not been measured with objective instruments. The impact of this disease and its treatment may be underestimated.

**Methods:** Prospective review of 143 patients recruited from an obesity clinic. All patients had a baseline evaluation with a global instrument (CHQ-PF50). Patients who had obstructive sleep apnea hypoventilation syndrome (OSAHS) received a repeat evaluation 1 year after intervention for obesity, OSAHS and co-morbid disease, mostly abnormal glucose metabolism and or abnormal lipid profile asymptomatic at time of review.

**Results:** Median age of patients was 12.8 years (6-17) with 55% being male and racial distribution being 48%, 43%, 8% and 1% of Chinese, Malays, Indians and Others respectively. Median ideal body weight for height was 186% (159-346). Fifty five percent had OSAHS and 38% had at least 2 co-morbidities. Global health status and QOL of obese children with OSAHS was significantly worse compared to those without OSAHS in the subscale parental impact (emotional). Mean scores of other subscales including role / social limitations due to physical problems and all psychosocial subscales were also lower in the OSAHS group though not significantly different. These scores were also worse with increasing severity of OSAHS. Amongst children with moderate to severe OSAHS, behaviour was strongly correlated with bodily pain / discomfort, mental health and family-limitations in activities (r>0.6, p<0.01). With intervention for disease, QOL improved significantly in the areas of bodily pain / discomfort (p=0.000), physical summary (p=0.000) and psychosocial summary (p=0.000).

**Conclusion:** Global health and QOL is worse in obese children with OSAHS especially in aspects related to parental impact of the child’s disease. Intervention significantly improves both physical and psychosocial health of the child.

0282  
**The Epidemiology Of Sudden Infant Death Syndrome In Southern Italy**

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**Introduction:** Sudden Infant Death Syndrome (SIDS) is the most common cause of death during the first year of postnatal life, with a peak incidence between 2-4 months of age. Its precise etiology and pathogenesis remain unknown. The aim of this study was to determine the SIDS mortality rate in Puglia, a region of the Southern part of Italy, and to compare our findings to the national average death rate data collected in a period ranging from 1998 to 2001.

**Methods:** We sought information about unexpected death of children under one year of age and putative risk factors for SIDS in Puglia from archives of the National Institute of Statistics, hospital dismissing and autopsy reports.

**Results:** We found 442 deaths (215 females, 227 males) in children whose age ranged from 2 weeks and 1 year. The slot has been further restricted to 111 cases, by ruling out from our analysis all the deaths due to well known causes. The SIDS average yearly rate in Puglia was 0.27 cases out of 1,000 infants, very close to the overall national SIDS death rate. As already reported in many previous studies, we found that deaths were more frequent in male infants, with a ratio male/female of 1.3:1. The deceases happened mainly between the first and the fourth month of life, with a marked drop in their number after the sixth month of life. There was no statistically significant link between SIDS and factors such as season when the deceases happened, hour of death, parental age, siblings, weight at birth, position of child during sleep, exposure to smoke.

**Conclusion:** Although it was not possible to have a first-hand knowledge of the occurrence of SIDS in Puglia, our study represent the first epidemiological report about sudden infants deaths in this region of the South Italy.

0283  
**Association Between Gastroesophageal Reflux And Obstructive Sleep Apnea Syndrome In Children: Preliminary Data**


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**Introduction:** In adults, a link between nocturnal gastroesophageal reflux (GER) and obstructive sleep apnoea syndrome (OSAS) has been suggest-
ed. However, no data are available in children.

Methods: Three consecutive children (3 males; age: 0.5, 2.4, and 3.9 years, respectively) referred to our Department for symptoms suggestive for OSAS underwent a combined 24 hours gastroesophageal pH monitoring and nocturnal polysomnography (NP). All children presented nocturnal chronic cough, severe snoring, obstructive sleep apnoeas, failure to thrive without gastrointestinal symptoms. OSAS was defined as Apnea-Ipnoeapnea Index (AHI)> 3.

Results: All enrolled children had both OSAS (AHI: 3.5, 6.5, 3.2, respectively) and GER (Reflux Index: 18.8%, 38.2%; 11.1%, respectively). NP detected: a) 3 episodes of central apnea in 2 children and one of these episodes was preceded by GER in one patient; b) 17 episodes of obstructive apnea in 2 children. One of them had 8 out of 12 episodes (67%) preceded by an episode of GER; c) 81 episodes of hypopnoea of whom 41 were preceded by an episode of GER; d) 48 episodes of arousals of whom 13 (27%) preceded by GER.

Conclusion: In our preliminary experience we have found a relationship between GER and OSAS: The two disorders may coexist and aggravate each other. GER seems to be a predisposing factor for OSAS in children even in absence of gastrointestinal symptoms (atypical GER) emphasizing the importance of 24-hour pH-gastroesophageal monitoring in evaluating patients with sleep disorders.

0284
Comparison Of A Parent Voice Smoke Alarm With A Pure-Tone Smoke Alarm: Can Children Be Effectively Awakened From Stage 4 Sleep?

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Introduction: Conventional 80dB smoke alarms fail to awaken the majority of children during slow wave sleep. We compared a personalized parent voice alarm with a conventional pure-tone smoke alarm, both presented at 100dB, with respect to their ability to awaken children 6-12 years old from Stage 4 sleep (S4).

Methods: Children 6-12 years old were trained how to perform a simulated escape procedure when they heard a smoke alarm. Each child s mother recorded a voice alarm message (i.e., NAME, NAME, wake up! Get out of bed! Leave the room!). For each child, one of the two smoke alarm stimuli was randomly selected and triggered during the first cycle of S4, and then the other alarm was triggered during the second cycle of S4. The number of children who awakened and escaped within 5 minutes was recorded.

Results: Twenty-four children 6-12 years old were enrolled. The median age was 9 years and 11 (46%) were male. One-half of the children received the parent’s voice alarm first, and one-half received the pure-tone alarm first; however, the order that the stimuli were presented was statistically associated with awakening and escaping. Twenty-three (96%) of the 24 subjects awakened to the parent’s voice alarm, compared with 14 (58%) to the pure-tone alarm. One child did not awaken to either stimulus. Nine children awakened to their parent’s voice but not to the tone, while those awakened only to the tone and not the voice (McNemar, p=0.008). Twenty (83%) of the subjects in the parent voice alarm group successfully escaped, compared with 9 (38%) in the pure tone alarm group (McNemar, p=0.003).

Conclusion: The parent’s voice alarm at 100dB successfully awakened 96% of children 6-12 years old from Stage 4 sleep with 83% successful-
Introduction: Obstructive sleep apnea (OSA) is closely associated with obesity, a growing epidemic in children, is a known risk factor for obstructive sleep apnea (OSA). However, little is known about the prevalence rates of OSA in obese children with additional risk factors including habitual snoring. Few reports discuss persistence of OSA following adenotonsillectomy (T&A) in obese children. The AAP recommends evaluation of all children with habitual snoring for OSA. Thus, the purpose of this study is to describe the prevalence of polysomnographically diagnosed OSA in habitually snoring obese children.

Methods: Anthropometric data were collected to stratify children by BMI from 2000 CDC growth curves. All pediatric patients referred with habitual snoring seen at the Strong Sleep Disorders Center in Rochester, NY from 9/01 through 10/04 were included.

Results: There were 256 children ages 18 evaluated with habitual snoring during the study period. 47.7%[n=122], were identified as obese, BMI >95%ile for age and gender. Of these, 64.8%[n=79] were male, with mean age of 10.8±4.1 years. Mean BMI percentile was 98.8±1.1 for age and gender. In the obese group, 18.0%[n=22] had associated medical disorders predisposing them to OSA. Thus, over 80% of obese children with habitual snoring had no other predisposing co-morbid medical conditions. Available polysomnographic data identified 91.5% with PSG evidence of OSA (AHI>5/hr or obstructive hypoventilation). 30.9% had already undergone adenotonsillectomy (T&A) and were seen for persistent symptoms. All were males and all still had post-operative PSG evidence of OSA. Their mean BMI percentile was 99.6%±0.3 and their mean Apnea-Hypopnea Index was 19 (range 5 to 63).

Conclusion: Our data demonstrating that overweight children with habitual snoring are at very high risk for OSA suggests that more intense screening is needed in this population. Furthermore, OSA can persist following T&A. Additional studies investigating disease resolution following T&A in overweight children and adolescents are needed.

0289
Nighttime Symptoms Of Sleep Apnea Are Predictive Of Daytime Symptoms And Neurobehavioral Difficulties In Children With Surgically-Repaired Cleft Palate
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Introduction: Obstructive sleep apnea (OSA) is closely associated with measurable impairments in cognitive function and mild hyperactive-impulsive symptoms in otherwise neurologically normal, healthy children. The impact of OSA in children with cleft palate remains unknown. This study was designed to 1) investigate the incidence of symptoms suggestive of OSA in a population of children with surgically-repaired cleft palate and 2) explore the impact of OSA on daytime and neurobehavioral symptoms.

Methods: Children with surgically-repaired cleft palate ≥ 18 months of age, cared for at the Golisano Children’s Hospital at Strong Pediatric Cleft and Craniofacial Center were included. Parents completed a 19-item questionnaire evaluating frequency of behaviors suggestive of OSA using a scale of 0 to 4. Children with nighttime symptoms suggestive of OSA, daytime sleepiness or hyperactivity/inattention were referred for polysomnography following an evaluation by a pediatric sleep specialist.

Results: 56 consecutive patients completed the questionnaire. 64%[n=36]...
were male. The average age at the time of survey completion was 90±60.8 months. 42.0% of enrolled children had a syndromic condition associated with cleft palate. 70.0% reported nighttime behaviors concerning OSA. Nighttime symptoms suggestive of sleep apnea, including habitual snoring, observed apneic pauses, struggling to breathe, parents shaking the child to make him/her breathe, cyanosis, parental concern about nighttime breathing, restlessness and enuresis predicted daytime symptoms of morning headache, mouth breathing and sleepiness (<0.001, r²=0.268). Likewise, nighttime symptoms predicted neurobehavioral symptoms of hyperactivity, short attention, difficulty staying on task and academic difficulties (<0.009, r²=0.121).

**Conclusion:** Nighttime symptoms suggestive of sleep apnea are common in children with surgically-repaired cleft palate. Furthermore, as in otherwise normal, healthy children, nighttime symptoms suggestive of sleep apnea are predictive of daytime symptoms and neurobehavioral difficulties. Further studies are needed to assess the impact of OSA on cognitive function in children with cleft palate.

**0290 Symptoms Of Sleep Apnea Are Common In Children With Surgically-Repaired Cleft Palate**

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**Introduction:** Sleep apnea is well described in cleft palate (CP) patients following secondary speech surgery. However, only limited reports describe sleep apnea (OSA) following isolated primary palatal repair. CP children have a laterally narrowed midface predisposing to OSA. Palatal reconstructive surgery narrows the pharynx, potentially producing OSA. This study was designed to investigate the prevalence of symptoms suggesting OSA in children with surgically-repaired CP to compare the frequency of symptoms following primary closure versus following secondary speech surgery.

**Methods:** A 19-item questionnaire inquiring about the frequency of nighttime symptoms suggesting OSA, daytime symptoms and neurobehavioral difficulties was completed by parents of CP children

**Results:** 56 consecutive children with surgically-repaired CP ≥18 months old, cared for at the Golisano Children's Hospital at Strong were included. 64.0% were male, aged 90±60.8 months. 42.0% had syndromic conditions associated with CP. 45.0% had secondary speech surgery including posterior pharyngeal flap (n=12), Furlow palatoplasty (n=6), or sphincter pharyngoplasty (n=7). Overall, 70% of parents described nighttime behaviors concerning for OSA (47.8% habitual snoring, 12.8% struggling to breathe, 11.4% observed apneic pauses, 8.5% cyanotic episodes). 26.1% of parents reported at least occasional concern over their child's nighttime breathing. Symptoms of daytime sleepiness were reported by 37.2% of parents, 42.2% described hyperactivity, 50.0% short attention span, and 46.6% had difficulty staying on task. 45.0% reported that their child was struggling academically. No difference in the frequency of any reported symptom was found comparing children with primary closure to those following secondary speech surgery (p=n.s.).

**Conclusion:** Nighttime symptoms of OSA are common in children with CP. A statistically significant increase in symptoms of OSA following secondary speech procedures was not found, suggesting that sleep apnea may be under-recognized following primary closure alone. Future investigation of non-syndromic cases of CP is needed to discern effects of OSA on neuropsychological outcomes in children with cleft palate.

**0291 Adolescent Sleep Before, During And After Vacation**

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**Introduction:** Sleep deprivation is common in adolescents. Factors including psychosocial and academic pressures, early school start times and circadian rhythm changes are reasons for insufficient sleep. Adolescents sleep about nine hours ad lib but only get about 7-7.5 hours during the school week. Our aim was to examine dynamic changes in sleep patterns and alerting behaviors when adolescents transition from a school week to vacation and back to school.

**Methods:** Subjects were randomly selected from a diverse high school in suburban New York. Thirty-nine adolescents, grades 9-12 (21 females, 18 males, 14-18 years, mean 15.6 years) completed sleep logs during a consecutive 3 week academic period (school start time: 7:45 AM); the weeks before, during and after vacation. Dependent variables included total sleep time (TST), bedtime (BT), arisetime, sleep latency, computer time, and caffeine intake. Subjects completed a modified questionnaire from the website: http://www.sleepforscience.org/

**Results:** Mean TST for school nights (Sunday to Thursday) before and after (7.02 hours and 6.93 hours, respectively) differed from mean TST weeknights during vacation (9.05 hours) (<0.01). Subjects significantly delayed bedtime on vacation weeknights (mean BT before:10:22 PM, during:11:38 PM, after:10:44 PM) (<0.01) but compensated for lost sleep by awakening ~3.5 hours later on vacation weekday mornings (9:45 AM) compared to before (6:17 AM) and after (6:19 AM) vacation (<0.01). Alerting behaviors such as caffeine intake (before ~1.5 cups, during=5 cups, after=5 cups) and computer use (before-119 min, during-94 min, after-109 min) showed changes. Subjects self-identified as poor sleepers showed larger changes in TST (before-7.27 hrs, during-10.24, after-7.78 hrs), S/W schedule and sleep latency.

**Conclusion:** Our results support the view that adolescent sleep is constrained by school schedules and circadian tendencies. The findings in the poor sleepers suggest that adolescents at risk for developing insomnia may be identified in their teens.

**0292 Symptoms Of Sleep-Disordered Breathing And Attention Deficit/Hyperactivity Disorder In A Population-Based Sample Of Adolescents**

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**Introduction:** Associations between sleep-disordered breathing (SDB) and attention deficit/hyperactivity behaviors has been reported in a number of clinic-based studies of children. However, population-based studies of adolescents have been limited. We examine the distribution of (SDB) symptoms in population-based sample of adolescents 13 to 16 years of age and examined the association of SDB with ADHD.

**Methods:** Data come from 1014 youth-parent pairs randomly selected from eligible households in a 400,000 member HMO in metropolitan Detroit. SDB was considered present if any symptoms were reported at least once per week: 1) loud snoring; 2) making choking, gasping or snorting sounds while sleeping; 3) awakening with feeling of gasping or choking; 4) stopped or abnormal breathing during sleep. DSM-IV psychiatric disorders were assessed using the Diagnostic Interview Schedule for
Children. Excessive daytime sleepiness was assessed with the SWAI. Generalized estimating equations (GEE) were used to estimate the association between SDB and ADHD in a logistic regression that allows for combining parent and adolescent reports.

**Results:** Prevalence of SDB was 6.0% according to both adolescent and parental report and twice as likely among African Americans as Caucasians (OR = 2.4, 95% CI 1.6, 4.5). Adolescents with SDB were twice as likely to have ADHD—inattentive subtype (OR = 2.4, 95% CI 1.2, 4.7), but not ADHD—hyperactive subtype (OR = 0.8 95% CI 0.3, 2.5), with or without adjustment for ADHD treatment, conduct or oppositional defiant disorders, and race/ethnicity. Although excessive daytime sleepiness was associated with SDB, adjusting for it did not affect the association of SDB with ADHD.

**Conclusion:** Weekly symptoms of SDB were as common as ADHD among this sample of adolescents according to both self and parental reports. In contrast with studies of younger children, SDB was found to be associated only with the inattentive subtype of ADHD.

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0293

Sleep In Youth Foster Centers: An Exploratory Study

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**Introduction:** Studies examining adolescent sleep patterns consistently report that many teenagers experience significant sleep disturbances. Data regarding sleep of adolescents in foster centers are sparse. Objectives of the present study are to document sleep quality of these adolescents and to examine the relationships between their sleep, mood, and daytime sleepiness.

**Methods:** Residents of two Quebec City foster centers participated in this study. These centers house youths facing psychosocial, parental, or legal difficulties. Assessment instruments included self-report questionnaires on sleep disturbance, the Beck Depression Inventory-2 (BDI-2), and the Epworth Sleepiness Scale (ESS). For sleep related questions, participants were asked to refer to the period since their arrival in the center.

**Results:** Data were obtained from 33 adolescents (16 boys, 17 girls; M age = 15 years) residing at the centers for an average duration of 9.4 months. Mean total sleep time reported was 8.4 hours. At least one sleep complaint was reported by 85% of the total sample. Specifically, 70% reported problems initiating sleep (M sleep latency = 67 minutes) and 58% reported problems staying asleep, with the main reasons being physical discomfort (73%) and noise (51%). Difficulties waking in the morning were reported by 50%, whereas only 9% reported feeling refreshed upon waking. Sleep difficulties were experienced more than 3 nights/week in 48.5% of the sample. Mean ESS score was 8.15 with 51% reporting a score above nine, corresponding to high daytime sleepiness. Mean BDI-2 score was 18.5, with girls showing a significantly higher score (M = 22.13) than boys (M = 14.93). BDI-2 score was correlated to morning functioning and ESS score to nightly awakenings, feeling tired, sleepy, and irritable in the morning.

**Conclusion:** These preliminary results suggest that adolescents living in foster centers experience important sleep difficulties which may have repercussion on their daytime functioning and mood. Environmental factors such as discomfort and noise seem to play a role in these sleep complaints, as well as psychological factors. Interventions focusing on these factors might contribute to alleviate sleep disturbances. Future studies should examine links between sleep complaints, environmental factors, depressive symptoms and daytime functioning in adolescents living in foster centers.

0294

Parasomnias And Correlates Among Children With Autism Spectrum Disorders

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**Introduction:** It is estimated that about two-thirds of children with autism exhibit sleep problems. Sleep disorders in children are commonly classified into two major categories: dyssomnias and parasomnias. All of these problems may exacerbate difficulties with behavior and emotion and therefore need to be addressed. However, most of the sleep research in children with autism has focused on problems associated with settling and insomnia. Little is known about parasomnias and their correlates in children with autism.

**Methods:** Subjects consisted of a community sample of 167 children with autism spectrum disorders (ASD), including 108 (65%) with autistic disorder, 27 (16%) with Asperger syndrome, and 32 (19%) with unspecified ASD. Mean age was 8.8 years (range = 2.1, 18.7 years), 86% were boys. Parents completed a self-administered child sleep and developmental and family questionnaire, including the Child Sleep Habits Questionnaire (CSHQ).

**Results:** Overall, 53.5% of the sample were reported to have frequent parasomnias (5 times or more per week), including bedwetting (26.3%), talking during sleep (7.8%), restless during sleep (28.7%), sleepwalking (3.6%), grinding teeth during sleep (18.6%), awakening screaming, sweating (5.4%), and alarmed by scary dream (5.4%). Parasomnias declined significantly with advancing age from 63.6% at ages 2-5 years to 40.5% at ages 13 and over. Parasomnias were more common in girls than in boys (60.9% vs. 52.1%) but no statistical significance was detected. Logistic regression analyses indicated that gastrointestinal symptoms (OR = 1.7, 95% CI = 1.1, 2.7), co-morbid epilepsy (OR = 3.8, 95% CI = 1.2, 11.8), use of medications (OR = 2.8, 95% CI = 1.4, 5.6), and bedtime rituals (OR = 2.4, 95% CI = 1.1, 4.8) were related to elevated risk for parasomnias.

**Conclusion:** Parasomnias are very prevalent in children with autism spectrum disorders. Further research is warranted to examine the causal relationships between comorbid gastrointestinal disorders and epilepsy and parasomnias in children with autism for better understanding etiology and development of effective treatment of autism.

0295

Parent And Child Reports Of Children’s Insomnia: An Assessment Of Their Concurrence

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**Introduction:** Pediatric sleep medicine has emphasized the importance of parental reports in identifying sleep disturbance in children. However, few studies of sleep disorders have examined the degree of agreement between parental and child reports. We examined agreement between reports of insomnia among a community-based sample of adolescents 13 to 16 years of age and their parents, and assessed the construct validity of those reports.

**Methods:** Data come from 1014 adolescent-parent pairs randomly selected from eligible households in a 400,000 member HMO in metropolitan Detroit. Insomnia was defined by DSM-IV criteria. DSM-IV psychiatric disorders were assessed using the Diagnostic Interview Schedule for
Sleep, Stress, And Infant Temperament Ratings Among First Time Parents

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Introduction: Transition to parenthood is a stressful period for first time parents. Disruptions in sleep, work schedules, and daily routines occur simultaneously, which may adversely affect parents’ well-being, parent-infant relationship, marital satisfaction, and coping mechanisms. The purpose of this study was to examine the quantity and quality of parental sleep and their relationship to stress and infant temperament ratings.

Methods: Data was collected from 73 first-time couples at one, two, and three months postpartum. Wrist actigraphy was used to estimate total sleep time (TST) and wake after sleep onset (WASO). Questionnaires were used to estimate sleep quality, stress, and infant temperament ratings.

Results: Parents in this sample slept an average of 394±69 minutes/night. Actigraphy measures were not correlated with ratings of stress or infant temperament. However, self-reported sleep disturbance was significantly correlated with stress for both mothers and fathers across all 3 postpartum assessments (r = .32 to .51). For mothers’ self-reported sleep disturbance was associated with all 3 infant temperament ratings (r = .26 to .39); father’s self-reported sleep disturbance was unrelated to their rating of infant temperament. Maternal stress was consistently correlated with infant temperament ratings, while fathers’ ratings became increasingly correlated over time.

Conclusion: Our findings highlight the importance in evaluating parents’ perception of sleep, despite the lack of association with actigraphy measures. The postpartum period is stressful for parents who are adjusting to role transitions while their emotional, social, and physical states are depleted. Thus, assessing for disturbed sleep is crucial in maintaining family health and well-being as well as parent-infant relations.

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Sleep Disordered Breathing and Obesity: Implications for Children’s Spatial Reasoning

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Introduction: Reduced cognitive functioning is associated with both sleep-disordered breathing (SDB) and obesity in children; however, these factors have rarely been considered conjointly. The primary goal of the current study was to examine potential relationships between SDB, obesity, and cognition in children.

Methods: 139 children ages 5-8 years were recruited by questionnaire through the Jefferson County, Kentucky public schools. All children underwent overnight polysomnography and neurocognitive assessments including the Differential Ability Scales (DAS). Participants were divided into 4 groups: 2 with AHI ≥ 1 (obese: OS, n = 15 and lean: LS, n = 28) and 2 with AHI < 1 (obese: ONS, n = 23 and lean: LNS, n = 73). A 2 X 2 ANCOVA was used to examine the proposed relationships with ethnicity as a covariate.
Results: No gender or racial differences were found between groups (total sample: 55% male, 53% Caucasian, 26% African American). A main effect of SDB on speed of information processing was found after controlling for ethnicity (p < .05), with slower rates of processing speed in children with AHI ≥ 1, regardless of obesity status. Significant interactions (p<.05) emerged for Pattern Construction and Spatial Cluster scores after controlling for ethnicity, with the highest mean in the LNS group and the lowest in the ONS group.

Conclusion: This is the first study to our knowledge to examine cognitive skills in obese children, taking into account both SDB and race. Children with SDB had slower speed of processing than children without SDB, independent of obesity status. Obese children without SDB had spatial reasoning skills 1/2 standard deviation lower than their non-obese counterparts. However, no other group differences in spatial reasoning emerged. Future research is necessary to determine the basis for the unusual crossover interaction between SDB and obesity found for spatial reasoning skills.

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0299

Broadly Distributed Delta Frequency Evoked Responses During NREM Sleep In Preadolescent Children

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Introduction: Adolescent development is associated with dramatic reductions in the amplitude and incidence of delta waves during NREM sleep. In adults, NREM evoked responses are dominated by a large delta frequency component (N550). Its scalp topography in adults of all ages is maximal at Fz with the amplitude falling off rapidly when measured at lateral or posterior sites. No studies have systematically evaluated evoked delta frequency responses during NREM sleep in children. Given Feinbergs hypothesis of delta reductions being due to dendritic pruning, we hypothesized that pre-adolescent children would produce delta frequency evoked responses that would be more broadly distributed over the scalp, especially during SWS, than those reported previously in adults.

Methods: Data were collected from all night recordings in 8 preadolescent children (5 girls) aged between 9 and 11, using 64 channel EEG caps, Neuroscan Synamp2 amplifiers and Neuroscan Scan 4 software, sampling at 1000 Hz. Auditory stimuli (52 ms 1000Hz tone pips at 80dB) were presented binaurally, and responses from stage 2 sleep and SWS averaged. The amplitude of N550 at all 8 midlines sites was measured and subjected to a two factor (scalp site and sleep stage ANOVA).

Results: Extremely large and broadly distributed N550 components were seen in both stage 2 and SWS. There was a significant effect of scalp site (p < .001) and a significant sleep stage by scalp site interaction (p < .01). In stage 2 the maximum values were seen at FCz (138 ±53 uV), with values greater than 85% of this maximum seen as far back as CPz. In SWS the maximum values were seen at Cz (164.5 ±70 uV) with values greater than 85% of this maximum being seen from Fz, to CPz.

Conclusion: The data indicate that pre-adolescent children, are able to synchronize large areas of cortex, extending substantially past the frontal regions seen in adults. Ongoing data collection in this project involving twins and older children, will assess the impact of Tanner stage and genetics on the age-related changes in scalp topography of these responses.

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0300

Factors Associated With Symptoms Of Childhood Obstructive Sleep Apnea Syndrome In A Predominately Caucasian Population

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Introduction: Obstructive sleep apnea syndrome (OSA) is a relatively common condition in children affecting about 2% of this population. Published studies examining risk factors for OSA have enrolled mainly minority children. The purpose of this study was to evaluate risk factors associated with symptoms of obstructive sleep apnea (OSA) in a group of predominately Caucasian, middle class children.

Methods: 140 children ages 4-10 years old undergoing annual well-child evaluation were enrolled in this study from 2 private pediatric practices in Rochester, NY. The subjects’ parents completed a short questionnaire including 7 breathing and snoring related questions selected from the Pediatric Sleep Questionnaire (PSQ). The pediatrician completed a brief form including assessment of tonsil size (using a standardized pictorial chart) and medical history including height and weight. BMI percentiles were calculated using 2000 CDC growth curves for age and gender. The parent’s responses on the 7 PSQ questions were summed (sum-PSQ), and a score of 3 or higher was utilized to define a group with symptoms strongly suggestive of OSA.

Results: 88% of the children were Caucasian, 8% African-American, and 3% Hispanic. 56% were male. The average age was 7.1 y.o. (S.D. 2.0). 20 (14%) children had sum-PSQ≥3. Tonsil size was the only individual variable significantly correlated with PSQ ≥3 (p<0.001). A forward logistic regression was used to determine which of the variables together predicted a reported PSQ-sum score of ≥3. The best predictive model for this population included tonsil size, asthma, allergies and BMI >85%ile. This equation correctly predicted 82% of the children with PSQ-sum score of ≥3 (2-log likelihood 78.006; X2(4)12.922; p=0.012).

Conclusion: Our data demonstrates that, in a predominately Caucasian, middle class population of children, factors associated with symptoms of OSA include tonsil size, asthma, allergies and BMI >85%ile. Future studies are needed to determine if these same variables accurately predict polysomnographically diagnosed OSA in this population as well.

0301

Prevalence Of Sleep Problems Among Children And Adolescents With Co-Morbid Psychiatric Disorders

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Introduction: There is increasing evidence that children and adolescents with psychiatric disorders have a high prevalence of sleep disturbances (1). Few studies have determined whether psychiatric problems induce sleep problems or vice versa. Additionally, side effects of some psychiatric medications can lead to changes in sleep.

Methods: A sleep questionnaire was given to parents of children participating in a study of psychiatric disorders (N=24, age range 7-17). Psychiatric diagnoses were confirmed with the K-SADS, CDI, Conners, and SCARED. Diagnoses included ADHD, conduct disorder, oppositional defiant disorder, mood and anxiety disorders, and elimination disorders; 96% of subjects had co-morbid psychiatric diagnoses. Subjects were divided into two age groups: children (n=12, 7-11 years) and adolescents (n=11, 12-17 years).

Results: Children reported having significantly earlier bedtimes (mean=2048hrs+1.08) than adolescents (mean=2148hrs+1.05), p<.05.
While both groups had reduced total sleep time they did not differ from each other: children (mean=8.67hrs ± 1.1) and adolescents (mean=7.67hrs±1.2), p<.07. Napping occurred more than once a week in 25% of children and 45% of adolescents, and 42% of children and 55% of adolescents were rated as having an increased propensity to doze during the day. Results yielded four key findings: 1) of the 22% that had symptoms of insomnia, all were diagnosed with an anxiety disorder; 2) 30% had significant symptoms of sleep disordered breathing; 3) 17% had parasomnias and 9% had frequent nightmares; and 4) 17% had nocturnal enuresis. Overall, 65% (n=23) endorsed symptoms suggestive of a diagnosable sleep disorder.

Conclusion: This study found a high prevalence rate of sleep disturbance in children and adolescents receiving treatment for co-morbid psychiatric disorders. These results highlight the variety of sleep disturbances in this population. In conclusion, clinicians should routinely evaluate sleep problems when conducting psychiatric evaluations of children and adolescents. Reference: 1. Ivanenko A., Crabtree V. M., & Gozal D. (2004). Sleep in children with psychiatric disorders. Pediatric Clinics of North America, 51(1), 51-68.

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0302
A Survey Of Pre-Kindergarten And Kindergarten Napping Policy In The United States
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Introduction: Napping has become a controversial topic for schools. As pressure has increased to maximize learning time, some school districts have eliminated napping in early childhood programs. There is a dearth of research on napping in early childhood. According to a poll by the National Sleep Foundation, 25% of 4 year-olds, 15% of 5 year-olds and 2% of 6 year-olds nap daily. Three-year-old children who nap were more adaptable than non-napping children (Weissbluth, 1984). After a 15-minute nap, sleep deprived students’ performance improved over controls on a logical reasoning task (Takahashi & Arito, 2000). Napping has recently been given more attention for its effects on learning in adults. For example, visual learning task performance declined in those not napping, remained stable in participants napping 30 minutes, and increased in those napping 1 hour (Mednick, Nakayama, & Stickgold, 2003). There is no similar research in children. The gap in pediatric research is manifesting itself as a gap in Preschool and Kindergarten policies.

Methods: Each state’s Department of Education was contacted to assess state policies toward napping in Kindergarten and Pre-Kindergarten. The Early Childhood Specialists were asked about napping policy, length of program, and any known disparity surrounding napping in their state.

Results: All 50 states responded. Fourteen states, 28%, have some policy addressing napping or quiet play in Kindergarten and/or Pre-Kindergarten. Nine states (18%) regulate Kindergarten naptimes and 10 states (20%) regulate Pre-Kindergarten napping. Three states (6%) restrict naptime or discourage napping, while 12 (24%) have policy requiring napping or quiet play. Thirty-six states (72%) have no policy towards napping, 16 of these states (32%) allow local control of policy for kindergartners. Two states (4%) do not mandate naptime but give teachers education regarding the needs of children.

Conclusion: Because only 28% of states have napping policies, there is an urgent need for new research to address the effects of napping on learning, behavior regulation, and development to guide the future creation of educational policy. With a growing emphasis on performance testing, required for state funding of educational programs, children’s health and developmental needs may lag behind other priorities.

0303
Apparent Life Threatening Event (ALTE) In Infants: Evaluation Of Risk Factors
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Introduction: Infant with an ALTE present to medical attention because of an acute unexpected change in behaviour reported as life-threatening (that occurs during sleep, awake or feeding). Up to 50% of all ALTE remained unexplained (idiopathic). Recurrent ALTE have been associated with obstructive sleep apneas, digestive, neurological abnormalities and metabolic disorders. A multidisciplinary approach is highly recommend-
ed. Altered autonomic function, reduced arousability, increased respiratory effort, obstructive sleep apnea, frequent episodes of hypoaxemia have been suggested as markers. The PSG evaluation may be important in particular in the idiopathic form. Aim of our study was to investigate wheter anamnestic information and objective data (pH monitoring, PSG, cardiorespiratory home monitoring) could identify infants at high risk for ALTE.

Methods: In a 4-years period 232 infants (106 F/126 M; median age 68.3 days) who had experience ALTE and 80 age_matched controls were studied. A complete clinical evaluation including information on anthropometric data, family history, exposition to passive smoking, alcohol and drug intake, delivery modality, Apagar score, prematurity, growth, specific circumstances of ALTE episode was performed. Moreover all patients underwent extensive emathological tests, cerebral ecography, ECG and instrumentation monitoring (pH-recording, PSG and cardiorespiratory home monitoring). All collected variables were statistically analysed in order to assess the best predictive risk factors for ALTE.

Results: No significant differences were observed between ALTE infants and controls in total sleep time, delay in sleep onset, time of awake, % of REM and non-REM sleep, number and duration of apneas. The major risk factors resulted: gastrointestinal disease (p<.001), smoking in pregnancy (p<.001), previous ALTE (p<.0001), reflux index and number of refluxes measured by pH monitoring (p<.001), Apagar 1 and 5 score (p<.005) and type of delivery (p<.005).

Conclusion: Our results confirmed that a detailed anamnestisce evaluation as well as objective evaluations are important for detecting infants at high risk for ALTE. The further evaluation of polysomnographic data and in particular of the autonomic nervous system functioning may give important indication both on the pathogenesis of this phenomena and on its management in order to contribute to the care of this common condition.

0304
Sleep Cyclic Alternating Pattern In Children With Juvenile Idiopathic Arthritis
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Introduction: Pain is associated with day and night time complaints. When occurring during the night pain can lead to sleep fragmentation. But the Rechtschaften and Kales and ASDA arousal scoring criteria do not describe all sleep changes seen with nocturnal pain. Cyclic alternating pattern (CAP) is an indicator of NREM sleep instability, and may add

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to the investigation of sleep disturbances associated with pain. The aim of this study was to investigate the nocturnal sleep of children with juvenile idiopathic arthritis (JIA), a syndrome of chronic pain infanto-juvenile subjects, adding CAP analysis to normally analyzed sleep patterns.

**Methods:** 12 children and teen-agers with JIA and 12 healthy children matched for age, gender and Tanner stage were monitored following one night of habitation in the sleep laboratory. Sleep and wake patterns were analyzed following published criteria and CAP analysis.

**Results:** JIA patients showed more sleep fragmentation than healthy controls. NREM sleep instability was much more important in patients. CAP analyses showed the following significant differences with p<0.01: CAP rate (65.2 (2.6) vs 52.8(8.6)%), CAP time in stage 3 in seconds (20.7(18.7) vs 13.4(5.7)), number of CAP cycle in stage 3 (54.5(49.9) vs 35.9(13.5)), percentage of CAP in stage 4 (93.6(6.3) vs 81.5(14.8)%). CAP phase-A indexes in JIA were significantly different of control group (p<0.01), with important increase in phase A2 subtype percentage (25.3 (4.6) vs 13.3 (7.8)).

**Conclusion:** This is the first study of CAP on a pain syndrome in pediatrics. It indicates that pain may lead to NREM sleep instability were even without presence of EEG arousals as defined by Atlases. CAP is important tool for sleep studies in pediatric cases with chronic pain.

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**0305**

**Clinically Significant Sleep Problems Across Three Populations Of Clinically-Referred Preschool Children**

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**Introduction:** The impact of sleep disordered breathing on children’s learning and behavior has received much attention. Less attention has been paid to the relationship between daytime behavior problems and disturbed sleep. Disrupted sleep appears to impact child behavior and emotional stability, but little is known about how emotional and behavior problems may affect sleep. The current study represents our initial effort toward investigating the bi-directional influences between sleep and daytime behavior in preschool children.

**Methods:** Participants included 212 preschoolers between 18 and 71 mos. participating across three treatment programs. Sixty-five were enrolled in a day treatment center for severe behavior disorders, 56 in an early intervention program for speech-language/behavior problems, and 91 were receiving services in an outpatient behavioral health clinic. Each family completed the Achenbach Child Behavior Checklist (CBCL) upon entering services. Raw scores were converted to age- and gender-adjusted T-scores(mean 50; SD 10) on the basis of published norms. The CBCL Sleep Problems syndrome scale was used to define clinically significant sleep problems.

**Results:** Data were combined across preschool populations(Total N = 212). CBCL scores reflected a high rate and severity of emotional/behavior problems:34% clinically significant internalizing;59% clinically significant externalizing behavior problems. Elevated sleep problems (93-97 percentile) were identified in 17 preschool children(8%). Clinically significant sleep problems (> 98 percentile) were identified in 42(20%), representing a 10-fold increase over the expected 2% based on the standardization sample.

**Conclusion:** These findings document clinically significant sleep problems across three separate populations of preschool children with identified behavior problems. Even using relatively stringent cut-off criteria (> 93rd percentile), 28% were identified with disturbed sleep, representing 59 children who could potentially benefit from the services of a sleep specialist. Limitations: these data do not identify directional influence. Daytime behavior problems (e.g., noncompliance, anxiety) may spawn sleep/settling problems. Sleep problems may instigate behavior problems, or a third factor (e.g., ineffective parental limit-setting) may potentiate both. Future analyses will focus on differences across the three preschool populations and the relationship between diagnostic profiles (e.g., Anxiety, ADHD, Oppositional) and sleep problems.

**0306**

**A Comparison Of Parent And Child Reports Of Sleep Problems Associated With Early-Onset Bipolar Spectrum Disorders**

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**Introduction:** Early-Onset Bipolar Spectrum Disorders (EOBPSD) are mood disorders of childhood-adolescence, characterized by mania and depression. Research on EOBPSD sleep difficulties is lacking. As sleep disturbances may occur without a child/parent’s awareness, and be differentially endorsed, the current study compares child/parent reports of EOBPSD sleep problems.

**Methods:** Participants included 104 8-11-year-olds with EOBPSD and their parents. The Mania Rating Scale (MRS) and Child Depression Rating Scale-Revised (CDRS-R) were administered separately to parents and children for current and worst episodes of mania and depression. Sleep variables included: MRS reduced need for sleep, CDRS-R sleep difficulty and, for depression-only, initial middle and early insomnia. Child/parent reports of the frequency of sleep problems was examined via Chi Squared analyses and severity ratings analyzed by Pearson’s correlations. Informant differences for the number of sleep problems were illustrated by Discrepancy Ratios (DR: sleep problem reported only by child/parent reported only by parent). Child/parent severity differences were illustrated via a Mean Absolute Value Discrepancy Score (MAVDS).

**Results:** No significant differences emerged between child/parent frequency and severity ratings. DR and MAVDS estimates of frequency and severity include: Current mania DR = 15/06 and MAVDS = 0.18 (SD = 1.26); Worst mania DR = 12/29 and MAVDS = 0.72 (SD = 1.9); Current depression DR = 25/14 and MAVDS = .38 (SD = 2.00); Worst depression DR = 24/27 and MAVDS = .23 (SD = 2.45); Current/worst initial insomnia: DR = 23/47/10 and 21/40/19; Current/worst middle insomnia DR = 16/56/08 and 17/46/17; and Current/worst early waking DR = 09/64/07 and 14/53/13.

**Conclusion:** Overall, parent/child reports of EOBPSD-related sleep problems were similar. However, as the DR and MAVDS indices indicate, informants do not always agree on presence/absence and severity of sleep difficulties. Results suggest that both parent and child reports are important when assessing EOBPSD sleep problems.

**0307**

**Detection Of Cortical Arousals In Children Using Frontal (Fz) EEG Lead In Addition To Conventional Central (C3/C4) Leads**

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**Introduction:** EEG arousal in sleep is defined as an abrupt shift in frequency (including alpha or higher frequencies, but not spindles) lasting 3
**Introduction:** Obesity is increasing in the pediatric population, with known associated short- and long-term health risks. Adenotonsillectomy is the accepted first line treatment for children with obstructive sleep apnea (OSA), but at least 20% of children have residual disease. Previous reports suggest that obesity and severity of initial disease contribute to the risk for persisting OSA in children. We evaluated the impact of obesity at diagnosis on treatment outcomes in pediatric OSA.

**Methods:** Children were included if they had both diagnostic and follow-up studies for OSA. Anthropological and polysomnographic data were collected at the time of both studies. Polysomnograms were scored using standard criteria and OSA was defined as a respiratory disturbance index (RDI) ≥5. Obesity was defined as a body mass index (BMI) greater than the 95th percentile adjusted for age and gender.

**Results:** For 79 children (54 males), mean age was 7.3 ± 3.9 years and 38 (48%) of children were obese. The RDIs of obese and non-obese children were similar before treatment (17.7 ± 19.3 vs. 11.9 ± 15.1; p=ns). However, after treatment the obese children had a significantly higher mean RDI (10.7 ± 15.6 vs. 3.7 ± 4.3; p=0.01). Disease resolution occurred in 83% of non-obese compared to 58% of obese children (p=0.05). The odds ratio (OR) for persistent OSA in obese compared to non-obese children was 2.9 (95% CI: 1.4 – 8.0, p=0.03). Given previous evidence that severity of disease at diagnosis correlates with treatment outcomes, using initial RDI as a covariate the adjusted OR was also calculated using logistic regression. The adjusted OR for persistent OSA after treatment for obese children was 2.5 (95% CI: 1.1 – 7.1, p=0.01).

**Conclusion:** For children, obesity at the time of diagnosis (BMI>95% for age and gender) is a major risk for persisting OSA after treatment, regardless of the severity of initial disease.

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**0310**

**Activity-Based Sleep Estimation In Teens Diagnosed With And Treated For ADHD: Comparisons With Polysomnography And Healthy Controls**

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**Introduction:** Actigraphy algorithms for estimating sleep are derived primarily from healthy sleepers and may have limited application in special populations. Children with Attention-Deficit/Hyperactivity Disorder (ADHD) may be a particularly poor fit for current algorithms, as reports suggest more nocturnal movement and greater risk for PLMs and RLS relative to non-ADHD samples. Furthermore, ADHD is often treated with stimulant medication, possibly increasing risk for abnormal nocturnal activity. To explore this issue, we present overnight recording with actigraphy and polysomnography (PSG) in a sample of teens diagnosed with ADHD and treated with stimulants and compare these data to archived recordings of healthy, medication-free controls matched for age, sex, and pubertal development.

**Methods:** Sixteen teens (ages 12-17, mean = 14 years; 6 girls) with ADHD were studied for one night (9.5 hours) in the laboratory. Volunteers followed normal medication routines on the day of study. We used a wrist-worn actigraph (AMI Inc.) and validated algorithm (Sadeh, Sharkey, Carskadon, 1994) for sleep/wake estimation. Nocturnal PSG was visually scored using standard criteria. Archival subjects had similar recording procedures, though time-in-bed tended to be longer (9.5 to 10 hours, mean = 10) and most archive protocols did not include leg EMG. T-tests...
were used for hypothesis testing, and we present group means in order: ADHD vs. Controls.

**Results:** Percent sleep ([TST/TIB]×100) from PSG did not differ between groups (91% vs. 89%), but percent sleep from actigraphy was significantly lower for teens with ADHD (79% vs. 87%; p < .05). As a result, our estimate of overall agreement between actigraphy and PSG -- the ratio of actigraphic percent sleep to PSG percent sleep -- was significantly lower for ADHD nights (.87 vs. .98; p < .01). More movement time was scored from PSG for ADHD nights (12 vs. 3 minutes; p < .001), but adding movement time to either sleep or wake totals did not affect the results.

**Conclusion:** While the actigraphy algorithm performed less well in estimating percent sleep among stimulant-medicated teens with ADHD than controls, estimated agreement with PSG of .87 was reasonably close to more rigorous epoch-by-epoch agreement rates from validation studies with healthy samples. Nevertheless, our findings suggest that actigraphy may systematically underestimate sleep in children diagnosed and treated for ADHD compared to PSG.

MH63199

**0311 Clinical Spectrum Of Childhood Narcolepsy**

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**Introduction:** Narcolepsy is a relatively uncommon sleep disorder in children. The core symptoms of excessive daytime sleepiness, cataplexy, sleep paralysis and hypnogogic hallucinations are rarely reported in children with narcolepsy. Presentation in children can be heterogeneous and maturational changes in central nervous system and difficulty in symptom expression are cited as possible reasons. We report the clinical spectrum of a series of children with proven narcolepsy who are currently followed at our institution.

**Methods:** We reviewed clinical records of 16 consecutive children with narcolepsy evaluated at Sleep Center at Childrens Hospital of Wisconsin between 1999-2004. All children had overnight polysomnographic studies followed by multiple sleep latency tests (MSLT). Mean sleep latency of less than 8 minutes with two sleep onset REM periods on the MSLT is considered as diagnostic of narcolepsy.

**Results:** Mean age at diagnosis was 10.3 years (range, 6-16 years). There were 7 (43.7%) boys and 9 (56.3%) girls. 13 (81%) children were Afro-Americans and 3 (19%) were Caucasians. Excessive daytime sleepiness is the presenting complaint in all children. Of the 3 children who are 6 years of age, sleep attacks was the presenting symptom. Cataplexy and hypnogogic hallucinations were reported in 3 (18.7%) children. Obesity was found in 5 (31%) children (>10 years) and Neurobehavioral symptoms were reported in 11 (68%) children. Of the 13 children for whom Human Leucocyte Antigen (HLA) typing was available, 10 were positive for DQ B1 0602.

**Conclusion:** In this small sample of children with narcolepsy, 1) higher prevalence in Afro-American children was an unexpected association, 2) the classic tetrad of symptoms is uncommon 3) younger children appear to present with classic sleep attacks, 4) obesity appears more common in older children 5) neurobehavioral symptoms are common. 5) clinical and PSG features of narcolepsy can occur in HLA DQB1 0602 negative children.

**0312 Sleep In Adolescents With Anxiety Disorders**

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**Introduction:** Adolescents with pathological anxiety readily report sleep disorders but this has rarely been studied polysomnographically. The purpose of the present study was to investigate sleep in young patients with anxiety compared to healthy controls.

**Methods:** Twelve adolescents (5 girls, 7 boys, 13.9 ± 1.1 years old) diagnosed with Anxiety Disorders using DSM-IV criteria were recorded in a sleep laboratory for one night and compared to 5 controls (2 girls, 3 boys, 15.8 ± 0.8 years old). Sleep stages were scored according to Rechtschaffen and Kales (1968) using 20 sec. epochs. Sleep disordered breathing and Periodic leg movements were also monitored.

**Results:** Compared to controls, patients showed a longer REM sleep latency (p < .04), less REM sleep time in the first third of the night (p < .02) and more microarousals throughout the night (p < .02). The density of periodic leg movements during wake time after sleep onset was also found to be higher in patients compared to controls (p < .04). None of the participants presented with sleep disordered breathing.

**Conclusion:** Adolescent with anxiety disorders showed a limited number of sleep disorders, the core of which was found during REM sleep. Since only 1 night of recording was performed, other sleep disorders may have been masked by the so-called “First-night effect”. Periodic leg movements during waking were also found to be prevalent in the clinical group, which points toward the necessity to investigate the presence of the Restless legs syndrome in future studies.

**Canadian Institutes of Health Research**

**0313 Measuring Sleep In Children With Autistic Spectrum Disorders - Is Actigraphy With Video A Useful Tool?**

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**Introduction:** Polysomnography has been described previously as being useful in characterizing unique sleep abnormalities in children with autistic spectrum disorders (ASD). The role of actigraphy (a less intrusive methodology) in this population is less well defined. This study attempted to define the utility of actigraphy in detecting sleep disturbances in children with ASD, by comparing this modality with polysomnography and video.

**Methods:** Three subjects (ages 5-8 years) underwent two consecutive nights of standard polysomnography with video and actigraphy. Actigraphic data was obtained using the AW-64 Actiwatch (Mini-Mitter Co., Inc.). Thirty-second epochs of data were analyzed for consistency between wake (on polysomnography) and activity (on actigraphy) using a kappa statistic. Using video observations of rest and activity, actigraphic scoring was revised to incorporate the video data. The same statistical method was then reutilized in comparing this “corrected” actigraphic measurement with polysomnography.

**Results:** The kappa values for each data set prior to correction were noted to be highly variable, with values ranging from 0.22 to 0.70. Original versus recalculated kappa values using the corrected actigraphy data were 0.31 versus 0.71, 0.70 versus 0.73, and 0.36 versus 0.39. Video observations were useful for the first subject, because movement scored incorrectly as inactivity was evident. In the second subject, video observations were confirmatory, yet did not provide additional information given the
limited amount of movement. The third subject was noted to have sleep-onset insomnia with inactivity - video was not helpful in this situation, as it could not differentiate quiet wakefulness from sleep.

Introduction: This investigation examined the sleep patterns and daytime behavior of preschool-aged children in child care centers of varying levels of quality. If daytime sleep is adversely affected in lower quality child care settings, the consequences of poor sleep for children in these settings would be compounded. This study examined the relationship between the quality of a child care setting and children’s sleep patterns, in an attempt to see whether the sleep of children is more disturbed if they attend low quality child care centers, and if so, if their daytime behavior reflects this. Data collection is ongoing and a full report will be presented at the meeting.

Methods: To date, 26 preschool-aged children (14 female) from a sample of community child care centers have participated. This includes 15 children in high quality centers and 11 in lower quality centers, as rated by the Early Childhood Environment Rating Scale-Revised. Children wore an actigraph for 5 consecutive days and nights. Teachers and parents kept a sleep diary concurrently. Teachers also filled out a measure of children’s behavior, the Child Behavior Inventory (CBI). Results from the diaries are presented here; the actigraph and behavioral data will be reported at the meeting with results from the full sample.

Results: Preliminary results suggest, contrary to our prediction, that the children in high quality child care settings slept less (M = 74.41 minutes) during the day than their peers in low quality settings (M = 133.10 min.; t = 3.63; p = .001). This relationship does not appear to be mediated by family demographic variables. No significant differences in nighttime sleep duration, as reported by parent diary, were found between the two groups. Interestingly, children who slept less during the day also had higher ratings on the Apathy subscale of the CBI.

Conclusion: Some literature on sleep in infants suggests that stress may induce a sleep response. Although our results are preliminary, they suggest the intriguing possibility that perhaps the stressful environment of a lower quality preschool setting may act similarly, at least affecting daytime nap duration. Further data are clearly needed in order to test this idea, and analysis of the full data set, with the addition of objective data from actigraphy, will help to clarify the possible relationship between quality of child care and children’s sleep.

Introduction: We previously demonstrated that fasting insulin levels correlated with the severity of obstructive sleep apnea (OSA) in obese children. However, since all children in that study were obese, it was not possible to evaluate the relative contributions of OSA as compared to obesity in that group. This study evaluated sleep and metabolic variables in children with a wide range of BMI values.

Methods: Children who presented to a tertiary pediatric sleep unit were invited to participate in this study. Children who participated had anthropometric and demographic data collected at the time of admission to the sleep unit, timed urine collection overnight, and fasting bloods collected on the morning after the study. Polysomnograms were scored using standard criteria. Obesity was defined as a body mass index (BMI) z-score greater than 2 for age and gender.

Results: A total of 247 children participated, aged 8.2 ± 0.3 yrs, of whom 176 (71.3%) were male, and 96 (38.9%) were obese. The respiratory disturbance index (RDI) was 7.9 ± 1.8 events per hour (range 0-163.4). Sleep variables were available for the entire group, and serological markers were obtained in 214 subjects. In a multiple regression model, fasting insulin levels correlated with age, log10RDI, and BMI SDS, R = 0.54, p<0.001, with b co-efficients of 0.42, 0.14, and 0.24, respectively.

Conclusion: Amongst children with symptoms of OSA, age correlated more strongly than the level of obesity with the severity of sleep disordered breathing. However, regardless of the severity of obesity, the severity of OSA continues to be a significant contributor to fasting insulin levels. Further studies will be required to evaluate the mechanisms for this association.

Introduction: The impact of upper airway obstruction (UAO) on daytime functioning in children is becoming greatly apparent. The literature suggests a number of neurocognitive deficits are evident in children with UAO, including global intelligence, attention, executive functioning, language skills, visuospatial ability, memory and learning. To ascertain these findings more carefully conducted studies comparing neurocognitive performance in such children with that of matched controls are required. This study examined the neurocognitive performance of a group of children awaiting adenotonsillectomy (T&A) for suspected UAO as compared to controls.

Methods: Children awaiting T&A for suspected UAO were invited to participate in the study. Those who participated were carefully screened for previous A&T, current upper respiratory infections and conditions that potentially could result in hypoxemia and/or sleep fragmentation. All children underwent standard overnight polysomnography (PSG) and neurocognitive testing using the Stanford Binet Intelligence Scale and a neuropsychological assessment tool (NEPSY). Non-snoring control children were recruited from the general community and matched for age, gender, socioeconomic status, BMI, and underwent overnight PSG and neurocognitive testing.

Results: To date, the neurocognitive data from 25 children awaiting A&T (8.3 years ±2.5(SD); 14 males) and 20 control children (9.1 years ±2.2(SD); 11 males) are analyzed. Children awaiting A&T scored significantly lower compared to controls on a range of scores including those...
for attention and executive function (101.6 ±16.7(SD) vs 112.6 ±10.9(SD), p<.05) language ability (94.5 ±13.2(SD) vs 108.9 ±13.5(SD), p<.005), visuospatial skills (101.1 ±12.9(SD) vs 110.7 ±10.6(SD), p<.05), memory (99.7 ±14.0(SD) vs 111.1 ±14.0(SD), p<.01), global intelligence (95.6 ±7.6(SD) vs 107.0 ±9.0(SD), p<.001), fluid reasoning (97.4 ±12.2(SD) vs 108.0 ±11.9(SD), p<.01), crystallized ability (91.8 ±8.0(SD) vs 103.3 ±10.1(SD), p<.001), and quantitative reasoning (99.5 ±7.7(SD) vs 105.8 ±10.3(SD), p<.05). Neurocognitive data collection and analysis of overnight PSG is currently ongoing.

**Conclusion:** Children awaiting A&T for UAO display a range of neurocognitive deficits when compared to matched non-snoring children. These findings confirm previous results which show similar neurocognitive deficits in children with UAO and extend our knowledge by incorporating well validated assessment tools in a rigorously controlled protocol.

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Age-Related Changes In Percentage Of REM Sleep In Adults

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Introduction: The purposes of this study were to describe changes in the percentage of REM sleep (REM%) across the adult lifespan and test two recently reported meta-analytic claims about age-related change in REM sleep percentage: 1) There is a linear decrease in REM% from young to middle-aged adults; 2) This decline in REM% ceases after age 60.

Methods: This was a research synthesis of published and unpublished research results from studies conducted between 1960 and 2002. All samples represented narrow bandwidths on age across the lifespan in order to detect changes in mean values for each decade of the lifespan. Study samples were composed of subjects described as normal or healthy. Approaches used by researchers to assure the health of subjects were coded. Two coders extracted information from manuscripts. Inter-rater reliability of coders showed no signs of coder drift and remained well above cutoffs for excellent reliability throughout the study. Discrepancies in coding were revisited and consensus achieved. Findings were analyzed using an approach to research synthesis that facilitates the detection of linear and nonlinear trends: Scatterplots for age and REM% were produced based on the sample size, age, REM% values for each sample, and the distribution of REM% values in the population. Next, Cubic B smoothing techniques were used to determine the magnitude of linear trends and whether significant nonlinear trends between age and REM% existed.

Results: Retrieved manuscripts provided means and standard deviations for REM% for 344 samples representing 4,171 subjects. Mean ages of samples ranged from 19.0 to 91.7 years. Standard deviations for age were less than or equal to 4.0 years for each sample. The relationship between age and REM% was essentially linear and decreased approximately 0.6% per decade. No meaningful change in the rate of linear decline, i.e. no non-linearity, was detected at any point across the agespan. No design or outliers were detected based on the sample size, age, REM% values for each sample, and the distribution of REM% values in the population. Next, Cubic B smoothing techniques were used to determine the magnitude of linear trends and whether significant nonlinear trends between age and REM% existed.

Conclusion: REM% appears to decline over the adult lifespan; however, for healthy subjects, the magnitude of decline may be smaller than previously reported in the sleep research literature. The decline appears to continue past 60 years of age and into the ninth decade of life.

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Quantitative EEG Analysis Of Sleep In Women With Menopausal Hot Flashes

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Introduction: Despite epidemiologic reports of increased sleep disturbance at menopause, recent laboratory studies have not confirmed this. We recently reported that postmenopausal women with and without hot flashes and cycling women of similar ages did not differ on any physiologic or reported sleep measure, on MSLT latencies, or on performance tests. Here we report quantitative sleep EEG analyses from that investigation.

Methods: 11 postmenopausal women with hot flashes (FL), 8 without them (NF), and 11 cycling women (CY) of similar ages (46-51) were screened to eliminate those with any sleep, physical, or mental disorder, drug use, or BMI > 30. They were recorded at 23 °C ambient temperature for 3 consecutive nights with standard PSG. C4-A2 EEG was digitized at 200 Hz; time and power in frequency bands (zero-cross) were computed in real time.

Results: There were no significant group differences (ANOVA) on any measure. For delta power (uV²): CY = 980 ± 468 (SD), FL = 1272 ± 1082, NF = 999 ± 542; theta: 137 ± 56, 114 ± 41, 159 ± 152; alpha1: 53 ± 24, 48 ± 28, 101 ± 91; alpha2: 13 ± 7, 12 ± 6, 17 ± 9; beta1: 25 ± 47, 55 ± 100, 38 ± 61. For delta % time-in-band: 54 ± 8, 58 ± 9, 56 ± 9; theta: 22 ± 3, 21 ± 3, 23 ± 3; alpha1: 14 ± 4, 13 ± 4, 13 ± 5; alpha2: 5 ± 2, 4 ± 1, 6 ± 1, beta1: 5 ± 1, 4 ± 1, 5 ± 1.

Conclusion: These results provide further evidence that hot flashes do not produce disturbed sleep in symptomatc postmenopausal women.

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Effects Of Caregiving On Sleep Appear To Be Particularly Salient Among Older Caregivers

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Introduction: This study examined differences in objective measures of sleep and subjective reports of sleep quality between caregivers of patients with Alzheimer’s disease (AD) and non-caregivers.

Methods: Seventy-three community-dwelling spousal caregivers (CG) of patients with AD and 40 non-caregiving (NCG) controls participated. All subjects completed a semi-structured interview consisting of socio-demographics, cognitive status of the care-recipient, self-reported sleep quality (Pittsburgh Sleep Quality Index, PSQI) and functional outcome (Functional Outcome of Sleep Questionnaire, FOSQ). A polysomnogram was conducted in the home within one week of the interview.

Results: Although CGs of patients with moderate-severe AD reported significantly more sleep problems (p<0.05) and more functional impairment as a result of sleepiness than NCGs (p<0.01), there were few differences between the groups in polysomnogram variables. The only significant difference in objective measures of sleep was in total sleep time, with older CGs of those with moderate to severe AD sleeping significantly less than older NCGs (p<0.05). There was also a main effect for age, with older CGs and older NCGs having lower sleep efficiency, less slow wave sleep and more stage 1 sleep than younger CGs and NCGs (p<0.05).

Conclusion: Results showed that caregivers slept less than NCGs, but that the amount of sleep fragmentation did not differ between the groups. Effects of caregiving on sleep appear to be particularly salient among older caregivers of those with moderate to severe AD as compared to younger caregivers and to non-caregiving controls. It is possible these older caregivers are more vulnerable to the effects of sleep disruption and thus have trouble falling back to sleep when the time is afforded them. Future work to examine differences by age may provide understanding regarding sleep differences. Studies to examine health consequences of shortened sleep in older caregivers’ are also needed.

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Sleep Apnea/Hypopnea Is Associated With Lower Memory Performance In APOE ε4 Allele Carriers Only

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Introduction: The Apolipoprotein E (APOE) ε4 allele is a well-established genetic risk factor for the development of cognitive decline and Alzheimer’s Disease. Presence of the ε4 allele also has been associated with an increased risk for the development of Obstructive Sleep Apnea/Hypopnea (OSAH). In addition, OSAH is associated with cognitive impairment. This raises the question of whether OSAH may account, in part, for the well-documented association between cognitive decline and APOE ε4 genotype among non-demented individuals.

Methods: Thirty-six community-dwelling non-demented older adults, 18 with and 18 without the ε4 allele, were assessed for cognitive performance and level of OSASH (12 men, 24 women; age 70.6±8.1; MMSE 28.7±1.2; BMI 25.9±4.5). Participants completed a comprehensive cognitive battery including the Mini-Mental State Examination (MMSE) and the Rey Auditory Verbal Learning Test (RAVLT). The APOE/Hypopnea Index (AHI) was assessed using unattended in-home ventilatory polygraphy (EdenTrace© Model II).

Results: No significant differences were observed between the ε4 and non-ε4 group with respect to demographic, respiratory and cognitive variables. However, a homogeneity of correlation test found the relationship between AHI and the delayed recall and short-term recall components of the RAVLT to be significantly different in ε4 versus non-ε4 carriers. Higher levels of respiratory events were associated with lower memory scores in the ε4 carriers only (AHI versus RAVLT delayed: r=-.46 in ε4 carriers versus r=0.21 in non-ε4 carriers; AHI versus RAVLT 6: r=-.49 in ε4 carriers versus r=0.24 in non-ε4 carriers).

Conclusion: This is the first study to provide preliminary evidence for a negative interaction of APOE ε4 and OSAH on memory function in older adults, suggesting that OSAH may account, in part, for the well-documented association of APOE ε4 allele to cognitive decline in community-dwelling older adults. This interaction may have significant implications for treating cognitive decline and delaying dementia onset.

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Sleep Disordered Breathing Lightens Sleep But Does Not Increase awakenings In Patients With Alzheimer’s Disease

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Introduction: Sleep disordered breathing (SDB) and Alzheimer’s disease (AD) both independently disrupt sleep and cause nocturnal awakenings. This study examined sleep architecture in AD patients with and without SDB, hypothesizing that sleep would be more disturbed with an increased amount of awakening in those with than without SDB.

Methods: 66 subjects (23 women) (mean age=78 years; SD=8) with mild-moderate AD (mean MMSE=24.7; SD=3.0) were enrolled. Each underwent polysomnography (PSG) with Embia (Flaga/Medicare, Iceland) recorders scored for TST, WASO, % of each stage of sleep, and oximetry. Mean apnea hypopnea index (AHI) was 20.1 (SD=15.5, range=0.6-76.4). The sample was divided into two groups: AHI<10 (n=18) and >10 (n=48). T-tests were performed.

Results: Sleep was disturbed in both groups (TST mean=352.3 minutes, SD=107.0; WASO mean=119.4 minutes, SD=75.1), but there were no significant differences in the amount of WASO or TST based on AHI. Those with AHI>10 had lighter sleep with statistically higher % stage 1 sleep (mean 25.8% vs. 15.5%, p=0.002) and lower % stage 3 sleep (mean 1.5% vs. 5.8%, p=0.005) than those with AHI<10. As expected, when compared to AHI<10, the AHI>10 group spent significantly more % of TST with SaO2<90% (mean 0.3% vs. 4.8%, p=0.001), had a lower saturation nadir (mean 82.7% vs. 87.1%, p=0.01), and a lower average SaO2 (mean 94.9% vs. 93.6%, p=0.007).

Conclusion: AD patients with SDB did not have more disturbed sleep than those without SDB although their sleep was lighter. The presence of SDB in these patients caused nocturnal hypoxia, but did not affect the
number of awakenings. Both groups had large amounts of WASO, suggesting perhaps that sleep was already so disturbed due to AD that the presence of SDB did not worsen it.

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0323
Mild Regular Exercise Consolidates Sleep-Wake Architecture In 24 Month Old F344 Rats
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Introduction: With aging there is increased sleep fragmentation, decline in sleep homeostasis, increased episodes of sleep during the normally wake active period and a severe loss of delta power. These changes are not due to a loss of sleep-active neurons in the VLPO (3) although a decline in adenosine A1 receptor in the basal forebrain (2) together with a decline in hypocretin levels (1) might be contributing factors. Since the elderly population is expected to double in the next ten years, interventions that can improve sleep quality are urgently needed. Here we investigate the effects of mild exercise on sleep in old rats.

Methods: Young (3 mo, n=4) and old (21 mo, n=6) male rats were exercised for one hour daily (at dark onset; 2 m/min) for 45 days. Age-matched control rats (young n=4, old n=4) were not exercised but kept awake by gentle handling for the hour. A 48h sleep recording was made immediately after exercise, 2 days later and 2 weeks after the end of exercise. Rats were housed in 12:12 LD with food and water available ad libitum.

Results: Compared to control old rats, old rats that were exercised lost weight and were awake more during the last third of the night, a time when hypocretin levels peak (1). In old rats exercise also significantly reduced nighttime sleep fragmentation by increasing length of wake, SWS and REM bouts. Exercise also lengthened SWS bouts during the light-on sleep period. These changes persisted two weeks after end of exercise. In old rats exercise also significantly increased theta power during REM sleep, and alpha power during waking. However, delta power during SWS was not changed. Exercise had no effect on any sleep parameters in young rats.

Conclusion: Here, the rats were exercised for one hour at the start of the normal wake-active period, and they were awake more during the last third of the light-off period. In humans, this would be analogous to exercise in the morning, and we suggest that it should keep them more alert and active during the day. We suggest that the increased waking might result from higher levels of hypocretin secreted as a result of the exercise. Thus, exercise produces weight loss and better sleep in old rats. 1. Desarnaud F, et al., (2004) Sleep 27: 851. 2. Murillo-Rodriguez E, et al., (2004) Neuroscience 123: 361. 3. Shiromani PJ, et al., (2000) Am J Physiol 278: R125.

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0324
Actigraphic Measures Of Sleep Are Associated With Decreased Daytime Functioning In Elderly Women
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Introduction: Excessive daytime sleepiness is associated with impaired daytime performance. Few studies have quantified sleep and performance with objective measures. We hypothesized that elderly women with disturbed sleep behavior would function more poorly.

Methods: Sleep was assessed using actigraphy (Sleep-Watch-O, Ambulatory Monitoring, Inc.) in 3127 women who wore actographs on the non-dominant hand (average 4.1(0.82) nights) during the 2001-2002 examination of the Study of Osteoporotic Fractures (SOF). SOF, a longitudinal study of 9704 community dwelling, ambulatory Caucasian women aged ≥ 65 began in 1986 and added 662 African American women in 1996. Sleep parameters assessed included total sleep time (TST) and minutes awake after sleep onset (WASO). Performance measures included self-reported difficulty with one or more of six activities of daily living (ADL’s) (range 0=no difficulty to 6=total difficulty), and observed gait speed (meters/second). Associations between quartile of TST and WASO and physical function were evaluated using General Linear Models adjusted for age, race, and other covariates known to be associated with sleep or function.

Results: Mean age was 83.57(3.79) years, 10.5% were African American. Women with TST in the lowest (<6 hours) and highest quartiles (≥7.6 hours) nightly were more likely to have ADL impairments, and walked slower than those with 6-7.6 hours TST. Adjusted means (standard error) by quartile for ADL’s were: 1.62(0.08), 1.47(0.07), 1.23(0.07), 1.64(0.07) (p<0.0001); and for walk speed 0.80(0.010), 0.84(0.10), 0.86(0.10), 0.83(0.10) m/sec (p=0.0001). Increasing WASO was also directly related to poorer performance. As WASO increased from <43.75 to 99.5 minutes, mean ADL score increased from 1.24(0.08) to 1.83(0.08) (p<0.001) and walk speed decreased from 0.88(0.01) to 0.78(0.01) m/sec (p<0.0001).

Conclusion: Older women with measured short or long sleep duration, and those with more fragmented sleep, functioned more poorly. Longitudinal studies are needed to determine if disturbed sleep is associated with subsequent decline in function.

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0325
CPAP Improves Cognitive Function In Alzheimer’s Disease Patients With Sleep Apnea: Preliminary Results
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Introduction: The hypoxia and sleep fragmentation of sleep disordered breathing (SDB) might make symptoms of Alzheimer’s disease (AD) worse. Studies in SDB have suggested that CPAP has a significant positive impact on neurobehavioral performance. This study tested the hypothesis that CPAP would improve cognitive functioning in patients with AD and SDB.

Methods: This was a randomized, double-blind, placebo controlled study. 24 men and 10 women (mean age=78.1 years, SD=7.0; range=53-91) with SDB (mean AHI=27.1, SD=14.62; range=11-76) and mild-moderate AD (mean mini-mental state exam=25.1, SD=3.0; range=18-30) participated. Patients were randomized to either 3-weeks of sham-CPAP
followed by 3-weeks of real-CPAP or to 6-weeks of real-CPAP. A complete neuropsychological test battery was administered at baseline, after the first 3 weeks of active CPAP treatment (p=0.012) in both groups; there was no improvement associated with 3-weeks of sham-CPAP. There was no further improvement after 6 weeks of active CPAP.

Conclusion: These preliminary results suggest CPAP might improve cognition in AD patients with OSA, even beyond that generally seen with ACh-E. These preliminary findings require replication in a larger sample, but if confirmed, then treatment of SDB in AD patients may prove an important component in the effort to improve patients’ quality of life and to postpone institutionalization.

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Effect Of Ambient Temperature On Sleep And Expectancies In Postmenopausal Women With Hot Flashes
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Introduction: Although some epidemiologic studies report increased hot flash (HF) frequency, we manipulated ambient temperature during sleep disturbance at menopause, recent laboratory research has not confirmed.

Methods: 14 postmenopausal women with HF (FL), 6 without them (NF), and 12 cycling women (CY) of similar ages were used. 11 women were screened out for: drug use (3), high estrogen level (2), psychiatric disorder (1), and 5 NF had HF in sleep. Subjects were run for 4 nights, 3-5 days apart, in random order: adaptation (23°C), warm (30°C), neutral (23°C), cold (18°C). Complete PSG was recorded, plus skin and rectal temperatures, and sternal skin conductance to detect HF. C3-A2-EEG was digitized at 200 HZ and time and power in band were computed online. The EDS, POMS, Fatigue scale, pre/post sleep questionnaire, and a scale to measure expectations of sleep quality at different temperatures were given.

Results: There were no significant effects for Group or Room Temperature on any physiologic sleep measure. For example, sleep efficiency: Warm = 80 ± 15% SD (FL), 88 ± 9% (NF), 88 ± 6% (CY); neutral = 86 ± 12%, 83 ± 15%, 85 ± 14%; Cold = 81 ± 13%, 90 ± 6%, 87 ± 8%. Skin temperature was colder in the cold (34.7 ± 0.1°C) than the warm (35.4 ± .05, p<.0001) room but HF frequency did not change (3.6 ± 8 vs. 4.4 ± .6). All subjects expected worse sleep in the warm than the cold room (p<.01) but only FL reported lighter and less refreshing sleep during the warm vs. cold night (p<.005).

Conclusion: Reports of worse sleep in FL at warm ambient temperatures are due to expectancies rather than physiological effects.

Effect Of CPAP On Daytime Sleepiness In Alzheimer’s Disease Patients With Sleep Disordered Breathing
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Introduction: Studies report that 33-70% of demented subjects have sleep-disordered breathing (SDB). Continuous Positive Airway Pressure (CPAP) treatment has been shown to reduce daytime sleepiness and improve health-related quality of life in non-demented elderly. No current data are available in demented patients. We assessed the effect of therapeutic CPAP treatment on a subjective measure of sleep in mild-moderate Alzheimer’s disease (AD) patients with SDB.

Methods: This was a randomized, double-blind, placebo-controlled trial. 34 patients (mean age=78.1 years, SD=7.0; range=53-91) with SDB (mean AHI=27.1, SD=14.6; range=17-76) and mild-moderate AD (mean mini-mental exam=25.1, SD=3.0; range=18-30) were randomly assigned to receive 6-weeks of therapeutic CPAP or sham-CPAP followed by 3 weeks of therapeutic CPAP. Epworth Sleepiness Scale (ESS) was administered at baseline, 3 and 6 weeks. The difference in mean outcome scores of the therapeutic CPAP group was compared to those of the sham-CPAP group.

Results: On average, both groups wore their CPAP for 4-5 hours a night. Patients receiving therapeutic CPAP for 6 weeks (n=17) showed improvement in ESS scores compared to sham-CPAP group (n=17) who received therapeutic CPAP for 3 weeks (p<0.05). Scores in the therapeutic CPAP group decreased from 9.06 (SD= 4.10) to 5.12 (SD=3.86) while those in the sham-CPAP group changed from 8.53 (SD=4.73) to 6.47 (SD=4.30).

Conclusion: Our study provides initial evidence of effectiveness of CPAP in improvement of subjective sleepiness in mild-moderate AD patients with SDB.

Keywords: Alzheimer’s Disease, Sleep Disordered Breathing, CPAP, Daytime Sleepiness, Dementia, Sleep Apnea.

Diurnal Cortisol Is Associated With Functional Improvement During Post-Acute Rehabilitation In Older Adults
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Introduction: Cortisol levels normally rise in the morning and decline in the evening. Sleep disturbance may alter this pattern. Within a larger study of older veterans undergoing inpatient rehabilitation after acute hospitalization, we found patients who sleep more during the day have less improvement in physical function. We hypothesized that daytime sleepiness is related to abnormal diurnal cortisol patterns and reduced functional improvement.

Methods: A sub-sample of 32 participants (mean age=77 years, 87% men) provided up to 6 saliva samples on one day, including samples at wake time (WT) and WT+45 minutes. They also wore wrist actigraphs (Octagonal Actiwatch-L, Ambulatory Monitoring) for one week to measure hours of daytime sleep (dTST; 0800-2000h; Action4; time–above–threshold; default settings). Cortisol levels (nmol/l) were assayed using time-resolved immunoassay with fluorometric detection (DELFIA), and the change in cortisol levels from WT to WT+45 minutes was calculated. Admission and discharge physical function was measured by the Functional Independence Measure (mFIM; validated for assessing physical function and instrumental activities of daily living) and the Functional Capacity Index (mFACI; a newly validated measure designed for use in rehabilitation settings). Cortisol data were analyzed at baseline, 1 week, and discharge using the linear mixed effects model, and Wilcoxon signed-rank tests were used to analyze within group differences in mFIM and mFACI scores.

Results: Cortisol levels were significantly lower in the WT compared to the WT+45 minutes (p<0.01) and were inversely correlated with mFIM score change from baseline to discharge (p<0.01) and with mFACI score change from baseline to discharge (p<0.01). Cortisol levels were not correlated with sleep measures in this sub-sample.

Conclusion: Cortisol levels are related to functional improvement in older adults undergoing rehabilitation for post-acute illness.
Introduction: Sleep disordered breathing (SDB) has been associated with hypertension, thus SDB might be related to the extent of atherosclerosis. Small case-control studies have suggested an association between SDB and increased carotid wall thickness. We examined this relationship among 1004 community dwelling older adults who participated in both the Cardiovascular Health and Sleep Heart Health Studies (mean age 79; 57% women).

Methods: The carotid wall thickness was assessed using ultrasound (average of left and right common or internal carotid intimad medial thickness, or CC- and IC-IMT). Home polysomnography was used to define the apnea-hypopnea index (AHI- average number of apneic and hypopneic events with > 4% desaturation per hour of sleep).

Results: CC IMT was weakly correlated with AHI (r(spearman) = 0.092, p<0.01) but this was not significant within gender strata (MEN r=0.07 Women r=0.07; both p=NS). The IC IMT showed a similar pattern (r(spearman) = 0.07, p<0.05). Those with AHI between 15 and 29.9 were shown to have a significantly thicker CC IMT (1.16 mm) after multivariable adjustment than the other groups (p<0.05), but without a clear linear trend (RDI<1.5 1.12mm, RDI 1.5-4.9 1.09mm, RDI 5-14.9 1.12mm, RDI>30 1.07mm). There was no significant association shown between AHI and IC IMT in the adjusted model. There were no substantial differences observed in the relationship between AHI and carotid wall thickness with and without adjustment for the BMI in the multivariable model.

Conclusion: In conclusion, there was not a strong positive correlation between carotid wall thickness and SDB in this large group of older men and women. This may be partly due to a survival bias and does not rule out the potential for a stronger relationship in middle aged adults.
Results: Sleep latency was inversely related to WAIS Verbal IQ, (p=.005), with more than 30 minutes being associated with lower scores. Multivariate regression confirmed that sleep latency contributed to the prediction of verbal intelligence when accounting for education, age, concentration, depression, and hypnic use, p=.02. Sleep duration was related to verbal short-term memory as evaluated by the Selective REMinding Task, p=.009, with less than 5 hours and more than 8 hours of sleep being associated with lower performance. Multiple regression revealed that sleep duration was the most significant variable in predicting verbal short-term memory, p=.006.

Conclusion: Insomnia symptoms were related to poorer verbal functioning and short-term verbal memory. Furthermore, sleep problems were more strongly associated with current cognitive functioning than depression, which has received considerable attention in the aging literature. Given the restricted range of this non-demented sample, these results probably underestimate the relationship and cognitive functioning in later life.

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0332
Non-Verbal Correlates Of Poor Sleep In Older Adults Without Dementia
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Introduction: Geriatric insomnia increases morbidity and may predict incident dementia but no large-scale studies have explored the effects of poor sleep on current neuropsychological functioning. This study examined the relationship between sleep indices, late-life insomnia and non-verbal abilities.

Methods: 373 non-demented participants in a large-scale community-based study on the effects of aging, aged 75-85, completed clinical interviews, neuropsychological assessments and a sleep index.

Results: Nearly half of respondents reported sleep-related problems. Sleeping less than 5 hours or more than 9 hours nightly was negatively associated with non-verbal ability, p<.02, visual-spatial ability, p<.02, processing speed, p<.05 and motor ability, p<.04. Sleep latency greater than 30 minutes was negatively associated with visual-spatial ability, p<.03, and processing speed, p<.05. When controlling for the effects of depression, as measured by the Zung scale, an overall MANCOVA for sleep latency remained significant, p<.02, whereas follow-up ANCOVA's were not. Also, when controlling for depression, an overall MANCOVA for sleep duration was not significant.

Conclusion: Geriatric insomnia appears to impair multiple nonverbal abilities. Too little or too much sleep appears to be equally impairing. Depression may mediate much of the relationship between sleep duration and cognitive functioning. However, after controlling for depression, sleep latency remained a significant predictor of nonverbal cognitive functioning, whereas sleep duration did not. These results may underestimate the true relationship between these variables given the restricted range due to utilizing a non-demented sample.

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0333
Geriatric Textbooks Address Insomnia But Not Sleepiness
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Introduction: Complaints of insomnia and hypersomnia are very common among the elderly. We quantified sleep medicine content of major geriatric textbooks to assess the emphasis on sleep disorders.

Methods: We selected seven major geriatric textbook published within the last four years. The following were reviewed: Clinical Geriatrics 2003, 1st Edition (660pp); Geriatric Medicine 2003, 4th edition (1261pp); The Merck Manual of Geriatrics. 2000, 3rd Edition (1382pp); Oxford Textbook of Geriatric Medicine, 2000, 2nd edition (1208pp); Practical Guide to Geriatric Medicine, 2002, 1st edition (901pp); Primary Care Geriatrics: a case-based approach, 2002, 4th Edition (655pp); and Brocklehurst’s Textbook of Geriatric Medicine, 2003, 6th edition (1503pp). For each of these textbooks we reviewed chapter headings and searched indices for the following subjects and terms: bruxism, cataplexy, Cheyne Stokes respiration, central sleep apnea, circadian, hypnagogic hallucinations, hypersomnia, hypoventilation, hypersonomolence, hypno- notics, idiopathic hypersomnia, insomnia, melatonin, myoclonus, naps, narcolepsy, nocturia, nocturnal, obstructive sleep apnea, parasomnia, periodic limb movements, polysonomography, rapid eye movement sleep, REM sleep behavior disorder, restless legs syndrome, snoring, sleep, sleepiness, sleep paralysis, sleepwalking, sleep apnea, snoring, and somnambulism.

Results: The seven text books devoted between 0.4 and 2.2% of their total content to sleep medicine topics. Most texts devoted a significant proportion (30%) of the sleep content to insomnia (mean of 4.2 pages) and this represented 0.39% of the total book pages. In comparison, only 1.4% of the sleep content was devoted to discuss “sleepiness” (mean of 0.2 pages) and this represented 0.02% of the total book pages.

Conclusion: Sleep problems receive little coverage in major geriatric textbooks. Whereas insomnia is commonly addressed to some extent, sleepiness remains virtually excluded despite its high prevalence in older persons.

0334
Daytime Sleepiness And Physical Function In Older Adults: Results From The National Sleep Foundation 2003 Sleep In America Poll
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Introduction: Although good physical functioning has been identified as important in maintaining wellness in older adults, few studies have explored the relationship of sleep on physical status. The purpose of this study was to assess the effect of excessive daytime sleepiness on physical function.

Methods: The design was a secondary analysis of self-report data from older adults from the National Sleep Foundation (NSF) 2003 Sleep in America Poll. A random sample (n=1,506) of geographically representative, community- dwelling older adults were polled by telephone. Approximately 26% (n=1,506) completed the brief survey. Daytime sleepiness was dichotomized as either ‘daily to frequently’ or ‘never or rare.’ The sum of 5 questions (walk 0.5 mile, climb stairs, pull or push heavy object, stoop or kneel, write, handle small objects) on a 1-5 scale (‘no difficulty’ to ‘unable to do’) was calculated with a score of 2.5 indicative of impaired physical status. Descriptive statistics, correlations, t-tests, and binary logistic regression analyses were conducted (p<.05)

Results: The average respondent was 66.9 ± 7.99 years of age, female (57.9%), overweight (Mean BMI = 26.9 ± 5.58), generally healthy (19% with >3 co-morbidities), and with good physical functioning (86%). While 11.4% of the sample with good physical functioning had daytime sleepiness, 32% of those with impaired physical functioning were sleepy (Chi-square = 57.2, p = .001). Physical function was significantly lower in elders with daytime sleepiness then non-sleepy (t= 8.1, p = .001).
Age, BMI, co-morbidities, and daytime sleepiness were entered into a binary logistic regression model in a hierarchical manner to predict impaired physical function. Daytime sleepiness was predictive (p = 0.001) of impaired physical function, while controlling for age, BMI, and number of comorbidities (Odds Ratio = 2.34, 95% CI=1.59-3.45).

**Conclusion:** Daytime sleepiness may have an independent negative impact on physical function separate from age, weight or co-morbidities.

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**3335**

**The Effect Of Acetylcholinesterase Inhibitors On Sleep Architecture In Patients With Alzheimer’s Disease**

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**Introduction:** Studies have suggested that some acetylcholinesterase inhibitors (ACh-EI) increase nightmares and REM sleep in Alzheimer’s disease (AD) but few have studied their effect on other sleep parameters. This study examined the effect of ACh-EI on sleep architecture in AD patients who were not receiving antidepressants. Sleep architecture was assessed with polysomnography (PSG) and actigraphy. ACh-EI groups included: donepezil (n=40), galantamine (n=16), rivastigmine (n=8) or none (n=8). General univariate linear model analyses were performed.

**Results:** There was a significant main effect for %-stage 1 (p=0.004) and %-stage 2 (p=0.002) sleep. The donepezil group (mean=17.5%, SD=11.8) had significantly less %-stage 1 than the galantamine (mean=29.4%, SD=14.4; p=0.02) and no ACh-EI groups (mean=32.5%, SD=19.7; p=0.027), but was not different than the rivastigmine group (mean=25.0%, SD=12.3). There were no differences in %-stage 1 between the other groups. The donepezil group (mean=63.6%, SD=13.5) had significantly more %-stage 2 sleep than the no ACh-EI group (mean=45.4%, SD=16.6; p=0.002) with no differences either the galantamine (mean=56.4%, SD=8.4) or rivastigmine (mean=56.9%, SD=8.4) groups. There were no significant differences in the amount of TST, WASO, %REM or other sleep parameters between the groups.

**Conclusion:** The ACh-EI had little effect on sleep overall. Although more nightmares are reported in patients taking donepezil, there were no differences between groups in REM sleep. Additional analyses will need to determine whether these changes can solely be attributed to the use of ACh-EI or might also be a result of other variables, such as additional medications.

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**3336**

**Polysomnographic Correlates Of Poor Sleep Determined By Actigraphy In Elderly Women**

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**Introduction:** Older women with poor sleep efficiency (SE) by actigraphy may be at risk for neurocognitive deficits, falls and mortality. Our objective is to determine to what extent SE determined by actigraphy differentially identifies older women with evidence of specific sleep disorders ascertained by polysomnography (PSG).

**Methods:** We assessed the association between PSG and actigraphy indices in a subset of elderly women participating in the Study of Osteoporotic Fractures who had both 5 day actigraphy and a single night PSG performed within one month of one another (n=461). Sample demographics were: 92% Caucasian, age: 82.9+/-3.5 [SD] years, and body mass index: 27.9+/-5.1 kg/m2. Actigraphy indices were SE (%) and total sleep time (TST, hours) and PSG indices were apnea-hypopnea index (AHI), periodic limb movement index (PLM-I), arousal index, and percentage sleep time less than 90% oxygen saturation. SDB was defined as AHI≥15 events/hour and PLMD as PLM-I≥5 per hour.

**Results:** There were statistically significant relations between decreasing SE categories, (ÅÜ90, >85-90, >80-85, ≤75) and increasing AHI (p<0.001), higher percentage of SDB (p<0.009), increasing arousal index (p<0.0001), increasing percent sleep time less than 90% oxygen saturation (p<0.0003), and increasing PLM-I (p<0.0001). To assess the relative contribution of SDB and increased PLMD to poor SE, four groups were evaluated: Group 1 (No SDB and no PLMD; n=209), Group 2 (No SDB, +PLMD; n=74), Group 3 (+SDB and no PLMD; n=122), and Group 4 (+SDB and +PLMD; n=50). ANOVA F-tests demonstrated statistically significant differences in SE and TST between Group 1 (mean SE=86.9% and TST=7.0 hrs) and Group 4 (SE=79.4% and TST=6.2), p<0.0001.

**Conclusion:** In elderly women, poor SE and decreased TST ascertained by actigraphy are associated with SDB, PLMD and nocturnal hypoxia as identified by PSG, with poorest sleep observed in women with both PLMD and SDB.

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**3337**

**Sleep And Restless Legs Syndrome/Periodic Limb Movement Disorder In Dementia**

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**Introduction:** Restless legs syndrome/periodic limb movement disorder (RLS/PLMD) may be a treatable cause for the severe sleep/wake disturbance persons with dementia often have. The purpose of this study was to determine if sleep differs in persons with dementia based on whether or not they have RLS/PLMD.

**Methods:** 49 persons with dementia had 1 night of attended polysomnography while sleeping in their usual nursing home environment. Inclusion criteria were Mini-Mental State Examination Score (MMSE) less than 24, less than 7 hours of nighttime sleep and at least 30 minutes of daytime sleep per actigraphy, stable medical status, and ambulatory. Since the sample had cognitive impairment and could not reliably report symptoms of RLS, diagnosis of RLS/PLMD was based on a periodic limb movement index (PLMI) greater than 20. Sleep was scored by a registered polysomnography technologist with documented competency in scoring of sleep in persons with dementia.

**Results:** The mean age was 83.4 years and MMSE was 14.3, indicating moderate to severe dementia. The mean PLMI was 17.3, while the mean PLMI with arousals or awakenings was 9.0. 12 (25%) had a PLMI greater than 20. When compared to those without RLS/PLMD, those with RLS/PLMD had greater sleep disturbance including significantly fewer
minutes non-rapid eye movement (NREM) sleep (258.0 versus 319.1 minutes, p = .03), less percent NREM sleep (52.5% versus 61.5%, p = .03), and longer latency to sleep onset (33.2 versus 18.0 minutes, p = .05). The apnea/hypopnea index was significantly less in those with RLS/PLMD (9.5 versus 20.1, p = .05).

Conclusion: When compared to those without RLS/PLMD, persons with dementia with RLS/PLMD had significantly greater sleep disturbance, even though their apnea/hypopnea index was significantly lower. Treatment of RLS/PLMD may lead to improved sleep/wake patterns and daytime alertness in persons with dementia.

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0338
Comparison Of PD2 Values Of The Frontal And Temporal EEG Activity Before And After CPAP Titration: Nonlinear Dynamical Analysis
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Introduction: In obstructive sleep apnea syndrome (OSAS), due to the repetitive upper airway obstruction, severe hypoxia and cognitive dysfunctions (as consequence of cortical involvement) can be found. Nonlinear dynamical analysis is used to determine the complexity of the given biological signal (EEG). Several investigations show changes in the nonlinear dynamical characteristic of the EEG to different conditions (awake and sleep, epilepsy). The main goal of this study is to investigate the effect of CPAP titration on the complexity of EEG activity (which represents the cortical neuronal activity) by nonlinear dynamical method (point correlation dimension - PD2).

Methods: EEG data of 15 non-treated OSAS and 12 control patients were recorded. Apnoe-hypopnoe index of OSAS patients was above 20 per hour and was below five per hour in the control group. The evaluated EEG channels were F8, T4, T6, F4, F7, T3, T5 and F3 accordingly to the international 10-20 system. 5000 data points (app. 20 seconds off EEG, 256 Hz sampling rate) of each channel was used to determine PD2. The PD2 values of control and OSAS patients were compared by Student T-test.

Results: PD2 values of the non-treated OSAS patients and control patients differed significantly in case of F8, F4, F7 and F3 EEG channels (the p values are 0.015, 0.014, 0.012 and 0.011 separately). PD2 values of the temporal EEG channels (T4, T6, T3, T5) showed no significant differences between the non-treated OSAS and control groups (p values are: 0.55, 0.97, 0.86, 0.89). The PD2 values determined after CPAP titration showed no significant differences.

Conclusion: The PD2 evaluation of the OSAS patient may be a useful additional tool to determine the cortical involvement of the disease and the effectiveness of CPAP titration.

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0339
Sleep Catastrophizing As An Implicit And Explicit Process In Older Insomniacs
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Introduction: The main difference between implicit measures and explicit outcome measures derived from self-reports is that implicit measures examine the attentional component of cognitive processing, whereas, explicit measures examine perceptual / interpretative processes, with the latter following naturally from the former. Therefore, the biggest problem with measuring sleep catastrophizing with a self-report questionnaire is that the measure is generating and directing the attentional aspect of cognitive catastrophizing and only measuring perceptual outcomes. For the purposes of the present study, a card-based implicit association task (IAT) was used to examine differences in response times between sleep-specific, non sleep-specific, pleasant and unpleasant stimuli, within samples of older insomniacs and normal sleepers. Reaction times were also compared to an explicit measure of sleep catastrophizing (the 24-hour Sleep Catastrophizing Scale).

Methods: Thirty-eight participants were recruited through a poster campaign in two counties within the U.K. (19 insomniacs and 19 matched controls). Participants were administered the PSQI, Sleep Catastrophizing Scale and the IAT, encompassing eight experimental conditions, four singular and four combined conditions.

Results: T-test analyses showed that insomniacs took less time to pair sleep related and unpleasant words than normal sleepers (t = 2.08, df = 36, p<0.05). Additionally, a significant correlation between total scores on the 24-SCS and reaction times pairing unpleasant words with sleep related words) was observed (r = -0.32, n = 38, p<0.05).

Conclusion: The main findings from this study suggest insomniacs tend to pair sleep related stimuli with unpleasant words more readily than normal sleepers. This preliminary data indicates that sleep catastrophizing has an implicit attentional component. The finding that the attentional measure of sleep catastrophizing was related to the perceptual measure of sleep catastrophizing (scores on the 24-SCS) adds to the validity of the 24-SCS and provides a cautious indication of how sleep catastrophizing may work.

0340
A Warm Footbath Before Sleep Onset Increased REM Sleep In Older Adults With Disturbed Sleep
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Introduction: A warm footbath may increase the distal (foot) - proximal (abdominal) skin temperature gradient (DPG), hasten sleep onset and improve sleep quality. This study used a randomized crossover design to examine effects of a warm footbath before sleep onset on core (rectal) temperature, DPG, and sleep in Taiwanese older adults with sleep disturbance.

Methods: Fifteen older adults (9 women, 6 men, mean age=64.7 years) with Pittsburgh Sleep Quality Inventory scores of >5 had standard polysomnography (PSG) recorded for 3 nights. A 41C warm footbath for 40 minutes was administered before usual bedtime randomly on night 2 and night 3. Rectal and abdominal temperatures were recorded at 1-min intervals continuously, and foot temperatures were recorded for 3 min before and after the footbath and continuously during sleep. DPG was calculated by subtracting abdominal from foot temperature. Paired t-tests were used to compare differences in temperature and sleep variables between the bathing and non-bathing nights.

Results: Mean rectal temperature increased 0.1C (t=4.40, p=0.01) after foot bathing. Mean DPG before lights off was -2.14C (SD=0.57) on the non-bathing night, but was reduced (-0.42C, SD=0.89, t=6.81, p<0.001) on the bathing night. The overall amount of REM sleep was increased (t=2.43, p=0.03) on the bathing night. There were no significant differences in other PSG sleep variables. However, when NREM cycles were examined separately, sleep efficiency was increased and wake time was decreased (both p =0.01) in the second NREM cycle, compared to the non-bathing night.
Conclusion: A warm footbath provided a sufficient heat load to increase core body and skin temperatures, and REM sleep in older adults with disturbed sleep. Water temperature, timing with respect to sleep onset, and duration of foot bathing are important considerations for future studies of local warming as an intervention to improve sleep in the elderly.

0341
Predictors Of Daytime Sleep Among Elderly Nursing Home Residents With Dementia
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Introduction: Studies have demonstrated signs of cortical arousal on the waking electroencephalogram (W-EEG) following caffeine administration. Recent reports have shown modifications of the adenosinergic system with age, but few studies have evaluated age-related effects of caffeine. This study aimed to establish a topographical profile of caffeine effects on W-EEG and to determine if this profile is modified through ageing.

Methods: A group of young adults (20-30 y.o.) was compared to a group of middle aged individuals (40-60 y.o.). All were submitted to a caffeine (200 mg) and a placebo (lactose) condition in a double blind cross over design, separated by one week. They received one 100 mg capsule three hours before bedtime and the remaining dose, one hour before bedtime. A W-EEG was performed 30 minutes after the second dose. EEG signals in F3, C3, P3 and O1 were submitted to spectral analysis. ANOVAs (groups, derivations, conditions) were made for each 1Hz frequency bins. P-levels were set to 0.05.

Results: Simple condition effects demonstrated that caffeine diminishes spectral power in theta and low beta frequencies similarly for all derivations. However, effects of caffeine on high beta frequencies were more prominent in posterior areas. Generally, young and middle-aged subjects displayed similar results. Nevertheless, compared to the middle-aged, young subjects were more sensitive to the effects of caffeine in delta and beta frequencies.

0343
Impact Of Gender On Sleep And Sleep-Related Growth Hormone (GH) Secretion In Older Adults
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Introduction: Older women report poorer sleep quality than older men, despite reports that they have better preserved slow-wave activity (SWA). This study examines gender differences on objective sleep quality and GH release in older adults.

Methods: Two groups of healthy non-obese subjects were studied: 10 men (59±2 years), and 10 post-menopausal women (63±2 years). Sleep was polygraphically recorded for two consecutive nights and blood samples were collected during the last 24hrs. An EEG spectral analysis was performed in delta (0.5-4.0 Hz) and alpha (8.5-12 Hz) bands.

Results: There were no gender effects on sleep stages. In the blood sampling night, total sleep time, sleep efficiency, and slow-wave sleep were significantly reduced. Sleep in women was more disturbed by catheterization. Absolute delta and alpha powers in both NREM and REM sleep were higher in women. SWA in NREM sleep was highly correlated with SWA in REM sleep in women (r=0.9, p=0.0011), but not in men. Delta power in NREM sleep was therefore normalized for the corresponding delta activity in REM sleep. This normalization reverted the gender difference in NREM delta activity as delta activity appeared to be lower in women than in men, consistent with lower sleep-related GH secretion in women. In men, normalized delta power in NREM sleep tended to be correlated with nocturnal GH secretion (r=0.6, p=0.06) but no such correlation was present in women. Relative delta power in NREM sleep was similar in both groups and did not correlate with nocturnal GH release.

Conclusion: Major gender differences in sleep quality and in GH release are present in healthy elderly. Normalizing delta activity in NREM sleep suggests that NREM sleep may actually be of lower intensity in women.
Daytime Sleepiness, Nocturnal Sleep Parameters And Neurocognitive Function In The Elderly

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Introduction: The prevalence of sleep disordered breathing (SDB) increases with age, and it usually causes daytime sleepiness and cognitive dysfunction. Therefore, SDB could be a possible etiology of the cognitive impairment in the elderly. There have been a few studies on the neurocognitive function of various domains related with SDB in the elderly. We aimed to examine the relationship of SDB and neurocognitive function in the elderly with daytime sleepiness.

Methods: Epworth Sleepiness Scale (ESS) was administered to elderly subjects who visited the Health Promotion Center at Kangwon National University Hospital. The subjects with abnormal laboratory tests were excluded. CERAD-K (Lee, J Gerontol: Psych Sci 2002;57B:P47-53) Neuropsychological Battery and Stroop test were done for 11 subjects (ESS>9) (X Age: 68.4, SD=5.1) and 19 subjects (ESS<10) (X Age: 71.1, SD=4.0). For eleven subjects, nocturnal polysomnographies were conducted.

Results: The scores of Word Recognition test were significantly higher in the higher ESS group, compared to the lower ESS group (p<0.05). Eight subjects had SDB, and 6 PLMS, 4 both SDB and PLMS among 11 subjects (ESS>9). The central apnea index was negatively correlated with the Word score of Stroop test (r=-0.507, p<0.05), and the lowest oxygen saturation positively with the score of Word Recall test (r=0.758). The limb movement index was negatively correlated with the score of Word Recognition test (r=-0.758), and the limb movement arousal index negatively with the score of Constructional Praxis test (r=-0.758). The ESS score was positively correlated with limb movement arousal index (r=0.758).

Conclusion: Our data showed SDB was associated with impaired executive function and verbal memory function, and increased arousals due to limb movements were associated with increased daytime sleepiness and visuospatial dysfunction in the elderly. It suggests both SDB and PLMS would be essential correlates of daytime sleepiness and neurocognitive dysfunction in the elderly.

Sleep Habits, Insomnia, And Hypnotic Use Among The Urban Aged Population Of Shandong, China

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Introduction: Little is known about epidemiology of sleep habits and sleep disorders in the elderly population of mainland China. This epidemiological study was conducted to examine sleep patterns, insomnia symptoms, hypnotic use, and demographic correlates of insomnia in the elderly population in Shandong Province, China.

Methods: A representative sample of the urban elderly in Shandong was obtained from five cities, using two-stage cluster sampling. Among 1,820 individuals aged 65 and over who were sampled, 1,679 (92.2%) were interviewed at home, including 770 men and 909 women. A sleep questionnaire which included the Pittsburgh Sleep Quality Index was used for interviews with participants.

Results: 21.3% of the sample went to bed at 21:18 (SD = 2.2h), and rose in the morning at 05:42 (SD = 1.0h). Average sleep duration was 7.1h (SD = 1.6) without age and gender differences. Average sleep latency was 31.0m (SD = 32.0) and tended to increase with age (F = 3.15, p < .01). 44.2% of the elderly men and 28.0% of women reported regular napping (Chi-square = 52.08, p < .001). 32.9% of the sample reported frequent insomnia symptom(s), with women reporting more insomnia symptoms than men (36.4% vs. 28.7%, p = .001). When the criterion for poor sleep quality was taken into account, the prevalence rate for insomnia markedly dropped to 5.3% (men 3.6% vs. women 6.8%; Chi-square = 7.97, p = .005). 6.5% of the sample had used hypnotics at least once a week during the past month. Women were more likely to use hypnotics than men (8.1% vs. 4.6%; Chi-square = 8.99, p = .003). Multivariate logistic regression analysis indicated that age 75 and over (OR = 2.0, 95%CI = 1.2, 3.2), unmarried status (OR = 1.8, 95%CI = 1.3, 2.4), residing with offspring (1.8, 95%CI = 1.2, 2.6), and napping (OR = 1.9, 95%CI = 1.5, 2.4) were associated with elevated risks for insomnia.

Conclusion: Total sleep duration in the elderly of China is about 7.5h, longer than that in western aged populations. Napping is very common in Chinese elderly, especially in men. One third of the elderly report frequent insomnia symptom(s), but most of them do not complain about poor sleep quality. Hypnotic use in Chinese elderly is less common than in western populations. Multiple demographic factors are associated with risks for insomnia in the elderly.
Introduction: Research has shown subjective and neurobehavioral benefits of napping in young adults. Since older adults have poorer sleep, longer naps were hypothesized to facilitate greater benefits. Moreover, since frontal lobe function is impaired by both sleepiness and aging, naps were expected to lead to improvements in frontal lobe function, particularly for older adults.

Methods: Three age groups [24-31 yrs (n=10); 33-51 yrs (n=10); 56-70 yrs (n=12)] participated in a repeated-measures dose-response paradigm (0, 20, and 60 minute nap conditions). Pre-post nap measures were subjective sleepiness, serial addition/subtraction, ERPs to novelty detection, and waking EEG (12 sites). Age by Trial (pre-post) by Condition (nap duration) ANOVAs were run.

Results: Condition Effects. Participants were less sleepy after longer naps; math accuracy improved after either nap. Theta power decreased after longer naps, and increased after no nap, indicating that participants were more alert after the long nap, and less alert after no nap. Waking beta power increased after the short nap and no nap conditions, representing more mental effort. Age Effects. As expected, amplitude of P2, novel P3, and P3b ERP components, reflecting allocation of attention, was smaller for older adults. Novel P3 latency, representing stimulus evaluation time, was shorter for younger adults. Older adults also had greater waking beta/gamma power, representing more mental effort. Three-way Interactions. In older adults only, waking gamma power increased following the no nap condition, but remained unchanged following either nap. Thus, greater mental effort may have been needed to combat sleepiness when prevented from napping.

Conclusion: There was little evidence that older adults benefited more from a longer nap, or had greater frontal recovery. Math accuracy indicated that working memory improved after naps for all age groups. Longer naps or more sensitive frontal tasks may have been needed.

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Association Between Sleep Duration And Mortality Is Partly Mediated By Higher Levels Of Inflammation In Older Adults

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Introduction: Sleep restriction is associated with changes in immune function and increases in circulating cytokines. Older adults report both longer and shorter sleep times. Health outcomes related to sleep duration might be mediated by higher levels of inflammation in older adults.

Methods: Sleep habits and disturbances were assessed by interview in the Category H—Aging

0347
Do Longer Naps Lead To Greater Benefits, Especially To Frontal Lobe Function, In An Older Population?

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Introduction: Sleep restriction is associated with changes in immune function and increases in circulating cytokines. Older adults report both longer and shorter sleep times. Health outcomes related to sleep duration might be mediated by higher levels of inflammation in older adults.

Methods: Sleep habits and disturbances were assessed by interview in the Health, Aging and Body Composition Study, a cohort study of 3075 men and women (42% black and 52% women). Serum samples collected at baseline were assayed for interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-alpha) and C-reactive protein (CRP). Medical history and medication use were assessed by self-report. Physical measures were assessed by in-clinic examination. Follow-up contacts were every 6 months. Vital status was confirmed by death certificates and medical records. Crude mortality rates after 5 years are reported. Cox proportional hazard models were used to produce crude and adjusted hazard ratios (HR).

Results: Race, obesity (BMI>30), diabetes and cardiovascular disease were all associated with sleeping <6 and >8 hours and women were more likely to report < 6 hours sleep than men. Levels of IL-6 were significantly elevated at the extremes of sleep time. After controlling for age, gender, race, SES, BMI and health status, mortality was related to sleep duration, with the highest rates in those with <6 and >8 hours of sleep (< 6 hours: HR: 1.56, CI: 1.11-2.18; > 8 hours: HR: 1.93, CI: 1.28-2.79). Further adjustment for inflammatory markers suggested that IL-6 may be an important mediator for the association of short sleep duration and mortality, but did not explain the elevated risk of mortality among long sleepers.

Conclusion: Mortality was higher in older adults with short (< 6 hours) and long (> 8 hours) sleep duration. These associations were partly explained by poorer health status and elevated inflammatory markers, particularly in those with shorter reported sleep duration.

0349
Sleep In Nursing Home Residents With Cognitive Impairment

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Introduction: Sleep has been described as severely disturbed in nursing home residents with cognitive impairment, but most of the studies to date have used actigraphy and observation to measure sleep. Few investigators have used polysomnography because it is difficult to obtain, and often those who did use polysomnography conducted the research in a sleep laboratory with scheduled bedtimes and risetimes. Unfamiliar settings and routines increase agitation in persons with cognitive impairment and may artificially disturb sleep. The purpose of this study was to describe the usual sleep patterns of nursing home residents with cognitive impairment.

Methods: Polysomnography was conducted for two nights on sixty cognitively impaired residents of six nursing homes. Inclusion criteria were diagnosis of dementia or mild cognitive impairment, ambulatory, stable psychotropic drug regimen (if any), and seven or fewer hours of nighttime sleep and at least 30 minutes of daytime sleep, based on five days and nights of actigraphy. Polysomnography was scored by a specially trained registered polysomnography technologist using modified scoring criteria whereby non-rapid eye movement (NREM) sleep categories were collapsed into one indeterminate NREM category and usual electromyogram criteria for rapid eye movement (REM) sleep was disregarded. Polysomnography times (lights out and lights on) were determined by participants’ usual bedtime and morning routines.

Results: The mean age was 83.4 years (sd=7.3). Sleep onset was in 22.1 minutes (sd=24.4). Sleep efficiency and total sleep time were decreased, while wake time was increased. Mean sleep efficiency was 68.0 (sd=14.5), total sleep time was 347.2 minutes (sd=93.0), and minutes awake were 159.1 (sd=80.3). Mean minutes of NREM sleep were 305.0 (sd=84.7) and percent NREM was 87.3 (sd=11.2). Percent REM sleep was 11.9 (sd=9.3). Participants averaged 36.0 awakenings. The apnea-hypopnea index was 18.0 (sd=16.4). Twenty-one of the participants had an apnea-hypopnea index greater than 20.
Conclusion: This sample of cognitively impaired nursing home residents spent less than 7 hours asleep and about 2 1/2 hours awake in bed each night. The seven hours of sleep were severely fragmented averaging 36 awakenings per night. About 1/3 had obstructive sleep apnea syndrome. Polysonmography in cognitively impaired nursing home residents is feasible in the nursing home environment and provides important information for understanding the etiology of disturbed sleep.

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0350

Sleep During The Menopausal Transition In A Multi-Ethnic Cohort: Feasibility And Preliminary Results

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Introduction: Mid-life women routinely complain that the menopause disrupts their sleep. Little is understood about the profile, causes and consequences of menopause-related sleep disturbances. We are conducting a multi-site study to characterize sleep and its correlates during the menopausal transition in a multi-ethnic cohort.

Methods: The SWAN Sleep Study is an ancillary study of the longitudinal Study of Women Across the Nation (SWAN). Participants were drawn from four sites (Pittsburgh, PA, Detroit, MI, Chicago, IL, Oakland, CA). The 35-day study protocol includes 3 nights of in-home polysomnography (PSG), up to 35 days of actigraphy and sleep diaries, and questionnaires related to sleep, lifestyle and mood. Data shown here are from an initial sample of 127 women. At study entry, participants were classified as pre-peri- or post-menopausal, as determined by bleeding patterns and sex hormones; none were using HRT. Descriptive data include the median and interquartile range (IQR) for visually-scored sleep on Night 2 and measures collected on Night 1 (AHI, PLM).

Results: Across study sites, 72% of eligible women elected to participate. The drop-out rate is 4% and data loss is less than 6%. The current sample includes 49 African-American, 58 Caucasian and 20 Chinese women, the majority of whom were classified as early perimenopausal (65%). Mean sample age is 51 years. Night 2 PSG sleep characteristics include: median total sleep time = 380 minutes (IQR 96.7), sleep latency = 14.3 minutes (IQR 15.0), sleep efficiency = 86.2% (IQR 10.0), % stage 1 = 5.9 (IQR 4.3), % stage 2 = 65.1 (IQR 10.3), % delta = 2.3 (IQR 6.1), and % REM = 24.5 (IQR 8.0). Night 1 data reveal a median AHI of 5.4 (IQR 8.3) and PLMI of 3.6 (IQR 5.0). Preliminary tests reveal a significant First Night Effect and sleep differences based on menopausal status, ethnicity and lifestyle factors.

Conclusion: It is feasible to conduct comprehensive, in-home sleep studies in a multi-ethnic sample of mid-life women. In some respects, Night 2 PSG sleep characteristics are similar to those reported in other studies of mid-life women. As we continue to collect and process data in this study, we will evaluate complex, temporal relationships between menopausal characteristics (hormones, hot flashes), sleep (quantitative EEG, heart rate variability), ethnicity, SES, lifestyle factors (smoking, exercise) and mood (depression, anxiety, stress).

0351

A Low Cost And Safe Physical Activity Program Improved Total Sleep Time And Sleep Quality In Elderly Women

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Introduction: Many factors influence quality of life in humans and one of them is the sleep quality. The subjective experience of non-satisfactory sleep results in an unpleasant experience and has consequences on behavior and wellbeing of a person. Sleep disorders in the elderly represent increased risk of death and also have a huge impact on quality of life. Sleep quality (SQ) in the elderly is associated to many variables including exposition to light and physical activity. Our objective was to evaluate total sleep time (TTS) and SQ in sample of sedentary elderly women submitted to a program of physical activity.

Methods: We randomly selected to perform physical activity 6 women (60 to 68 y.o, mean = 63.3) from Vila Sao Vicente de Paulo in Lavras, MG, Brazil. The exercise program consisted of walking during afternoon for 60 minutes, 2 times a week, for 4 months. TTS and SQ were evaluated through a sleep diary during 30 days and the Visual Analog Scale in the beginning and in the term of the program.

Results: The average TST before the physical activity program was 7.81 hours and 8.97 hours after the program (p<0.01). The average perception of the SQ by the Visual Analog Scale before the physical activity program was 7.14 cm and 8.61 cm respectively (p<0.01).

Conclusion: A low cost and safe physical activity program increased the total sleep time and improved sleep quality in previous sedentary elderly women. Simple tools like sleep log and visual analog scale are simple but valuable tools to inform health professionals about sleep in elderly.

0352

High And Low Frequency Napping Behavior In Relation To Total Sleep Time In Older Adults

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Introduction: Insomnia is a major health concern for older adults. Daytime napping has been associated with impaired nocturnal sleep. Two mechanisms, the circadian system and homeostatic drive, explain the association between napping and sleep. Napping may disrupt these systems resulting in increased polyphasic sleep. The current study examines napping in relation to subjectively (sleep diary) and objectively (actigraphy) measured sleep.

Methods: 103 community-dwelling elderly (M=72.81 years, SD=7.12) participants were recruited from North Central Florida. Inclusion criteria: absence of sleep disorders other than insomnia, absence of severe psychiatric disorders, no cognitive impairment; and no sleep altering medications. Sleep diary and actigraphy were collected for 14 days.

Results: Two MANOVAs examined napping frequency (low, medium-low, medium-high, and high frequency) in relation to sleep diary and actigraphy variables. Four sleep variables were analyzed (SOL, WASO, TST, SE). Main effect of napping was significant for sleep diaries (Roys =.01, F (3,98)=3.32, p <.01) and actigraphy (Roys =.02, F (3,98)=3.13, p <.05) variables. Univariate tests revealed significant differences for napping frequency for total sleep time for sleep diaries (F (3,98)=3.63, p <.05) and actigraphy (F (3,98)=3.84, p <.05). Post hoc testing revealed significantly shorter TST for high frequency nappers compared to low and medium-low frequency nappers as measured by sleep diary and actigraphy. High frequency nappers on average slept 50 minutes less per night.
than low and medium-low frequency nappers. Average nap duration for high frequency nappers was 42 minutes.

**Conclusion:** These findings indicate that higher frequency of daytime naps are associated with significantly shorter total sleep times for older adults. Interestingly, the sleep deficit of high frequency nappers (40-50 minutes) corresponds with the average duration of their daytime naps (42 minutes). Although the total 24 hour sleep for both high and low frequency nappers is similar, the sleep of high frequency nappers is more polyphasic.

0353

**Physical Active Elderly Women Have Longer Total Sleep Time And Better Sleep Quality: The Roles Of Sleep Logs And The Visual Analog Scale**

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**Introduction:** Population studies carried out in many countries has shown that while the individual ages, the sleep becomes more and more a motive of complaints, and some sleep disorders appear to be more frequent in the third age that in any other age range. There is a body of experimental evidences showing that a program of regular physical exercise can prevent illnesses, diminish risk of falls, reduce physical incapacity, improve humor and sleep quality of elderly individuals. Sleep diary is an important tool to assess sleep issues on elderly, but sometimes total sleep time do not reveal the real problem behind that almost normal amount of sleep, being necessary additional information such as the subjective perception of sleep quality by the individual to give us a more complete impression. This study compares the total sleep time and sleep quality in sedentary and active elderly women, using a sleep log and the Visual Analog Scale.

**Methods:** We evaluated 66 elderly women: 37 women have practiced physical activity for at least 3 years and 29 were sedentary. All included elderly completed a sleep diary for 30 days and answered about their sleep quality using a Visual Analog Scale daily.

**Results:** The elderly women that practiced regular physical activity slept on average 7.43 hours and the sedentary women slept 6.44 hours (p <0.01). On average sleep perception for the elderly active women was 7.56 cm and for sedentary women was 4.68 cm (p <0.0001).

**Conclusion:** Total sleep time and sleep quality were much better for regular physical active women than for sedentary women. We suggest that sleep logs should include a daily Visual Analog Scale should as part of sleep evaluation, for it can bring valuable additional information in assessing sleep in elderly.
0354

Effects Of Prolonged Wakefulness And Lead Vehicle Characteristics On Headway Distance And Brake Reaction Time During Simulated Driving

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Introduction: The effects of a lead vehicle’s speed, brake lights and braking intensity on headway distance (HD) and brake reaction time (BRT) were examined in alert and sleepy participants.

Methods: Participants (15M, 15F, mean age 18.9 yr) completed each of two counterbalanced test sessions, evening (7-9 p.m.) and early morning (3-5 a.m.), one week apart. They drove along a straight four-lane highway for 45 minutes. At intervals they were passed by a vehicle which pulled in front of them. The lead vehicle’s behaviour was determined by the factorial combination of speed (60, 90, 120 km/h), braking (braked, did not brake) and brake lights (lights, no lights). Each scenario was presented three times in random order. Stanford Sleepiness Scales were completed before and after each test session.

Results: Data were analysed by ANOVA. Participants were significantly sleepier in the early morning (F[1,28]=210.58, p<0.0005). Overall: HD increased with speed of lead vehicle (F[1,28]=148.49, p<0.0005), after braking at the two lower speeds (F[1,28]=4.64, p=0.019) and when the lead vehicle’s brake lights came on (F[1,28]=6.06, p=0.02); BRT increased (F[1,28]=85.74, p<0.0005) with speed of lead vehicle. Contrary to prediction there was no significant change in BRT (F[1,28]=0.37, p=0.85) or HD (F[1,28]=0.25, p=0.87) in the early morning condition compared to the evening condition. However, males left a greater HD in the early morning and males in the evening (F[1,28]=6.02, p=0.02). There was an increase in the number of crashes in the early morning condition (F[1,28]=6.4, p=0.02).

Conclusion: Although more crashes occurred in the early morning, HD and BRT did not appear to be the main factors related to these events. In fact, most crashes occurred when there were no other vehicles on the road suggesting that the presence of other vehicles may act as an alerting factor, at least for short periods of time.

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0355

Gender Differences In The Relation Between Alcohol Consumption And Daytime Sleepiness

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Introduction: Alcohol interferes with the quality of sleep and subsequent daytime functioning. Males tend to consume more alcohol than females (Geisner et al., 2004; Russell et al., 2004), while females tend to report higher rates of insomnia, sleep difficulties, and daytime sleepiness (Lee et al., 1999; Li et al., 2002; Lindberg et al., 1997). Gender differences in alcohol metabolism (Graham et al., 1998) and recent studies that report differential effects of alcohol on physical and mental health as a function of gender (Green et al., 2004), suggest that any study of the effects of alcohol should look for potential gender interactions. The present study assessed gender differences in the relation between alcohol consumption and daytime sleepiness.

Methods: 1700 randomly-selected undergraduate students were surveyed concerning their use of alcohol, tobacco, and caffeine, their sleep, physical activity, and work habits, and their levels of depression (CES-D, Radloff, 1979) and daytime sleepiness (Epworth Sleepiness Scale, Johns, 1991). A total of 903 surveys were returned. Linear regression was used to predict Epworth scores. The following known or suspected correlates of daytime sleepiness were entered first: sex, age, BMI, average hours of sleep per weeknight, number of hours of paid employment per week, tobacco use, physical activity level, caffeine use, and depression. Then typical number of drinks per week was entered, followed by the interaction of Gender X Number of Drinks.

Results: Higher Epworth Sleepiness Scores were predicted by gender (females), age (older), sleep (less), work hours (more), depression (higher), and number of drinks per week (more). After controlling for all of these effects, the addition of a Gender X Number of Drinks interaction term revealed that female sleepiness was more strongly affected by drinking.

Conclusion: Increases in alcohol consumption among college students lead to higher levels of daytime sleepiness, especially among females.

0356

DNA Microarray And RT-PCR Analysis Of Basal Forebrain Cholinergic Neurons Isolated Using Fluorescently Activated Cell Sorting Showed Sleep Deprivation-Induced Decrease In Glyceraldehyde 3-Phosphate Dehydrogenase mRNA

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Introduction: Previously we reported that sleep deprivation (SD) induced an increase in extracellular adenosine in cholinergic basal forebrain (CBF). Adenosine, acting via the A1 adenosine receptor, mobilizes calcium from intracellular stores and induces nuclear translocation of NF-kB in the cholinergic neurons (CN) of CBF. To further examine SD-induced changes within CN, we developed a novel technique of isolating CN from CBF.

Methods: CN were labeled retrogradely by fluorescence-tagged anti-p75 receptor IgG injections into lateral ventricles. Six days post-injection one group of rats were sleep deprived (6h SD, 8AM-2PM) while another were allowed to sleep. Rats were sacrificed at the same circadian time. Cells of the CBF were dissociated using trypsin and fluorescent CN were sorted using fluorescence activated cell sorting (FACS). Pooled RNA (N=4/group) were amplified and differential gene expression examined using Affymetrix GeneChip rat genome 230 2.0.

Results: Surprisingly, one of the genes that showed 5-fold reduction with SD (p<0.001) was the most widely used housekeeping gene glyceraldehyde 3-phosphate dehydrogenase (GAPDH). Next, we performed real time RT-PCR of RNA from CN of individual animals (N=5/group) as well as whole tissue extracts of CBF, cingulate cortex and hippocampus (N=4/group) using ribosomal 18S RNA as the normalizer. We confirmed that the GAPDH mRNA levels decrease considerably (3-5 fold) in FACS sorted CN following SD compared to sleeping controls. Moreover, the level of GAPDH mRNA was 18-20 fold higher (p<0.003) in isolated CN when compared with whole tissue extracts of CBF, cortex or hippocampus with no differences between the latter three regions with or without SD.

Conclusion: Long considered a classical glycolytic protein, GAPDH has recently been linked to apoptosis, dementia and receptor phosphorylation. The higher levels of GAPDH mRNA and SD-induced regulation suggest that GAPDH may be involved in other functions, in addition to its role in glycolytic pathway in rat CBF cholinergic neurons.

Supported by VA Merit Award (RB) and NIMH Grant MH 39683 (RWM)
Methods: Five healthy participants (4M:18-27yr) performed a psychomotor vigilance task (Johns Test of Vigilance, JTV) in the morning when alert, then repeatedly after 34-40 hours of wakefulness. The JTV requires a push-button response to a change of shapes lasting 400 msec on a PC screen at random intervals of 5-15 sec. A lapse involved either no response or a response >2 sec after the stimulus began. Eyelid movements were recorded during JTVs by an infrared reflectance method (Optalert™) using 500 samples per sec. Blinks were distinguished from saccades and other movements. The duration of eyelids closing, remaining closed, reopening, and the total blink duration were measured in Ss when alert, and during the minute before their last lapse in performance when drowsy.

Results: The duration of each component of blinks increased significantly with drowsiness: eyelids closing (103+/-18 SD msec vs 165 +/-118, n=250,133, p<0.001), reopening (162+/-49 vs 273+/-100, n=250,133, p<0.001) and total blink duration (265+/-57 vs 586+/-592, n=250, p<0.01).

Conclusion: The duration of each component of blinks increases with drowsiness caused by sleep deprivation. These results are consistent with those from earlier experiments using magnetic search coils. By contrast, video-camera methods have mostly given underestimates. The ratios of amplitude to maximum velocity of these eyelid movements are described in a companion report. These blink parameters should be useful for monitoring the alertness of active people.

0359
The Amplitude-Velocity Ratios Of Eyelid Movements During Blinks: Changes With Drowsiness
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Introduction: The amplitude of each blink is highly correlated with its maximum velocity. The ratio of amplitude to maximum velocity (AVR) of eyelid closure during blinks has been shown to increase with drowsiness and to predict lapses in a vigilance task. This investigation compared AVRs for eyelid closure and reopening when Ss were alert and when drowsy.

Methods: Five healthy subjects (4M: 18-27 yr) performed a 10-min psychomotor vigilance task when alert and again after 34-40 hr of wakefulness when drowsy and with lapses in performance. Eyelid movements were monitored by an infrared reflectance method (Optalert™) using 500 samples per sec. The AVR for each movement was calculated from its amplitude (change of position) divided by its maximum velocity (change of position per 50 msec). AVRs for eyelid closure and reopening were compared when Ss were alert and when drowsy.

Results: In each condition (eyelids closing or reopening, alert or drowsy), very high correlations between the amplitude and maximum velocity of eyelid movements were confirmed (Spearman r = 0.88 - 0.95, n = 133 - 250, p<0.001). AVRs for eyelids reopening were significantly higher than for closing (1.4 +/- 0.2 SD vs 1.2 +/- 0.2, n=250, 250, p< 0.001, Mann-Whitney U). Both increased significantly with drowsiness, to 2.7 +/- 0.9 and 1.5 +/- 1.0 respectively (p<0.001). In all conditions, AVRs for closing were only moderately correlated with those for reopening (Spearman r = 0.31, n = 633, p< 0.001).

Conclusion: The AVRs for eyelid closure and reopening are different, i.e. for the same amplitude of movement, the eyelids close more quickly than they reopen. The two velocities are only moderately correlated. Sleep deprivation increases AVRs for both closing and reopening. Consequently, the duration of those movements increases with drowsiness, as described in a companion report.
0360
Adverse Health Outcomes Associated With Inadequate Sleep In Late Pregnancy
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Introduction: Our previous research indicates that <6 hours of sleep/night during late pregnancy is associated with longer labors and increased risk for cesarean delivery. This study describes the prenatal sleep quality and well-being of pregnant women who obtained <7 hours compared to those with longer sleep times.

Methods: As part of a randomized clinical trial, data were collected during the last month of pregnancy prior to intervention. Wrist actigraphy and sleep logs were used to estimate mean total sleep time (TST), percent wake after sleep onset (%WASO), and time in bed (TIB) for 48 hours. Participants also completed self-report measures of sleep (General Sleep Disturbance Scale), fatigue (Lee Fatigue Scale), and well-being (CES-D and Perceived Stress Scale).

Results: Women with TST of <420 minutes per night (n=61) were compared to those with 420 minutes or more per night (n=77). Controlling for infant birthweight, women who slept <7 hours had later bedtimes (23:27 ± 1:16 vs 22:54 ± 0:56, F=6.31, p=.013), less TIB (8.2 ± 1.1 hrs vs 8.9 ± 1.0 hrs, F=9.27, p=.003), and higher %WASO (17.7 ± 8.3 vs 9.8 ± 5.0, F=28.75, p<.001) compared to women who slept at least 7 hours/night. In addition, women who slept <7 hours reported more sleep disturbance, more morning fatigue, more daytime sleepiness, more depressive symptoms, and higher stress levels than those who slept 7 or more hours/night. Women who slept <7 hours/night also had longer labors and were 4 times more likely to have a caesarean delivery.

Conclusion: Women who sleep at least 7 hours/night in late pregnancy have better sleep quality and well-being, as well as better labor and delivery outcomes than women who sleep less. Given group differences in TIB, women should be advised to spend more time in bed to compensate for the increased WASO associated with pregnancy.

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0361
The Relationship Between Cortical Activation And Vulnerability To Fatigue
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Introduction: The factors underlying individual differences in fatigue vulnerability have yet to be determined, but studies indicate that an individual who is fatigue-resistant on one occasion will be similarly resistant on another. It remains to be determined whether this trait can be predicted and used for practical purposes. However, recent evidence suggests underlying patterns of cortical activation may partially account for an individual's responsiveness to sleep deprivation.

Methods: Ten active-duty Air Force pilots were subjected to 37 hours of sleep deprivation to quantify the impact of fatigue on individual piloting skills. Eight of these pilots subsequently traveled to the Medical University of South Carolina (MUSC) to undergo non-sleep-deprived fMRI evaluations. First, their baseline levels of cortical activation were compared (as a group) to those obtained from previously-studied fatigue-resistant and fatigue-vulnerable non-pilots. Second, the pilots' fMRI regional activation data were correlated with their earlier-obtained flight-performance data.

Results: ANOVA indicated that the number of activated voxels for the pilots as a group was more similar to fatigue-resistant non-pilots than to fatigue-vulnerable non-pilots. Correlations between fMRI data and performance data within the pilot group revealed that the number of activated voxels were significantly related to fatigue vulnerability in simulator flight performance.

Conclusion: These preliminary data suggest baseline fMRI-scan activation may help predict fatigue susceptibility. However, due to the small number of subjects in this study, follow-up studies should be conducted to validate these findings.

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0362
Efficacy Of Modafinil For Supporting The Performance And Alertness Of Sleep-Deprived Aviators
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Introduction: Modafinil is a relatively new alertness-enhancing compound of interest to the military aviation community and others required to work long hours without sufficient sleep. Although modafinil has been well-tested in clinical settings, additional studies are required to establish its safety and efficacy for use in pilots. The objective of the study was to determine whether modafinil (100 mgs after 17, 22, and 27 hours without sleep) will attenuate the effects of fatigue on fighter-pilot mood, alertness, and performance during 37 hours of continuous wakefulness.

Methods: A quasi-experimental, single-blind, counterbalanced design tested the effects of modafinil on simulator flight performance, self-ratings of mood, and slow-wave electroencephalographic activity in 10 Air Force F-117 pilots.

Results: Modafinil significantly attenuated flight performance decrements on six of eight simulator flight maneuvers (p<.05). Under modafinil, overall performance (with all flight maneuvers collapsed) decreased only by an average of 27 percent, whereas performance under placebo fell by an average of 82 percent. Modafinil improved several aspects of subjective mood as well. Self ratings of depression and anger were lower under modafinil than under the no-treatment condition, and self ratings of vigor were improved (p<.05). In addition, modafinil administration attenuated fatigue-related increases in slow-wave EEG activity (delta and theta) recorded from Cz, Pz, and Oz (p<.05). The benefits of modafinil were most noticeable after 24 to 32 hours of continuous wakefulness—the times at which untreated fatigue created the most serious performance and alertness difficulties. There were no problematic side effects.

Conclusion: Modafinil's positive effects on simulator flight performance, mood, and alertness suggest that it is an appropriate counter-fatigue strategy for demanding situations in which operators must perform critical tasks despite the presence of significant sleep deprivation.

0363
Severely Obese Sleep Disorders Center Patients Sleep Less As Documented By Polysomnography
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Introduction: General medical practice patients who are overweight and obese, report sleeping less than do normal BMI patients (Vorona et al, in press). Here we examine the relationship between polysomnographic (PSG) sleep and obesity in SDC patients.
Methods: Patients >18 years completing polysomnography (PSG) during 2002 and 2003 were examined. Patients were allowed eight hours in bed. We attempted to permit patients their normal bed and awakening times. We excluded those with a previous PSG, as well as those who had split-night or CPAP studies, those who had PSG sleep times <120 minutes, or reported home bed times outside of 120-900 minutes. We categorized patients as normal (BMI < 25 kg/m2), overweight (BMI 25-29.9 kg/m2), obese (BMI 30-39.9 kg/m2), and severely obesity (BMI > 40 kg/m2) for analyses.

Results: 1255 patients met inclusion/exclusion criteria. 584 were male and 671 were female. Mean age (±SD) was 49 +13 years. BMI ranged from 17-72 kg/m2 with a mean of 34±8. There were 114 patients with normal BMIs; 280 were overweight; 267 were obese; and 231 were severely obese. AHI ranged from 0-141 (mean = 10 ±15). Nard SAO2 ranged from 41-99% (mean = 86±8). Mean PSG sleep time was 347±73 minutes (range, 120-484 minutes). Men slept less than women (388 versus 355 minutes, p<0.001). Total sleep time decreased as BMI increased from overweight to severely obese. Overweight patients slept 353±72, obese 348±71 and the severely obese 339±72 minutes. Normal BMI patients slept 351±86 minutes. Overall, sleep times among BMI groups were significantly different (F = 11.1, df = 3/1246, p = <0.001).

Conclusion: BMI increased as PSG total sleep time decreased in SDC patients. These results further support the linkage between restricted sleep and obesity shown in other data. These findings may be hormonally mediated, for example, through leptin and ghrelin.

0364 Individual Differences In Auditory Vigilance Performance During Total Sleep Deprivation And Sleep Restriction
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Introduction: Stable individual differences in cognitive and visual vigilance performance have been reported in response to repeated episodes of total sleep deprivation. Whether stable differences in auditory vigilance performance occur in individuals during total sleep deprivation and sleep restriction was examined in the current study.

Methods: Fifteen healthy men and women aged 28.63 ± 9.4 (Mean ± SD) years participated. Participants were scheduled to sleep 8-h per night for 3 baseline weeks at home, verified by wrist actigraphy, sleep diaries, and call-ins to a time stamped recorder. The 10-day inpatient portion of the protocol consisted of three baseline days (16:8 wakefulness:sleep schedule) with sleep at subjects’ habitual bedtimes; 40-h of total sleep deprivation (TSD) following 8-h scheduled sleep. On average, subjects were awake less then 30 sec prior to scheduled waketime (0.22 ± 0.26 min, range 0-0.5 min). In the last 30 min prior to scheduled waketime, average time awake was 0.44 ± 0.46 min (range 0-1 min). Prior to awakening, six subjects were in stage 2 and three subjects were in REM. Cognitive performance was assessed with a computerized mathematical addition test ~1, 21, 41, and 61 min after EEG verified awakening, and then every 2-h beginning ~120 min after awakening. Repeated measures ANOVA with Hunyh-Feldt and modified Bonferonni correction factors were used to analyze z-scored data. Percent of peak performance was also calculated.

Results: Cognitive performance immediately upon awakening from sleep was significantly worse than performance at all but one time point measured during TSD (p < 0.0134) and was on average 64% of peak performance. After 21 min of wakefulness, cognitive performance was on average 83% of peak performance and not-significantly different from performance at other times measured.

Conclusion: The current findings demonstrate that cognitive performance immediately upon awakening from sleep is worse than virtually all performance bouts examined across 40-h of sleep deprivation. This finding suggests that sleep inertia following a night of normal sleep has greater impact on performance than previously recognized.

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0366 Cross-Sectional Relationship Of Sleep To Obesity, Diet And Physical Activity: Results From The Third National Health And Nutrition Examination Survey
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Introduction: Daytime fatigue may be a marker for inadequate or non-restorative sleep, but it is likely influenced by other modifiable risk factors. We hypothesized that daytime fatigue and non-restorative sleep are associated with less favorable lifestyle factors, including higher BMI, suboptimal nutrition, and limited physical activity.

Methods: Using data from the Third National Health and Nutrition Examination Survey (NHANES III), we examined cross-sectional relationships between responses to the question, Right now would you say you are feeling energetic, fresh, average, tired or exhausted? and BMI, waist circumference, leisure time physical activity, and dietary intake. Analyses were conducted among people who reported getting their usual amount of sleep the night before the evaluation, and controlled for age, gender, and ethnicity. Analyses were performed with and without responses of participants who were depressed.

Results: There was a U-shaped association across the sleep categories of energetic, fresh, average, tired, and exhausted for physical activity, BMI, and waist circumference, with the healthiest lifestyle factors being associated with reporting feeling fresh. For example, relative to the fresh group, exhausted, tired and average participants were 3.8, 1.9 and 1.6 times more likely to report insufficient physical activity, all statistically different from the fresh group. This pattern was also observed for BMI and waist circumference, and persisted when we adjusted for covariates and when we excluded individuals who were depressed. In none of the dietary analyses did we observe any discernable intake pattern across the alertness categories.

Conclusion: In this cross sectional analysis of U.S. adults who report having a typical night of sleep the previous night, self-reported non-restorative sleep is associated with higher BMI, higher waist circumference and a reduced likelihood of getting recommended levels of physical activity.

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0367
A Comparison Of Performance On A Range Of Tasks Under Sleep Deprivation Conditions
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Introduction: Few studies on sleep deprivation have tried to compare performance across a variety of types of tasks. The purpose of the current study was to examine performance on several cognitive and vigilance tasks under sleep deprivation conditions.

Methods: Twenty-four college students (mean age: 20.2, SD 1.9) were paid to stay awake for one night. Three short cognitive tasks were completed: math processing, grammatical reasoning, and code substitution. The Cardinal Direction Task required participants to provide directions about the position of objects on a display. The Wombat task significantly improved across the night (p=.008). Reaction time on the PVT (p=.004) and on the longer vigilance task (p=.007) significantly increased during the night while accuracy on the longer vigilance task significantly decreased across the night (p=.000). Performance on the Process Control task decreased significantly across the night (p=.004).

Conclusion: Performance was more negatively affected on the vigilance tasks than the cognitive tasks. The type of cognitive tasks, however, could have an effect on performance. Cognitive tasks that focused on one particular type of processing (e.g., grammatical reasoning) seemed to be more susceptible to sleep deprivation than tasks that require a more global cognitive activation to successfully complete.

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0368
Combining Alpha Attenuation Test With Pupillometry
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Introduction: This study combined two promising objective physiological sleepiness tests, the Alpha Attenuation Test (AAT) and Pupillometry, into a single 10 min sleepiness test. The AAT is based on measuring alpha activity eyes closed and eyes open. In Pupillometry, spontaneous pupil size fluctuations are measured in darkness for 10 minutes. The combination of these tests is obtained by measuring pupil size during the eyes open condition in AAT. The sensitivity of test parameters was compared in a partial sleep deprivation study.

Methods: The test was performed in dark room with a distant fixation point. Alpha power (8-12 Hz) was calculated from O2-A1 using a 2 s Discrete Fourier Transform (DFT). A commercial eye gaze tracker was used to monitor pupil size fluctuations and blinks. EEG was scored visually using the standard sleep stages with adaptive epoch lengths (minimum epoch duration of 2 s). Fifteen male subjects were measured four times (around 10 AM, 1 PM, 3 PM, 5 PM) after a normal nights sleep and four times after a sleep deprivation (2 hours sleep) night. The measurements were made also around 10 AM after the recovery night in both conditions. The Wilcoxon signed rank test was used for statistics.

Results: In AAT, alpha power during eyes closed was lower during sleep deprivation (p<0.0001) and remained lower after the recovery night (p<0.05). In Pupillometry, there were no difference in blink frequency and pupil size fluctuations between the conditions. Blink durations (p<0.01) and the amount of eye closures (p<0.01) were increased under sleep deprivation. The amount of visually scored sleep during the 10 min test was higher after sleep deprivation (p<0.001) and remained higher after the recovery sleep (p<0.05).

Conclusion: This study showed that AAT and Pupillometry can be can be performed simultaneously in darkness. In pupillometry, blink duration is more sensitive than blink frequency in measuring sleepiness. Commercial eye gaze trackers can have limitations in measuring pupil size fluctuations in sleep deprived subjects. In AAT, the indicators of physiological sleepiness are still elevated after a single recovery night following partial sleep deprivation. Combination of AAT and Pupillometry enables to study further various voluntary and involuntary physiological processes eyes open or eyes closed during sleepiness and sleep onset.

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Category I—Sleep Deprivation

0369
The Percent Of Optimal Sleep And Daily Activities Across A 24-Hour Period
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Introduction: This study investigates how the amount slept relative to optimal amounts impacts time spent on common daily activities across a 24-hour period.

Methods: 14 female (mean age 19 years; range = 18-26) and 16 male (mean age 19 years; range 18-29) undergraduate students participated. On a planned activities questionnaire, participants indicated how much time they planned to spend on 23 activities during the 24-hour period following their awakening the next morning. Following that awakening, participants completed a sleep diary and an activities and mood chart over the 24-hour period that followed and reported their data by calling in to an answering machine every four hours except while sleeping.

Results: Participants were divided into 3 groups according to percent of optimal sleep obtained. The correlation between planned and actual time spent working, attending class and using the computer for work was not affected by percent of optimal sleep. Planned and actual time spent studying was significantly and positively correlated for participants who had 93% or more of optimal sleep (p=.05), only. For those who had 93% or more (p=.01) and those who had 82-92% of optimal (p=.01), the planned and actual time spent socializing were significantly and positively correlated. For those who had less than 82% there was no significant correlation. Planned and actual time on the phone was significantly correlated for those who had 93% or more of optimal. Those with 92% or less, showed no correlation.

Conclusion: Percent of optimal sleep did not impact the relationship between planned and actual time spent working, attending class or using the computer for work or school. Amounts of sleep close to optimal resulted in stronger relationships between time planned and actual time spent studying, socializing and talking on the phone. Additional analyses will further clarify the relationship between sleep and next day activities.

0370
Language-Related Performance During A Night Of Sleep Deprivation
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Introduction: While the effects of some stressors, such as background noise, have been examined in relation to language performance, few studies have examined the effects of sleep deprivation on language skills. The purpose of the current study was to examine performance on language-related tasks under sleep deprivation conditions.

Methods: Twenty-five participants (mean age: 20.4, SD 2.1) were paid to remain awake for one night. The verbal SAT test consisted of three portions: sentence completion, word analogy, and reading comprehension. The Speech Perception in Noise (SPIN) auditory task required each participant to repeat the last word of 50 sentences either with a noise background or a clear background. In 25 sentences, the last word of the sentence was easy to predict based on the context of the sentence. The last word of the other 25 sentences was not easy to predict. The participants completed both tasks five times during the night (8 - 10:30PM, 10:45 - 1:15AM, 1:45 - 4:15AM, 4:30 - 7:00AM, and 7:30 - 10AM). All tasks were counter-balanced.

Results: Repeated-measures ANOVAs were completed on the SAT test, on the over-all verbal ability score (calculated by averaging across the three portions of the SAT test), and on the SPIN test. Performance on the SAT word analogies (p=.005), the SAT reading comprehension (p=.000), and on the average SAT verbal (p=.000) decreased significantly across the night. Performance on the SPIN task remained relatively stable across the night, however, participants performed worse under the noise condition than the clear condition (p=.000) and worse on the low predictability sentences than on the high predictability sentences (p=.000).

Conclusion: The current data indicate that complex language skills are negatively affected by one night of sleep deprivation. This result is relevant in many work situations where language skills are an integral part of the required work.

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0371
The Expected Impact Of Sleep Loss On Common Daily Activities
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Introduction: The purpose was to examine students’ expectations concerning the impact of sleep loss on time spent in daily activities including home chores, work, personal hygiene and social life.

Methods: Thirty male (mean age = 18.51 years; SD= 1.21 ) and 47 female (mean age = 18.5 years; SD = 1.21) students completed a general sleep questionnaire and indicated their expectations concerning the impact of sleep loss on time spent in daily activities including home chores, work, personal hygiene and social life.

Results: Participants indicated that they were less likely to participate in home chores (t = 10.40, p < .0038), go to work (t= 8.02, p < .0038), attend class (t = 6.37, p < .0038), attend to personal hygiene (t = 4.09, p < .0038), watch TV (t = 7.41, p < .0038) and attend a party (t = 8.75, p < .0038) after having insufficient sleep. Participants also expected to feel less refreshed (t = 14.99, p < .0038), to be less active (t = 13.49, p < .0038) and to have a shorter attention span (t=14.48, p < .0038) after a night of insufficient sleep. There was no significant difference in the amount of time participants expected to spend exercising after a good or poor night’s sleep (t=2.22, p < .0038). Participants expected to be less willing to work late (t=9.14, p < .0036), work on the computer (t=6.84, p < .0038) or to pick up a sibling after school (t=9.05, p < .0036) following sufficient sleep than following insufficient sleep.

Conclusion: Participants expected that short-term insufficient sleep would reduce the likelihood of performing daily activities including going to work and school, attending to personal hygiene and socializing. Expected exercise time was not affected by anticipated sleep loss. Assessment of time spent in daily activities following sleep loss will clarify whether expectations are supported by actual behavior.

0372
REM Sleep Deprivation Selectively Impairs Memory For A Conditioned Fear Response At A 21-24 Hour Post - Training REM Sleep Window In Rats
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Introduction: 24 hours of post training REM sleep deprivation has been found to impair memory for a conditioned fear response (freezing). It was hypothesized that a smaller 4 hour period of REM sleep deprivation (REMD) would impair memory for this conditioned fear task during the
Conclusion: showed significantly less freezing than the Normal controls (p<.05). post hoc Newman-Keuls revealed that only the REMD 21-24 hour group mixed ANOVA on the 8 test trials during tone presentation showed an Between groups \[F(6,63) = 4.47, p= .0008\]. A post hoc Newman-Keuls apparatus with no tone presented). A significant difference was found frequency among the 7 groups during contextual testing (animals in the control mice were not significantly altered during the same periods. Significant sleep rebound was observed after sleep restriction. Sleep patterns (X2(4)=16.48, p<0.0025) by about 30% compared to the baseline. No sig- Frequency among the 7 groups during contextual testing (animals in the control mice were not significantly altered during the same periods. Significant sleep rebound was observed after sleep restriction. Sleep patterns (X2(4)=16.48, p<0.0025) by about 30% compared to the baseline. No significant sleep rebound was observed after sleep restriction. Sleep patterns in the control mice were not significantly altered during the same periods.

Conclusion: These results indicate that selective REM sleep deprivation for a short 4 hour period between 21-24 hours after the end of a fear conditioning task impairs memory for the experience. Activity during this REM sleep window appears to be important for the long term consolidation of contextual and conditioned fear memories.

This research was supported by a Discovery Grant from the Natural Sciences and Engineering Research Council of Canada.

0373 Sleep Patterns During Sleep Restriction In Mice Fang J, Guan Z Psychiatry, Pennsylvania State University College of Medicine, Hershey, PA, USA

Introduction: Chronic sleep restriction (CSR) induces excessive daytime sleepiness and impairs cognitive performance in humans. However, the impacts of CSR on the brain at cellular and molecular levels are unknown due to the lack of animal models. The goal of this study was to develop a mouse model of CSR.

Methods: Male C57BL/6 mice (n=10) were implanted with chronic EEG and EMG electrodes. The animals were placed into a disc treadmill system, in which each animal cage was made of a round pan as the bottom and a suspended Plexiglas tube with a divider at the bottom. The animal was awakened by the rotation of the pan driven by a motor. Baseline EEG and EMG were recorded for 1 day. In the next 3 days, animals (n=5) were allowed to sleep 60% of time during the day, and 20% during the night. The pan rotation was triggered by high EEG and low EMG under the control of a computer program (Sleep Wave) we developed. The disc rotated in 1-sec pulses until the animal was awake. Each CSR animal was matched with a control animal, which received the same amounts of stimuli but with all disc rotations occurring in the last 10-min of each 120-min block.

Results: Sleep restriction significantly reduced both rapid eye movement sleep (REMS) (F(4,16)=36.56, p<.00001) and non-REMS (NREMS) (X2(4)=16.48, p<0.0025) by about 30% compared to the baseline. No significant sleep rebound was observed after sleep restriction. Sleep patterns in the control mice were not significantly altered during the same periods.

Conclusion: Sleep in mice can be effectively restricted by the disc treadmill method in the experimental mice without reducing sleep in the control mice received the same amounts of physical stimuli. This method will be useful for further studying the impacts of CSR on the brain and behaviors.


Introduction: The study examined the effects of one-night partial sleep debt, rest pauses, and the following recovery sleep on sleepiness and executive cognitive functions.

Methods: 16 healthy men (age 19-22 yr) completed normal sleep and sleep deprivation (SD) conditions in our laboratory in a counterbalanced order. Both conditions included a 2 or 8-h night sleep depending on the condition, a test day followed by an 8-h night sleep, and a morning test. The test day included four multitask sessions of 70 min and every second session included a physically active rest pause of 10 min. The multitask contained four simultaneously active cognitive subtasks, which were presented on one screen. Task difficulty was set individually. Alertness was measured with an EEG/EOG recording and the Karolinska Sleepiness Scale during the multitask sessions. Self-estimation of performance was measured with a 100-mm analogue scale. Sleep was measured with polysomnography.

Results: The subject obtained 75% (sd 11) of the maximum score in the multitask after normal sleep, but only 41% (40) after SD (p<.001). SD also increased physiological and subjective sleepiness during the multi- task sessions (p<.001). The rest pause improved performance (p<.01) and physiological alertness (p<.05) for only 15 min. The self-estimations of performance were realistic before (69% of the maximum score, sd 13) and after (66%, sd 16) the multitask sessions after normal sleep. Under SD, the anticipatory evaluations of performance were too positive (59%, sd 18), whereas the retrospective evaluations were realistic (47%, sd 22). Multitask performance and alertness remained somewhat poorer in the SD condition than in the normal sleep condition after the recovery sleep (p<.05).

Conclusion: In addition to alertness, one-night partial sleep debt severely impairs complex cognitive performance and the ability to predict one’s own performance. Full recovery does not occur after one 8-h night sleep. Benefits from an active rest pause are short-lived.

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0375 Chronic Sleep Loss Has Long-Lasting Effects On Serotonin 1a Receptor Sensitivity Meerlo P, Roman V, Walstra I, Luitjen P Department of Molecular Neurobiology, University of Groningen, Haren, Netherlands

Introduction: Chronic sleep loss is a rapidly increasing problem in modern society. Several studies have shown that shortage and disruption of sleep is linked to poor mood. Also, several lines of evidence suggest that the serotonergic system is impaired in mood disorders. Particularly changes in the serotonin 1A receptor system are often implied in depression. However, whether such changes in the serotonergic system can be caused by chronically disrupted sleep is unknown. Therefore, the aim of this study was to test the hypothesis that chronic sleep loss leads to desen- sitization of the 5-HT 1A receptor system.

Methods: Our model of chronic sleep loss consisted of keeping rats awake for 20h each day by placing them in slowly rotating drums. The remainder of the time rats were allowed to sleep. In order to examine 5-HT 1A receptor sensitivity, rats received injections of the serotonergic...
agonist 8-OH-DPAT (0.25 mg/kg). The sensitivity of the receptors to 8-OH-DPAT was determined by measuring the acute hypothermic response by means of radio telemetry.

Results: The sensitivity of the serotonin 1A receptor system was not affected by 2 days of restricted sleep, but it was significantly reduced after 8 days of sleep restriction. This desensitization did not appear to be a consequence of stress since the sleep restriction procedure did not have a major effect on plasma levels of corticosterone. Moreover, the change in receptor sensitivity was not a consequence of forced locomotion since it did not occur in exercise controls. Importantly, the sleep loss-induced desensitization of the 5-HT 1A receptors did not rapidly recover and was still present after 1 and 2 days of unlimited recovery sleep.

Conclusion: The present data show that chronic sleep restriction causes persistent alterations in the serotonergic system that may change the susceptibility of the brain to psychopathologies.

0376
A New Approach To Understanding Of The REM Sleep Relation To Waking And Non-REM Sleep
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Introduction: Although interaction of wakefulness and sleep stages is examined in several studies, researchers are often confronted with questions: Does REM sleep (REMS) propensity accrue only during slow wave sleep (SWS), wakefulness or both? We propose a new approach to elucidating REMS relation to SWS and wakefulness and represent convincing experimental data obtained on cats exposed to SWS deprivation through its partial substitution by active waking.

Methods: Mature cats (n=8) chronically implanted with electrodes were recorded for sleep-wakefulness cycle (SWC). A week after surgery and 3 days of adaptation to a digital multichannel polygraph system SWC was recorded continuously (24h) during basal and deprivation days. After establishment of baseline SWC animals were awakened from each deep SWS (DSWS) by electrical stimulation of the posterior hypothalamus and required to remain awake during the time equaled to average length of baseline REMS. Observation on behavioral and EEG correlates was made continually. Frequency, amount and percentage ratio of SWS phases as well as latency of sleep stages were determined in both baseline and deprivation days. Significance of difference was verified by t test.

Results: High correlation between DSWS and REMS and negative correlation between wakefulness and REMS was found. The most striking finding was a disappearance of REMS from SWC during deprivation. Reduced light SWS and DSWS decrease, an increase of delta rhythm amplitude was observed. No REMS signs were revealed in other phases. Although delay of even one awakening from DSWS resulted in REMS appearance, its latency did not differ from baseline. The number of interventions in DSWS did not exceed the REMS baseline frequency.

Conclusion: Active wakefulness prevents REMS propensity while DSWS promotes REMS triggering. The primary basis for this hypothesis is the fact of REMS full elimination from SWC if active wakefulness is regularly maintained after awakening from DSWS.

0377
REM Sleep Deprivation Produces Hyperalgesia
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Introduction: A previous study indicated that a 4-hr sleep restriction produced hyperalgesia. However, general sleep loss from a 4-hr sleep restriction is confounded with differential REM sleep loss. This study was done to specifically eliminate REM sleep in order to determine its effects on pain threshold.

Methods: Six healthy adults with normal sleep, 18-35 yrs, without psychiatric disease, primary sleep disorders, or drug abuse, participated. Each underwent four sessions of 2 nights and days: 8 hrs uninterrupted time-in-bed (TIB), 2 hrs uninterrupted TIB, 9.5 hrs TIB with REM deprivation, and 9.5 hrs TIB with yoked NREM awakenings. In the REM deprivation (RD) the subjects were awaken each time they went into REM sleep and required to stay awake for 15 min before going back to bed, and at corresponding times during the NREM awakening (NR) condition. Pain threshold was assessed (1030 and 1430 hrs) using radiant heat stimulation. Finger withdrawal latency (FWL) in sec was measured for 5 randomly presented intensities directed to the index finger pad.

Results: Total sleep time for the RD (5.3 hrs) and NR (5.2 hrs) conditions did not differ, but both differed from T8 (6.7 hrs). The percentage of REM sleep in the RD condition (3.68%) was significantly reduced relative to NR (14.33%, p<.01), and the NR condition also differed from T8 (21.72%, p<.02). Treatment effects were found in the morning pain testing (p<.003). The RD condition shortened FWL (7.76 sec, p<.025) relative to the T8 (11.36 sec) and NR (10.05 sec) conditions, which did not differ from each other. The T2 FWL (7.23 sec, p=.022) differed from the T8 and NR conditions and was similar to the RD FWL.

Conclusion: These are the first data to show that REM deprivation differentially produces hyperalgesia. This is clinically significant in that opioid analgesics suppress REM sleep.

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Relationships Among Mood And Neurocognitive Tasks After Five Nights Of Partial Sleep Deprivation
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Introduction: The neurobiological and cognitive correlates of changes in mood over days of chronic partial sleep deprivation are not known. Sleep deprivation degrades performance mediated by the prefrontal cortex (PFC) which is also thought to be involved in emotion regulation. This study investigated relationships among neurocognitive tasks with and without high PFC demand and changes in mood over 5 nights of 4h TIB.

Methods: Preliminary analyses were conducted on 20 healthy subjects (age M=33+/-6.9, male=10) out of 45 who participated in a protocol in a controlled laboratory setting. After 2 nights of 10h TIB and 5 nights of 4h TIB, 3 PFC-mediated tasks were administered: the Tower of London (TOL), Haylings Sentence Completion Task (HSC), and the Controlled Oral Word Association Task (COWAT). The psychomotor vigilance task (PVT) and the Profile of Mood States (POMS) were administered daily at 2h intervals.

Results: Mood after 4 nights of sleep restriction was different from baseline (p=0.050) on 4 of the 6 POMS subscales (fatigue, confusion-bewilderment, vigor, depression-dejection) and total mood disturbance. Correlations were assessed between individual differences in change scores across days of sleep restriction on the POMS and performance on the neurocognitive tasks. Increases in the Anger-Hostility subscale scores were associated with poorer performance on the TOL (r=-0.59, p=0.006). Poorer performance on the PVT was related to greater levels of Depression-Dejection (r=-0.50, p=0.023), but not to fatigue or vigor.

Conclusion: Sustained partial sleep deprivation had deleterious effects on mood overall, but these changes were not strongly associated with PFC-mediated tasks. PVT performance was strongly related to the depression-dejection subscale, but not to subscales related to sleepiness such as fatigue and vigor. We did not find much evidence from these preliminary findings to support the hypothesis that PFC-function is associated with mood changes observed during partial sleep deprivation.

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0380

The Effects Of Sleep Deprivation On Component Processes In Working Memory
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Introduction: Many studies have reported that total sleep deprivation (TSD) alters working memory (WM) performance, although the nature of alteration is not consistent across studies. One possible reason for this inconsistency is that overall performance is typically measured, with little consideration for specific components of WM. Here, we utilized a verbal WM task that allowed us to tease apart the effects of TSD on different cognitive processes involved.

Methods: Twenty-two adults (age 19-32, 9M) performed a parametric n-back test after normal sleep (NORM) and after 42 hours TSD. Tests were composed of continuous sets with alternating conditions: study of target without high PFC demand and changes in mood over 5 nights of 4h TIB.

Results: Multivariate ANOVA revealed significantly worse overall performance after TSD. A priori repeated contrasts revealed a significant interaction between sleep condition and lag. The performance drop from lag 0 to lag 1 was greater after TSD than NORM. All other contrasts and paired-sample t-tests for levels of lag between sleep conditions were not significantly different.

Conclusion: Prior research suggests TSD impacts basic attention processes, reflected here as the ability to identify stimuli immediately after presentation (lag 0). Our results suggest that sleep deprivation does...
not impact basic attention to verbal material, but rather impairs maintenance of information in WM. Importantly, the effect manifests at lag 1 and then remains constant across greater lags, suggesting that encoding and retrieval processes remain relatively preserved. In sum, these data suggest that 42 hours TSD adversely affects the verbal WM rehearsal buffer, but not attention to stimuli or encoding and retrieval processes.

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0382
Sleep Extension Improves College Athletic Performance
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Introduction: Many studies explore the relationship between sleep quantity and human performance but few studies address this relationship in the context of athletic performance. This pilot study tested the hypothesis that sleep extension in college varsity tennis players improves athletic performance.

Methods: Women and men varsity tennis players at Whitman College (NCAA Division III) were recruited. The number of “2nd” serves hit within a 6 foot radius of the outer deep quadrant of the deuce and add courts (25 attempts in each court per participant) were recorded at baseline (habitual sleep condition) and after 1 week of 9 hours of nocturnal time in bed. It was assumed that the baseline reflected a sleep deprivation condition. Testing was done at the same time on both test days and in an indoor tennis facility to minimize circadian and weather variables. Sleep diaries were kept and the Stanford Sleepiness Scale and the Epworth Sleepiness Scale were administered. Participants were paid $20 upon completion of the study.

Results: Seven female and 5 males agreed to participate. One male dropped out because he could not obtain 9 hours in bed during the second week. The results showed no sex differences and are combined. Subjects averaged 7.138 hours of reported sleep during the habitual condition confirming that this indeed represented a sleep deprivation condition. This increased to 8.854 hours (p<0.05) during the sleep extension week. The Stanford Sleepiness Scale improved from 3.561 to 2.673 (p<0.05) and the Epworth Sleepiness scale improved from 12.154 to 5.667 (p<0.05) from habitual sleep condition to sleep extension condition. Total serves in the combined target areas improved from 17.833 (out of 50 attempts) to 20.917 (p<0.05); serves to the deuce court improved from 9.25 (out of 25 attempts) to 10.66 (p<0.05); serves to the add court improved from 8.583 to 10.25 (p<0.05).

Conclusion: Significant improvement occurred in self reported sleepiness and in athletic performance after one week of sleep extension (7 hours to nearly 9 hours) in college varsity tennis players. Adequate sleep should be a part of college athletic training programs.

Private support ($240) was obtained from one of the authors (RDS)

0383
Expanding The Two-Process Model To Describe Cumulative Performance Impairment From Chronic Sleep Loss
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Introduction: The homeostatic process S of the two-process model (TPM) saturates rapidly for schedules involving chronic sleep restriction, and cannot predict the waking performance deficits accumulating over days. The equations for process S have fixed asymptotes (U and L), as seen when writing the equations as follows: S(t)=U(t)=S(t–Δt)=U(t–Δt)exp(–Δt/Tr) during wake; S(t)=L(t)=S(t–Δt)=L(t–Δt)exp(–Δt/Td) during sleep; where U(t)=1 and L(t)=0; Tr and Td are time constants; and Δt is the time step. Based on an idea by Johnson et al. (2004), we expanded the TPM to predict the effects of chronic sleep restriction on psychomotor vigilance task (PVT) performance, by manipulating the asymptotes U and L.

Methods: The asymptotes were modified as a function of prior sleep and wake: U(t)=U(t–Δt)+MrΔt during wake; U(t)=U(t–Δt)+[1–U(t–Δt)][1–exp(–MdΔt)] during sleep; where Mr and Md are rate constants. It was postulated that L(t)=U(t–1). The model parameters were tentatively fixed at previously published values: Tr=18.2h, Td=4.2h, Mr=0.137/h and Md=0.0092/h. Closed-form versions of the equations were derived to assess goodness-of-fit relative to performance in a laboratory sleep restriction experiment involving n=35 subjects (see companion abstract by Avinash et al.). Goodness-of-fit was compared with a null model (i.e., straight line); the original TPM; and our previously hypothesized excess wakefulness model (EWM). To provide an equal basis for comparison, the latter was formulated with fixed critical wake duration ¼=15.84h and computed using scheduled TIB.

Results: Akaike’s Information Criterion (AIC) was employed to quantify goodness-of-fit (smaller is better). Expressed relative to the expanded TPM, the AIC was 681.7 for the null model; 322.4 for the original TPM; and –88.2 for the EWM.

Conclusion: The expanded TPM qualitatively captured the pattern of PVT performance changes across days of chronic sleep restriction, and constituted a considerable enhancement of the original TPM. While the EWM provided more accurate predictions of cumulative performance impairment, goodness-of-fit of the expanded TPM will likely increase following optimization of the time and rate constants.

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0383.5
Systematic Individual Differences In Delta Wave Expression In The NREM Sleep EEG
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Introduction: Previous investigations in our laboratory revealed systematic individual differences in sleep architecture. New investigations extend these observations to delta waves in the NREM sleep EEG.

Methods: As part of a larger study, 5 healthy subjects (age 29.4±5.3; 2 females) each participated in two laboratory experiments with 12h TIB (experiment 1) or 6h TIB (experiment 2) for baseline sleep, 36h controlled total sleep deprivation, and 12h TIB for recovery sleep. Sleep periods were recorded polysomnographically (VitaPort 3; TEMEC), sampled at 128Hz, and scored manually. Artifacts in the EEG (C4—Ax) were removed, and the average amplitude spectrum was computed for every 30s epoch. Subsequently, the mean amplitude of EEG delta waves (0.75—4.75Hz) during NREM sleep was determined for each recording (VitaScores; TEMEC). Analyses were completed for experiment 1 in 2 subjects, experiment 2 in 1 subject, and both experiments in 2 subjects, yielding a total of 14 records. The delta amplitude data were entered into mixed-model ANOVA to assess differences between baseline vs. recovery
considerable individual differences (ICC=89.7%; x[1]=14.8, P<0.001). Systematic individual differences in mean NREM delta amplitude ranged from 291µV to 3,681µV.

Conclusion: There was insufficient statistical power to investigate effects of TIB (6h vs. 12h) and prior sleep deprivation (36h) on NREM delta waves. However, this preliminary investigation yielded evidence of substantial individual differences in the mean amplitude of NREM delta waves (cf. Finelli et al., 2001)—which were systematic across baseline and recovery nights regardless of TIB. Further analyses on a larger sample will confirm if individual differences in NREM delta amplitude constitute a trait.

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0384
Effects Of Sleep Restriction And Recovery Sleep On Driving Simulator Test (AusED) Performance

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Introduction: It is known that sleep loss has a detrimental effect on driving performance. The aim of the current study was to measure the sensitivity of driving simulator performance to a night of varying sleep dose following a week of chronic sleep restriction.

Methods: Preliminary analyses were conducted on 10 subjects (age 30 +/- 7.5, 5 females) out of 20 subjects, in a controlled laboratory. The study consisted of 2 nights of baseline sleep (10h TIB) and 5 nights of chronic sleep restriction (4h TIB), followed by randomization to a sleep dose of either 8h TIB or 0h TIB. The 15-minute AusEd was administered every evening between 1830h-2000h and was set to simulate a monotonous rural road at night. Driving performance measures included reaction time (to appearance of trucks on the road ahead), steering deviation from median lane position, and speed deviation beyond the range of 60km/h-80km/h.

Results: On the fifth day of chronic sleep restriction, none of the driving simulator parameters differed significantly from baseline (steering deviation, P=0.4; speed deviation, P=0.3; and reaction time, P=0.2) due to subjects continuing to learn the task. After the 0h TIB condition, there was an increase in steering deviation (P=0.05), and trends toward greater speed deviation (P=0.06) and longer reaction times (P=0.09), compared to the 8h TIB sleep dose condition.

Conclusion: Results from these initial analyses on 10 subjects suggest that following a week of sleep restriction, a night of total sleep deprivation causes a decrease in driving simulator performance relative to an 8h recovery sleep period. Data from additional subjects will resolve the extent to which simulated driving is affected by varying dosages of recovery sleep.

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0385
REM Sleep Deprivation Reduces Cell Proliferation In The Dentate Gyrus Of The Hippocampus

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Introduction: The subgranular cell layer (SGZ) in the dentate gyrus (DG) of the adult hippocampus contains progenitor cells, which have potential to differentiate into neurons. Previously we reported that 96 h of sleep deprivation (SD) reduced neurogenesis in the DG of adult rats. Both NREM and REM sleep were reduced in our previous study; NREM or REM sleep could contribute differentially to this effect. The aim of the present study was to assess the effect of selective REM deprivation on cell proliferation.

Methods: Male Sprague-Dawley rats were implanted for polysomnographic recording. REM deprivation for 4 days was achieved by brief treadmill movement initiated by automatic online detection of REM sleep based on integrated EMG and the EEG power spectrum. A yoked control rat was placed in the same treadmill and experienced the identical movement regardless the stage of the sleep-wake cycle. The thymidine analog 5-bromo-2-deoxyuridine (BrdU) was injected after the first 48 h of the experimental procedure in both groups (50 mg/kg, i. p.).

Results: REM sleep was reduced by 86% in deprived rats and by 45% in yoked controls, compared to cage control animals (n = 5 per group). NREM sleep was mildly reduced in both REM-deprived rats and yoked controls. Proliferation in REM sleep deprived rats was reduced by 77% compared to cage control. Yoked controls exhibited a 53% reduction in proliferation. Across all animals, cell proliferation exhibited a positive correlation with the percentage of REM (r = 0.78, p < 0.01).

Conclusion: These results show that REM sleep deprivation reduces cell proliferation in the DG of the adult hippocampus.

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0386
Food Cravings: Chronic Sleep Restriction And Mood

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Introduction: There have been few studies that examined the relationship between sleep loss and food cravings. The aim of the present study was to investigate the effects of chronic sleep restriction on food cravings and its association with mood states.

Methods: Preliminary analysis was conducted on 20 healthy subjects (10f, 10m, aged 22-43y, BMI< 30) out of n=45 participating in a sleep restriction protocol with two baseline nights of sleep 10h TIB, followed by 5 nights of sleep restriction to 4h TIB. A validated Food Craving Inventory, with four subscales (sweets, fats, fast-foods and carbohydrates) was administered daily at 2100h during the protocol. The profile of mood states (POMS), with seven subcategories, was given at 2h intervals beginning at 0800h every day. POMS scores were averaged over the day. Food was limited to hospital diets, but food intake was not controlled.

Results: Repeated-measures ANOVA revealed no significant change in total food cravings over the sleep restriction period (p=0.47), and no detectable gender difference (p=0.79). There was a trend for a relation-
ship between BMI and average food cravings (p=0.07). Positive correlations between the tension/anxiety subscale of the POMS and cravings for sweets were found each day during the sleep restriction period (r=0.27 to 0.51). Additionally, by the end of the sleep restriction period, subjects who reported greater fatigue on the POMS had less cravings for all food subcategories (fats: r=-0.46; sweets: r=-0.23; carbs: r=-0.45; fast-foods: r=-0.45).

**Conclusion:** It appears that for subjects in a controlled laboratory environment, food cravings are not significantly increased by chronic sleep restriction when food intake is not controlled. However, those subjects who reported being more tense and anxious craved more sweet foods during the sleep restriction period. Furthermore, those subjects who were most fatigued craved less food in general after five days of chronic sleep loss.

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**Sleep Deprivation Affects Inhibitory Ability**

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**Introduction:** Total sleep deprivation (TSD) affects both attention and executive processes. The ability to inhibit responses lies at the intersection of these two domains. Here, we examined performance changes on an inhibition task across 2 nights TSD and 2 nights of recovery sleep (REC).

**Methods:** 23 subjects (age 23.9 ±4.0 years; 13F) participated. The protocol involved one night baseline sleep (BL), 64hrs TSD, and 2 nights recovery sleep (REC). We administered a go-no-go test every day at 14:00 (7, 31, 55hrs TSD) and 05:00 on TSD1 (22hrs TSD). We used MANOVA and planned contrasts to analyze d’ (the ability to discriminate among targets and non-targets) and response bias. Further analyses of hits and false+ responses helped elucidate the source of errors.

**Results:** All variables showed a significant effect of Time. d’ decreased linearly throughout TSD. 22hrs, 31hrs, and 55hrs TSD had significantly worse d’ than BL. Subjects showed a significantly bias towards greater responding at 22hrs TSD and after REC1 with a similar trend at 31hrs TSD. Hit rate showed a significant decline at 55hrs TSD and a significant increase after REC2. False+ responses were significantly greater at 22hrs, 31hrs, and 55hrs TSD.

**Conclusion:** TSD leads to impaired inhibitory abilities. Subjects showed diminished ability to effectively discriminate targets and non-targets throughout TSD. At 22hrs and 31hrs TSD, this inability was due to disinhibition generating increased false+ responses. At 55hrs TSD, it resulted from a bias to underrespond. Circadian influences may underlie the bias to overrespond, as it was strongest at 05:00. These results suggest errors in operational settings during TSD may result from a decreasing ability to quickly judge whether to take or withhold action. Furthermore, they suggest that the mechanisms underlying this inability may differ depending on both the length of TSD and the time of night.

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**Short Term Sleep Deprivation Increases SOD And GPX Activities In Several Rat Brain Regions**

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**Introduction:** We propose that free radicals accumulate during waking and give rise to the physiological and pharmacological changes associated with sleep deprivation. The accumulation of free radicals such as superoxide (O2-) and hydrogen peroxide (H2O2) depends on the rate of their production and the rate of their removal. Superoxide dismutase (SOD) and glutathione peroxidase (GPx) are the major antioxidative enzymes involved in scavenging these free radicals. We previously reported that long-term (5-11 days) total sleep deprivation significantly decreased SOD activity in the brainstem and hypothalamus, and GPx activity in the brainstem and cerebellum.

**Methods:** Male Sprague Dawley rats (400-500 g) were subjected to total sleep deprivation for 6 hours by gentle handling (n=12). All animals were sacrificed by halothane anesthesia followed by decapitation. Different brain regions were quickly dissected on ice and stored at -80°C. Samples were homogenized in buffer containing 50mM Tris HCl (pH 7.5), 50mM MgCl2 and 5mM EDTA. After centrifugation at 2,000 rpm for 10 mins. at 40°C, the supernatant was re-centrifuged at 14,000 rpm for 30 mins. at 40°C and this supernatant was used for measuring SOD and GPx activities. The paired t-test was used to determine statistical significance at the level of p<0.05.

**Results:** Short-term sleep deprivation significantly increased SOD activity in the brainstem (12%, t=-2.2, df=11, p=0.05) and hypothalamus (16%, t=-2.2, df=11, p=0.05). It also significantly increased GPx activity in the brainstem (9%, t=-2.6, df=11, p=0.03) and cerebellum (10%, t=-3.0, df=11, p=0.01).

**Conclusion:** We conclude that the initial increase in free radicals resulting from short-term sleep deprivation increased the activities of SOD and GPx. Prolonged sleep deprivation further enhanced the production of free radicals, which lead to the damage of these enzymes resulting in their decreased activity.

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**REM Sleep Deprivation Selectively Increase REM Sleep Propensity Without Affecting NREM Sleep**

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**Introduction:** Selective deprivation of REM sleep stage in rats has been achieved mainly by using the island technique. When deprived rats are allowed to sleep, a significant increase of REM sleep can be observed. However, it has been suggested that during the first 48 hours of REM deprivation there is also a similar loss of non-REM sleep. On the other hand, the propensity to sleep in rats has been assessed using a technique that resembles the multiple latency test used in humans. Rats are allowed to sleep for short periods and latencies to NREM and REM sleep are recorded. In this study we analyzed the effect of 24 and 48 hours of selective REM deprivation using the island technique on multiple latencies to sleep in rats.
Results: ICC between the two samples (likelihood ratio test).

The variance as a percentage of total variance. For every outcome variable, the class correlation coefficient (ICC), which expresses between-subjects differences over the two TSDs, in each study were quantified with the intrahostal variance.

Behavioral outcomes across the circadian cycle. Systematic individual differences in neurobehavioral deficits during total sleep deprivation (TSD) are substantial and constitute a trait. To further study this trait, we compared neurobehavioral deficits from TSD between two independent samples.

### 0390

**Comparison Of Individual Differences In Neurobehavioral Impairment From Sleep Loss Between Two Independent Samples**

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**Introduction:** A recent study in our laboratory demonstrated that individual differences in neurobehavioral deficits during total sleep deprivation (TSD) are substantial and constitute a trait. To further study this trait, we compared neurobehavioral deficits from TSD between two separate studies.

**Methods:** In study 1, 21 healthy subjects (age 29.5±5.3; 9 females) were twice exposed to 36h laboratory-based TSD. In study 2, another 21 healthy subjects (age 28.9±5.5; 11 females), drawn from the same general population, were also twice exposed to 36h laboratory-based TSD. In both studies, impairment on a battery of neurobehavioral tests was assessed every 2h during TSD. The battery contained a serial addition/subtraction task, digit-symbol substitution task, word detection task, repeated acquisition task, psychomotor vigilance task, and self-ratings of sleepiness and mood. In study 1, the battery took 60 min to complete; in study 2, test durations were evenly reduced to 30 min. Data from the last 24h of each TSD were averaged within subjects to assess neurobehavioral outcomes across the circadian cycle. Systematic individual differences over the two TSDs in each study were quantified with the intraclass correlation coefficient (ICC), which expresses between-subjects variance as a percentage of total variance. For every outcome variable, the two studies were analyzed in a single mixed-effects regression analysis controlling for study, which allowed direct statistical comparison of the ICC between the two samples (likelihood ratio test).

**Results:** Across the 13 outcome variables, the ICC ranged from 68.6% to 92.6% in study 1, and from 60.8% to 95.2% in study 2. The ICC differed significantly between studies for correct responses on the serial addition/subtraction task (study 1: ICC=79.0±5.4%; study 2: ICC=95.2±1.6%; x<7.5, P=0.006), but not for the other 12 neurobehavioral outcomes (x>3.6, P>0.05).

**Conclusion:** Despite the difference in test durations, systematic individual variability in neurobehavioral impairment during TSD was similarly considerable for the two studies. Thus, trait differential vulnerability to sleep loss persisted across independent samples.

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### 0391

**Sleep Propensity And Performance: Evaluating A Brief Protocol In Health Care Providers**

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**Introduction:** Historically, it has been difficult to obtain physiological sleep and performance measures in operational settings (e.g., hospitals), due to the time commitments of the subjects’ from lengthy protocols. The following describes a brief protocol designed to test sleep propensity and performance.

**Methods:** After IRB approval, 46 physicians and nurses (23 female, mean age 33.8 ± 8 years) participated in this study. All subjects were studied between 0630 and 0900 after sleep restriction the night before (usually after hospital duty). A week prior to their study, the subjects received a sleep diary in which they recorded seven days of sleep data, and a training session on the performance battery: Stanford Sleepiness Scale (SSS), a six item Probe Recall Memory (PRM) test, and a 10-minute Psychomotor Vigilance Task (PVT). On the morning of the study, the subjects completed the performance battery followed by electrode placement (C3,O2, EOG). The subjects’ EEG was recorded in a recumbent position for 12 minutes in a dark and sleep conducive environment. The test was terminated after 12 minutes regardless of whether or not they had slept. Time to sleep onset (NREM stage 1) was scored by a registered sleep technologist blinded to the purpose of the study. The prior nights sleep and sleep propensity are presented as mean ± SD. Sleep propensity was compared to performance measures by regression analysis. Significance was considered at P < 0.05.

**Results:** Average total sleep time (TST) over the seven days prior to the study day was 421 ± 41 minutes and TST for the 24-hrs prior to the study was 330 ± 134 minutes. Mean sleep onset was 7.1 ± 4.4 minutes. Sleep propensity was correlated to TST average for seven days (P < 0.04, R2=0.10), TST in the previous 24-hrs (P < 0.004, R2=0.19), mean reaction time on PVT (P < 0.04, R2=0.09) and SSS (P < 0.002, R2=0.21). Full test administration averaged 60 minutes in length.

**Conclusion:** Sleep propensity was short in our diverse cohort of nurses and physicians. Generally, these subjects showed a cumulative and acute sleep debt that was correlated to a short sleep onset, reduced performance, and subjective sleepiness. Overall, this brief protocol shows promise as a means to examine sleep propensity and performance in real work settings.

### 0392

**Goodness-Of-Fit Of An Expansion Of The Two-Process Model To Predict Cumulative Performance Impairment Due To Chronic Sleep Restriction**

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**Introduction:** In a companion abstract (Amin et al.) we proposed an expansion of the two-process model of sleep regulation to predict cumulative performance impairment due to chronic sleep loss. Here we quantified explained variance to evaluate predictions of the expanded model for psychomotor vigilance task (PVT) performance in a laboratory experiment involving 14 days of sleep restriction to 4h, 6h or 8h TIB in n=35 subjects.

**Methods:** To assess explained variance, we derived closed-form equa-
**Conclusion:** the variance.

**Methods:** We evaluated the effects of a one-night SD on cardiac sympathovagal balance and hormonal profile (plasmatic cortisol, ACTH, aldosterone and renin) in a group of 15 healthy medical residents. Subjects stayed awake for 26 hours (from 7:00 a.m.) and spend the night of SD at the ER, joining the medical staff on duty. Two recording sessions were scheduled the morning before and after the SD. ECG, arterial pressure (AP) and respiratory activity were recorded during rest (10 min) and head-up tilt (10 min). Blood samples were drawn between the rest and the tilt period. Autoregressive spectral techniques were used to extract cardiovascular variability oscillations: a low frequency (LF, -0.1 Hz) and a high frequency (HF, synchronous with respiration) components, markers respectively of sympathetic and vagal modulation of heart rate (HR) when expressed in normalized units (nu) whereas the LF/HF ratio is an index of the sympathovagal balance.

**Results:** After SD, HR, AP and respiratory frequency were not significantly modified, despite a significant increase in the LF component (from 0.43% to 1.6% nu) and the LF/HF ratio (from 1.4 to 2.9 nu). Sympathetic activity induced by tilt was abolished after SD (LF nu: +12±4% before vs -1±2% after SD). No significant changes were observed in the plasmatic levels of any hormones.

**Conclusion:** These data suggest that SD alters primarily cardiac sympathovagal balance, yet in absence of endocriine modifications. This could play a role in the complex mechanisms linking SD to cardiovascular morbidity.

**This work was supported in part by a PRIN 2003 Grant**

**0395**

**Sustained Nocturnal Performance Can Be Predicted By Specific Periods Of Daytime Alertness In Normal Humans**

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**Introduction:** In our 24-h society, nocturnal sleep-related accidents are common. Because all individuals are not equal in their responses to sleep loss, it is very important to identify the most vulnerable subjects.

**Methods:** We monitored cognitive performances (measured every hour using a 10-minute simple reaction time test.), EEG theta/alpha power (recorded every 2 hours during daytime), subjective sleepiness (measured every hour using Karolinska Sleepiness Scale) and two circadian markers during quiet waking is a marker for the rising sleep propensity during extended waking.

**0394**

**One-Night Sleep Deprivation Alters Primarily Cardiac Sympathovagal Balance**


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**Introduction:** The mechanisms underlying the increased cardiovascular morbidity and mortality associated with chronic sleep deprivation (SD) are still unclear, although different endocrine, neural and immunologic alterations have been hypothesized. The interruption of the alternating parasympathetic/sympathetic predominance of the night/day hours may alter the sympathovagal balance. Little information is available on the interplay between autonomic and endocrine systems following an acute SD.

**Methods:** We evaluated the effects of a one-night SD on cardiac sympathovagal balance and hormonal profile (plasmatic cortisol, ACTH, aldosterone and renin) in a group of 15 healthy medical residents. Subjects stayed awake for 26 hours (from 7:00 a.m.) and spend the night of SD at the ER, joining the medical staff on duty. Two recording sessions were scheduled the morning before and after the SD. ECG, arterial pressure (AP) and respiratory activity were recorded during rest (10 min) and head-up tilt (10 min). Blood samples were drawn between the rest and the tilt period. Autoregressive spectral techniques were used to extract cardiovascular variability oscillations: a low frequency (LF, -0.1 Hz) and a high frequency (HF, synchronous with respiration) components, markers respectively of sympathetic and vagal modulation of heart rate (HR) when expressed in normalized units (nu) whereas the LF/HF ratio is an index of the sympathovagal balance.

**Results:** After SD, HR, AP and respiratory frequency were not significantly modified, despite a significant increase in the LF component (from 0.43% to 1.6% nu) and the LF/HF ratio (from 1.4 to 2.9 nu). Sympathetic activity induced by tilt was abolished after SD (LF nu: +12±4% before vs -1±2% after SD). No significant changes were observed in the plasmatic levels of any hormones.

**Conclusion:** These data suggest that SD alters primarily cardiac sympathovagal balance, yet in absence of endocriine modifications. This could play a role in the complex mechanisms linking SD to cardiovascular morbidity.

**This work was supported in part by a PRIN 2003 Grant**

**0393**

**Theta-Activity In The Waking EEG Is A Marker Of Sleep Propensity In The Rat**

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**Introduction:** In humans EEG power in the theta frequency band (5-8 Hz) increases during sleep deprivation (SD). Theta activity was proposed to be a measure for increased sleep propensity in the waking EEG. Goodness-of-fit will likely increase after optimization of parameters Tr, Td and Mr and Md, for which analyses are ongoing.

**Conclusion:** This result suggests that the expanded two-process model has potential for the prediction of PVT performance impairment due to chronic sleep restriction. Goodness-of-fit will likely increase after optimization of parameters Tr, Td and Mr and Md, for which analyses are ongoing.

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(core body temperature and melatonin) of 18 healthy men during a 36-h sleep deprivation in constant routine protocol. Sleep need (assessed by questionnaire) and sleep history (polysomnographic recordings) were also investigated. Night-time performance impairment was defined as the percentage difference between the mean nocturnal reaction time (0.30 am to 7.30 am) and the preceding mean diurnal reaction time (7.30 am to 8.30 pm).

**Results:** Feeling fully alert in the morning just after awakening (beta = -0.63, p=0.0005) and/or sleepy in early mid-afternoon (beta = 0.51, p=0.036) were the only two factors (backward stepwise regression analysis, Multiple R= 0.82) able to predict performances impairment associated with prolonged wakefulness.

**Conclusion:** This study suggests that very simple questions (i.e.: Are you fully alert in the minutes following your morning awakening and/or in early mid afternoon?) can discriminate at-risk normal subjects for nocturnal activities such as work or driving.

**CHU BORDEAUX**

**0396**

**Chronic Sleep Restriction And Resatiation. I. Recovery Of Psychomotor Vigilance Performance**

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Department of Behavioral Biology, Division of Psychiatry and Neuroscience, Walter Reed Army Institute of Research, Silver Spring, MD, USA

**Introduction:** We reported previously (Belenky et al., J. Sleep Res. 12, 1-13) that 3 nights of 8 hours time in bed (TIB) per night were insufficient for recovery from chronic (7 nights) sleep restriction (3, 5, or 7 hours TIB per night). In the present abstract, we report immediate and near-complete recovery from chronic sleep restriction with 8 hours TIB.

**Methods:** Volunteers (N=9) underwent a 7-night sleep restriction phase (3 hours nightly TIB, 0400-0700) followed by a 7-night recovery phase (8 hours nightly TIB, 2300-0700). Daytime performance was measured hourly. Due to equipment malfunction, hourly sleep latency tests were conducted in only 3 volunteers; because of potential differences in total accumulated sleep, those 3 volunteers data were excluded from analyses. Results for subjective sleepiness are reported in a companion abstract (Balkin et al., this volume).

**Results:** PVT speed decreased across the first three sleep restriction days, then increased slightly from E3 to E4 (day, p = 0.008). Thereafter, speed continued to decrease from E4 to E7. Substantial recovery was evident after one night of recovery sleep (from E7 to R1); and with the exception of R2, no further gains were seen during the recovery phase. Mean speed across recovery was not different from BL (Tukey HSD, p > .05).

**Conclusion:** In sharp contrast to our previous findings, near-complete recovery occurred following one night with 8 hours TIB. Two factors may account for this difference: (1) Age: volunteers in the present study were younger (mean age = 22.7 years) than those in our previous study (3-hour group = 39.2 years); (2) Sleep satiation status prior to study: volunteers in the present study were more alert following one night recovery sleep. Two factors may account for this difference: (1) Age: volunteers in the present study were younger (mean age = 22.7 years) than those in our previous study (3-hour group = 39.2 years); (2) Sleep satiation status prior to study: volunteers in the present study were more alert following one night recovery sleep.

**0397**

**Testosterone Alterations In Adventure Male Racers**

Antunes HK, Andersen ML, Lourenzi VP, Mello MT, Tuñik S

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**Introduction:** The present purpose was to verify the effects of sleep deprivation (SD) on testosterone concentrations in athletes participating in a six days of competition of Ecomotion Pro Multisport adventure endurance race in Chapada Diamantina (Brazil, 2003).

**Methods:** Five healthy men, (29.33 ± 6.50 years) were evaluated before (baseline) and post exercise (immediately after race). These results indicate that testosterone was 72% reduced compared to baseline (538.9 ± 122.1 vs. 153.5 ± 56.3 pg/mL; p<0.001). To extend these data, the participants were submitted to indoor simulation during 84 h of SD and blood samples were collected in five different conditions: baseline; immediate-ly after exercise; after the first period of sleep, and 24 and 72 hours after first period of sleep. The simulation was carried out in three groups of participants (sedentary; athletes submitted to uninterrupted exercise or maintained as control).

**Results:** At baseline, sedentary males showed a significantly reduced testosterone levels compared to athletes not exposed to exercise. Immediately after the exercise, a markedly decrease was observed only the sedentary and athletes under the exercise condition in relation to baseline. The lower levels were maintained until 72 h after the sleep period in sedentary group. In the athletes, the hormone levels were normalized after 24 h of sleep. Interestingly, in athlete group not submitted to exercise no statistical significance was observed in the different time-points analyzed.

**Conclusion:** Our data showed the relevance of physical conditioned exercise that elevated the testosterone concentration in relation to a sedentary group. Secondly, the long-term SD condition decreases testosterone in exercised and sedentary groups, whereas in control athlete the hormone levels were unaltered. Thus, a continued exercise program seems to be efficient to enhanced testosterone levels and SD should be considered as a condition able to disrupt the male reproductive system.

**AFIP, CAPES and FAPESP.**

**0398**

**Chronic Sleep Restriction And Resatiation. II. Recovery Of Subjective Alertness**

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**Introduction:** In a previous study (Belenky et al., J. Sleep Res. 12, 1-13) we reported a dissociation between rates of recovery for objective versus subjective measures following chronic sleep restriction. In the present study and in a companion abstract (Wesensten et al., this issue) we report immediate and near-complete subjective alertness and psychomotor vigilance performance recovery from chronic sleep restriction with 8 hours TIB.

**Methods:** Volunteers (N=9) underwent a 7-night sleep restriction phase (3 hours nightly TIB, 0400-0700) followed by a 7-night recovery phase (8 hours nightly TIB, 2300-0700). Daytime performance was measured hourly. Due to equipment malfunction, hourly sleep latency tests were conducted in only 3 volunteers; because of potential differences in total accumulated sleep, those 3 volunteers data were excluded from analyses. Results for subjective sleepiness are reported in a companion abstract (Balkin et al., this volume).

**Results:** PVT speed decreased across the first three sleep restriction days, then increased slightly from E3 to E4 (day, p = 0.008). Thereafter, speed continued to decrease from E4 to E7. Substantial recovery was evident after one night of recovery sleep (from E7 to R1); and with the exception of R2, no further gains were seen during the recovery phase. Mean speed across recovery was not different from BL (Tukey HSD, p > .05).

**Conclusion:** In sharp contrast to our previous findings, near-complete recovery occurred following one night with 8 hours TIB. Two factors may account for this difference: (1) Age: volunteers in the present study were younger (mean age = 22.7 years) than those in our previous study (3-hour group = 39.2 years); (2) Sleep satiation status prior to study: volunteers in the present study obtained 10 hrs TIB for 7 days prior to the study. The relative contribution of these and other factors is under investigation.

**0397**

**Testosterone Alterations In Adventure Male Racers**

Antunes HK, Andersen ML, Lourenzi VP, Mello MT, Tuñik S

Psychobiology, Univ Fed Sao Paulo, Sao Paulo, SP, Brazil

**Introduction:** The present purpose was to verify the effects of sleep deprivation (SD) on testosterone concentrations in athletes participating in a six days of competition of Ecomotion Pro Multisport adventure endurance race in Chapada Diamantina (Brazil, 2003).

**Methods:** Five healthy men, (29.33 ± 6.50 years) were evaluated before (baseline) and post exercise (immediately after race). These results indicate that testosterone was 72% reduced compared to baseline (538.9 ± 122.1 vs. 153.5 ± 56.3 pg/mL; p<0.001). To extend these data, the participants were submitted to indoor simulation during 84 h of SD and blood samples were collected in five different conditions: baseline; immediate-ly after exercise; after the first period of sleep, and 24 and 72 hours after first period of sleep. The simulation was carried out in three groups of participants (sedentary; athletes submitted to uninterrupted exercise or maintained as control).

**Results:** At baseline, sedentary males showed a significantly reduced testosterone levels compared to athletes not exposed to exercise. Immediately after the exercise, a markedly decrease was observed only the sedentary and athletes under the exercise condition in relation to baseline. The lower levels were maintained until 72 h after the sleep period in sedentary group. In the athletes, the hormone levels were normalized after 24 h of sleep. Interestingly, in athlete group not submitted to exercise no statistical significance was observed in the different time-points analyzed.

**Conclusion:** Our data showed the relevance of physical conditioned exercise that elevated the testosterone concentration in relation to a sedentary group. Secondly, the long-term SD condition decreases testosterone in exercised and sedentary groups, whereas in control athlete the hormone levels were unaltered. Thus, a continued exercise program seems to be efficient to enhanced testosterone levels and SD should be considered as a condition able to disrupt the male reproductive system.
Introduction: Sleep restriction or extended wakefulness decrease performances possibly because of sleep state instability. All persons are not equal with regards to sensitivity to sleep loss: some are more resistant than others. These differences are not correlated with needs for sleep, nor with differences in term of circadian process. We tested the hypothesis that a difference in the evolution over time of the homeostatic pressure between resistant and vulnerable subjects could explain this inter-individual vulnerability.

Methods: We submitted 20 healthy normal participants (10 vulnerable, 10 resistant) to 25 hours of sleep deprivation. They had to rate their sleepiness on the Karolinska Sleepiness Scale and to perform a 10-minutes Simple Reaction Time every 2 hours, from 20H to 8H. Sleep pressure was measured by EEG power spectral analysis on the alpha-theta band (6.0-9.0 Hz). The waking EEG signal was recorded during 4 minutes eyes-open session every hours from 20H to 8H. Waking EEG was normalized through Z-scores and performances were transformed in percentage (20H value = 100%).

Results: Initial performances, EEG spectral power and KSS score did not differ between both groups (ANOVA ; NS). Performances of vulnerable subjects significantly increased during the night (rANOVA ; F = 10.008, p = 0.005) whereas resistant subjects globally sustained their performances. Homeostatic pressure and subjective sleepiness significantly increase during the night (rANOVA ; F = 10.008, p = 0.005), but not for the 4h and 6h TIB recovery conditions. All TIB doses (2h, 4h and 6h) yielded MWT MSL significantly below those at baseline (p<0.001).

Conclusion: Five nights of CSR to 4h TIB significantly increased subjects’ sleepiness measured by MWT. Further restriction of sleep to 2h on the recovery night reduced MSL, but the 4h and 6h did not provide improvement. Longer doses of recovery sleep are being studied to determine at what sleep duration MWT normalizes.

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0401
Stimulant Countermeasures And Risk Propensity Across 2 Nights Of Sleep Deprivation
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Introduction: Metabolic activity within the prefrontal cortex, the brain region most critically involved in the inhibition and control of voluntary behavior, is reduced during sleep deprivation. Limited field studies suggest that sleep loss may lead to increased risk-taking behavior, but this hypothesis has not been evaluated in a laboratory setting. Moreover, the combined effects of prolonged wakefulness and stimulant countermeasures on risk propensity are not known. In the present study, we examined the effects of two nights of sleep deprivation with countermeasures on risk propensity. Subjects were administered baseline, sleep deprived, following administration of stimulant medication, and following recovery sleep.

Methods: Fifty-four (29 men) healthy volunteers were selected for the study. Volunteers were randomly assigned to two conditions to receive either placebo or a fixed dose of 200 mg caffeine or 400 mg modafinil. Baseline testing was conducted on both nights to obtain baseline data. On the second baseline night, after the fifth sleep restriction night and after the sleep dose recovery night. Mean sleep latency (MSL) was defined as time to the first appearance of a brief sleep (10sec microsleep).

Results: MWT MSL after 5 nights of CSR was 13.6±10.4min, which differed significantly from baseline (21.1±10.6min; p=0.01). The 2h, 4h and 6h TIB doses after 5 nights of CSR yielded MSL of 5.1±3.4min, 6.6±7.1min and 7.3±3.1min, respectively. The 2h TIB recovery condition resulted in shorter MWT MSL than the final night of 4h TIB (p=0.007), but not for the 4h and 6h TIB recovery conditions. All TIB doses (2h, 4h and 6h) yielded MWT MSL significantly below those at baseline (p<0.001).

Conclusion: Contrary to expectations, sleep deprivation was associated with lowered RISK, which returned to baseline following recovery sleep. Caffeine and modafinil had no significant effect on RISK scores, whereas dextroamphetamine increased RISK scores, but only back up to baseline levels. Ongoing studies are now examining the relationship of these self-report measures of RISK with behavioral indices.
0402
The Effects Of 24 Hours Of Sleep Deprivation On Odor Identification Accuracy
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Introduction: Although we rely most heavily on our senses of vision and hearing, the sense of smell plays a considerable role in our everyday life. One of the cortical sites to which olfactory information is relayed is the prefrontal cortex, specifically the orbitofrontal region. Brain imaging studies have confirmed that sleep deprivation reduces activity in the prefrontal cortex. It has been suggested that reduced activation of the prefrontal cortex is, in part, responsible for reduced cognitive functioning following acute sleep deprivation. However, the effects of sleep deprivation on olfactory perception are unknown. The present study tested the effects of one night of sleep deprivation on odor identification accuracy using the University of Pennsylvania Smell Identification Test (UPSIT). The UPSIT has been shown to be sensitive to lesions of the orbitofrontal cortex.

Methods: Fifty four healthy volunteers (29 males) participated. Volunteers were tested 6 hours after waking from a full night of sleep (baseline) and then following 24.5 hours awake. The UPSIT is a reliable, self-administered test that consists of 4 booklets, each containing ten scratch & sniff odors. Two UPSIT booklets were administered at baseline. Volunteers remained awake and were administered 2 additional booklets when sleep deprived. Booklet order was counterbalanced across sessions. Earlier studies have demonstrated that olfactory functioning is correlated with age and sex. Therefore these variables were co-varied in the analyses.

Results: A mixed model ANCOVA controlling for age and sex indicated that accuracy of odor identification decreased significantly (p=.05) after 24 hours awake. Booklet form did not interact significantly with session order.

Conclusion: These data suggest that 24 hours of sleep loss significantly affects the ability to accurately identify odors. These findings are consistent with studies suggesting decreased prefrontal metabolism during sleep deprivation. Future studies will evaluate olfactory functioning following longer intervals of sleep loss.

0403
The Association Of Sleep Deprivation In Internship With Depression, Burnout And Empathy Prior To The Implementation Of Duty Hour Reform
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Introduction: Despite the high prevalence of sleep deprivation among physicians-in-training, it remains unclear how work hour limitations will affect sleep quantity. This study characterized the relationships between sleep deprivation and the evolution of mood disturbances, empathy and burnout among a cohort of interns.

Methods: Forty-seven interns at a university-based internal medicine residency program completed baseline and year end instruments inquiring about demographic data, sleep quantities, the Epworth Sleepiness Scale (ESS), the Beck Depression Inventory--Short Form (BDI-SF), the Interpersonal Reactivity Index (IRI) and the Maslach Burnout Inventory-Human Services Survey (MBI). Monthly, interns on the acute medical services at the main tertiary care hospital were asked about sleep amounts and subjective sleepiness as well as the BDI-SF, IRI or MBI. Absolute comparisons between means of baseline and year-end data were investigated. Associations between chronic sleep deprivation (CSD) and mood, empathy or burnout were evaluated. Plots of at least quarterly prevalences of CSD, subjective sleepiness, depression and burnout characterized general trends.

Results: The prevalence of CSD (9% to 43%, p < .001), sleepiness (11% to 36%, p = .004), moderate depression (4.3% to 29.8%, p < .001), and a high level of burnout (4.3% to 55.3%, p < .001) all increased by the end of internship. Scores that were originally more favorable than general population norms (p < .001) subsequently approached norms at the end of the year for empathic concern (p = .15) and perspective taking (p = .069). Many unfavorable changes in scores were identifiable by the fourth month of internship. There was an association between becoming chronically sleep deprived and becoming depressed (OR = 7, p = .014).

Conclusion: Given the association between chronic sleep deprivation and mood disturbances during internship, attention to preventing sleep deprivation with guidelines for sleep amounts and use of countermeasures is warranted.

0404
Post-Stimulant Hangover: The Effects Of Caffeine, Modafinil, And Dextroamphetamine On Sustained Verbal Fluency Following Sleep Deprivation And Recovery Sleep
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Introduction: Sleep deprivation reduces metabolic activity within the prefrontal cortex, a region critical to the ability to think divergently and generate response alternatives. Verbal fluency tasks are commonly used for assessing divergent thinking but have yielded mixed results during sleep deprivation. Whether verbal fluency deficits during sleep deprivation are counteracted by stimulant medications is not known, nor is the effect of such medications on post-recovery sleep performance. We compared the effects of three stimulants and placebo on Controlled Oral Word Association Test (COWA) performance.

Methods: Fifty-four (29 men) healthy volunteers remained awake for 61 hours, followed by 12 hours of recovery sleep. After 44 hours awake, volunteers received a double-blind oral administration of caffeine 600 mg, modafinil 400 mg, dextroamphetamine 20 mg, or placebo. COWA was administered daily. Total score was the sum of all words produced for all three letter prompts (e.g., C+F+L; 60 seconds for each letter). Sustained performance was evaluated by calculating the ratio of the number of words generated in the last 15 second interval relative to the first 15 second interval.

Results: Although there was no significant effect of drug group or session on total score, a mixed-model ANOVA (age and verbal IQ as covariates) yielded an interaction between drug group and testing session on sustained performance, p=.001. There were no differences in sustained performance at any session except post-recovery sleep, p=.021. Following recovery sleep, the three stimulant groups together demonstrated significantly poorer sustained fluency performance than placebo, p=.015. Individually, the dextroamphetamine group demonstrated poorer sustained performance than placebo, p=.013.

Conclusion: Although total verbal fluency score was not affected, administration of stimulant medications during sleep deprivation adversely impacted sustained verbal fluency performance after recovery sleep. Consideration should be given to the potential effects on post-recovery cognitive performance when stimulants are employed in an operational environment.
**0405**

**Impaired Decision-Making Following 49 Hours Of Sleep Deprivation**

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**Introduction:** Recent functional neuroimaging studies suggest that sleep deprivation reduces metabolic activity within the prefrontal cortex, the brain region most responsible for higher-order cognitive processes, including judgment and decision-making. The degree to which sleep loss affects decision-making has not been adequately explored. We evaluated the effect of two nights of sleep loss on risky decision-making using the Iowa Gambling Task (IGT), a computerized card game that presents subjects with choices that differ in the reward values of immediate versus long-term payoffs.

**Methods:** Thirty-four (24 men) healthy volunteers (M age=24.9, SD=5.5) participated. Following arrival on Day 1, volunteers received a full night of sleep (8 hours time in bed). After awakening at 0700 on Day 2, volunteers completed a baseline administration of the IGT. Subjects remained awake and were tested again on an alternate version of the IGT at Day 3 (following 49.5 hours awake). For baseline and sleep-deprived conditions, Net Scores were calculated, indicating the ratio of risky versus advantageous deck selections for each 1/5 of the game.

**Results:** Mixed model ANOVA indicated that sleep deprivation significantly affected decision-making on the IGT, p=.001. At baseline, volunteers performed normally, shifting away from selection of risky decks and toward advantageous decks as the game progressed, p=.001. After two nights of sleep loss however, volunteers gradually shifted their choices away from advantageous decks as the game progressed, p=.019. Under conditions of sleep deprivation, increased age was associated with more risky decision-making r=-.40, p=.019, an effect that was not present at baseline, r=.07, ns.

**Conclusion:** The sleep deprived pattern is similar to (though less severe than) that reported in studies of patients with lesions to the ventromedial prefrontal cortex. These findings suggest that executive functions mediated by the ventromedial prefrontal cortex may be particularly vulnerable to sleep loss, an effect exacerbated by age.

**0406**

**Sex Differences In The Homeostatic EEG Response To Sleep Loss**

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**Introduction:** Information about sex differences in sleep regulation is limited. The amplitudes of low-frequency EEG components during non-REM sleep in women are significantly and substantially (40%) higher than those in men, as is EEG power density in a large frequency range (0.25-11.00 Hz). Here, we investigated whether the relative EEG response to 40-h sleep deprivation differs between men and women.

**Methods:** The sleep EEG was recorded in 16 young (20-31y) and 16 older (57-74y) volunteers (8 men and 8 women in each age group) during the night preceding and the recovery night following 40h sleep deprivation under constant routine conditions. Visually scored EEGs were subjected to spectral analysis and instantaneous frequency analysis for detection of sleep spindles.

**Results:** Older men showed a significantly higher response in relative EEG slow-wave activity (0.75-4.5 Hz) to sleep deprivation than older women, an effect not present in the young (p < 0.05, age x sex). Independent of age, EEG activity in the high sigma range (14.75-15.75 Hz) and the time incidence of high frequency sleep spindles (13.75-15.0 Hz) was significantly reduced after sleep deprivation in men but not in women. This reduction was due to a peak shift in the sigma range to lower frequencies, which was clearly absent in women. Changes in sigma peak frequency correlated positively with changes in core body temperature (CBT) in both men and women (r=0.8, p<0.004), with women being on a higher CBT level (independent of hormonal status).

**Conclusion:** Since our female sample showed significantly higher CBT levels than men during the recovery night, the shift to lower sigma frequencies, typically reported for men after sleep deprivation, was not present. The homeostatic regulation of sleep spindles in response to high sleep pressure shows sex differences which may be related to a sex difference in thermoregulatory mechanisms.

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**0407**

**How Much Sleep Is Needed To Recover From Sleep Debt? The Impact Of Sleep Dose On Recovery**

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**Introduction:** People commonly attempt to recover from chronic sleep debt by extending sleep durations on weekends and days off. However, no systematic scientific data has been published on the relationship between varying doses of sleep obtained after a typical period of sleep restriction and the degree of recovery of neurobehavioal functions. A series of experiments were undertaken to provide such data.

**Methods:** Preliminary analyses were conducted on 20 subjects (age range 21-45yr; 10 females) out of N=45 participating in a laboratory-controlled chronic sleep restriction protocol. Subjects underwent 2 nights of baseline sleep (10h TIB) followed by 5 nights of sleep restriction (4h TIB) and a recovery night where TIB was given in different doses (0, 2, 4 and 8h TIB). Subjects were monitored during sleep with polysomnography. They completed a neurobehavioral test battery every 2h during wakefulness, which included the psychomotor vigilance task (PVT), the Karolinska Sleepiness Scale (KSS) and a fresh-tired visual analog scale (VAS). Test results were averaged within days (1000h-2000h).

**Results:** For each variable a linear mixed-model regression analysis was performed. Linear and quadratic models were fit to the sleep dose responses, and goodness-of-fit was compared with a likelihood-ratio test. The linear models provided an accurate description of the sleep-dose recovery function for all variables (t(17)≥4.45, p≤0.001). The quadratic models did not significantly improve goodness-of-fit (χ²(1)≥0.04, p≥0.84). The linear model was extrapolated to 100% recovery predicted. For PVT lapses (RT>500ms) this value was TIB=9.3±0.6h; for VAS it was TIB=7.3±1.0h and for KSS it was TIB=8.8±2.4h.

**Conclusion:** These preliminary data suggest that recovery of neurobehavioral functions from chronic sleep restriction occurs linearly with increases in TIB up to 8h. Additional subjects and conditions are being added to resolve whether a linear recovery dose-response relationship continues to be supported. If it does, this has profound implications for sleep homeostasis.

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Activation Of A Proinflammatory State And Failure To Eradicate Viral Disease Factors In The Sleep-Deprived Laboratory Rat

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Introduction: Our understanding of the physical systems and mechanisms affected by sleep deprivation that pose risk factors for disease can be advanced through comparative research. Sleep deprivation in laboratory rats results in transient systemic infections and eventual lethal septicemia by opportunistic microorganisms. The present study evaluated blood leukocytes, serum cytokines and chemokines, and serum endotoxin, to clinically assess parameters relevant to elucidating immunopathology in sleep-deprived rats.

Methods: Adult rats were operated for polysomnography and sleep deprivation by the Bergmann-Rechtschaffen method, which entails 6 seconds of locomotion upon sleep onset. Comparisons included operated animals administered the same ambulatory requirements (yoked) or permitted unrestricted sleep (baseline controls). Blood leukocyte differentials were determined in 10 catheterized animals studied for ≤22 days. Serum cytokines (IL-1ß, -2, -4, -6, -10, -12, TNF-α, IFN-γ), chemokines (MCP-1, MIP-2), and endotoxin were determined by ELISA and kinetic LAL in rat serum collected by cardiac puncture after 0, 5, 10, 15, and 20 experimental days (N = 5-8/treatment). Data were tested for significant differences by planned comparisons and P < 0.025.

Results: Neutrophils increased progressively to 61 ± 8% then 70 ± 3% of circulating leukocytes in sleep-deprived animals (vs. baseline, 46 ± 9%, each P < 0.001). An initial 3-fold increase in immature neutrophil number (left shift) was followed by a 3-fold increase in monocyte number (mono-cytosis), while lymphocytes declined proportionally (vs. baseline, all P < 0.01). Serum endotoxin and IL-1ß showed markedly increased incidence of detection and concentration in sleep-deprived rats throughout the experimental period (all comparisons, P < 0.025), while detection of IL-2, IFN-γ, and MCP-1 occurred sequentially.

Conclusion: A finding of neutrophilia is consistent with findings in sleep-deprived humans. Serum cytokine detection revealed a proinflammatory state in sleep-deprived rats. Cytokines are not normally detected in serum, and therefore high prevalence in sleep-deprived rats points to abnormal effector activities and systemic disease. Despite activation of innate immune cells, the sleep-deprived host failed to remove endotoxin, consistent with our previous report of host failure to control opportunistic microorganisms. These findings implicate immunopathology as an important health consequence of sleep deprivation.

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Sleep Restriction Does Not Significantly Impair Automatic Cognitive Function, But Increases The Facilitatory Role Of A Masked Prime In A Word Recognition Task

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Introduction: The detrimental effects of sleep loss on psychomotor performance have been extensively studied. However, our understanding of which, if any, cognitive functions are impaired by sleep loss is limited. We examined the effects of two consecutive nights of restricted sleep (60%) on the automatic processes supporting word recognition using the masked priming paradigm. The masked priming paradigm has been extensively used to explore the processes of lexical access, without contamination from extra-lexical cognitive processes.

Methods: Twelve healthy volunteers (mean age 24.5 yrs) were recruited. The study had a within subjects design, with each subject exposed to two conditions in a counterbalanced order: (i) habitual sleep schedule; and (ii) restricted sleep schedule. After a baseline sleep-wake assessment with sleep diaries for 7 days, subjects were asked to maintain a habitual sleep schedule or restricted sleep schedule for 2 nights in their normal environment. Subjects then attended the laboratory to complete the performance test battery in controlled conditions. The test battery consisted of the Psychomotor Vigilance Task (PVT), Karolinska Sleepiness Scale (KSS), and the masked priming word recognition task.

Results: Significant increases in subjective sleepiness and PVT reaction time were observed in the restricted sleep condition. In contrast, response time on the masked priming task was not significantly affected by sleep restriction. However, the magnitude of the masked priming effect, which is used as an index of automaticity of lexical processing, increased following sleep restriction.

Conclusion: We suggest that the increase in automatic processing after sleep restriction may occur as a consequence of compensatory mechanisms.

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0411
Endocrinological And Catecholaminergic Alterations During Sleep Deprivation And Recovery In Male Rats

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Introduction: Since previous data of our group showed increased concentrations in HPA axis hormones in sleep deprived rats, we hypothesized that this augmentation could produce effects in other hormonal systems, particularly in the sexual system. Considering that little is known about how the hormonal system changes during the recovery period after sleep deprivation (SD), our objective was to examine from what point SD alters sexual and stress-related hormones along with plasma catecholamine concentrations during four days. We also sought to verify the time course of their recovery after an equivalent period of recovery sleep.

Methods: Rats were deprived of sleep by the platform technique for 1 to 4 days and were allowed to recover for the same period. Plasma catecholamines (dopamine, DA and noradrenaline, NOR), testosterone, estrone, progesterone, prolactin, corticosterone and ACTH concentrations were measured.

Results: Comparisons between groups showed that the SD procedure used in the present study produced marked alterations in almost all studied hormones from 24 hours of SD, except for estrone and prolactin (which required 96h of SD to become altered). Testosterone and estrone decreased, whereas progesterone, prolactin, corticosterone, ACTH, DA and NOR increased. During recovery period, progesterone, prolactin and corticosterone concentrations returned to control levels, whereas testosterone, estrone, NOR and DA did not. In addition, after 48 hours of recovery ACTH and NOR decreased below control concentrations, remaining low until 96 hours of sleep recovery.

Conclusion: Thus, SD showed long lasting, differential effects upon these neurochemicals suggesting that each has its own pattern of responses to SD as well as variable periods of recovery.

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0412
The Effects Of Active Sleep Deprivation On The Developing Brain

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Introduction: Studies investigating the role of AS in early brain development suggest AS deprivation during critical stages of development, results in behavioral and morphological changes in adult animals. Rat pups between the ages of postnatal day 5 to 14 are in a critical period of development that requires a sustained high level of activity within the central nervous system (CNS). We proposed that AS deprivation during this period with induction of prolonged quiet sleep (QS) would precipitate an abnormal increase in apoptosis in the CNS as well as an overall reduction in brain mass resulting from AS deprivation. In addition, waking the animal after clonidine or clomipramine exposure did not result in the same level of PCD as either drug given independently, suggesting that AS deprivation precipitates PCD. This data suggests a possible function of AS to maintain the high level of CNS activity that is necessary during this critical period of development.

0413
Are Pilots Well-Rested Upon Entering A NASA Flight Simulation Protocol?

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Introduction: Aviation operations, which can involve erratic schedules, are often associated with sleep loss. As a result, it is challenging to ensure that pilots enter operationally-based research protocols without an accumulated sleep debt. To confirm that participants were well rested, as determined by Psychomotor Vigilance Task (PVT) performance, and had stable sleep/wake cycles prior to beginning a Boeing 747-400 flight simulation protocol, sleep patterns were evaluated in the 4 days preceding the protocol.

Methods: Participant sleep patterns were recorded by an actigraphy monitor during the 96 hr prior to beginning the protocol. All participants were male and consisted of two captains and six first officers. Participants were 46.36 ± 8.96 years, flew on average 68.00 hr per month ±21.09, and completed 15.00 duty days per month ±2.33. To assess performance, five 10-min PVT trials were administered over a 13 hr period. The PVT sessions consisted of one training trial and four baseline trials that occurred between 0900 and 2200 PST.

Results: A repeated measures ANOVA revealed no significant differences in the amount of time in bed obtained per day by participants during the 96 hr period, F(3,18)=.31. Analyses of participants’ PVT reaction time revealed no significant differences across trials for mean (M=258.16 ±4.10), F(3,21)=1.85, median (M=247.28 ±4.28), F(3,21)=1.71, fastest 10% (M=199.34 ±4.68), F(3,21)=2.63, and slowest 10% (M=370.88 ±4.85) F(3,21)=.26.

Conclusion: The data suggest that participants are not significantly different in the amount of time in bed obtained prior to entering the protocol and perform at levels consistent with normal, alert individuals (i.e., M=250 milliseconds) throughout baseline testing. Additionally, participants do not show unstable sleep/wake cycles. Therefore any differences in performance across the protocol are due to factors other than beginning the protocol with insufficient rest.

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0414
Diurnal Variation In The Genital Reflexes And Hormone Levels Induced By Paradoxical Sleep Deprivation And Cocaine In Male Rates

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Introduction: The purpose was to ascertain whether the genital reflexes induced by paradoxical sleep deprivation (PSD) in male rats show diurnal variation, and whether the hormonal rhythm of testosterone and proges-
terone is involved in these behaviors.

Methods: Genital reflexes (penile erection-PE, and ejaculation-EJ) and hormone levels were assessed during a 24-h period at four testing times (0900, 1600, 2100 and 0400 h) in PSD rats injected with saline or cocaine.

Results: Results indicated that PE in PSD rats given saline or cocaine did not show diurnal variation while EJ responses were significantly reduced at 0400h in the PSD-cocaine group. The home-cage control group testosterone concentrations were lower at 1600, 2100 and 0400 h than at 0900 h. At 0900 h, testosterone levels were significantly lower in the PSD groups than in the control group. In contrast, progesterone levels were significantly higher in PSD groups in relation to the control group at the four testing times.

Conclusion: Thus, we observed strong diurnal variation in testosterone and progesterone in control rats whereas only EJ responses in PSD-cocaine seemed to be influenced by the time of day. These results suggest that progesterone may influence the modulation of male genital reflexes displayed by sleep-deprived rats.

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0415

Neutrophil Infiltration Into Liver And Lung Tissue Resulting From Sleep Deprivation In Rats

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Introduction: The purpose of this study was to determine whether neutrophils infiltrate lung and liver tissue during sleep deprivation in rats. Recent analyses of sleep-deprived rat blood and serum revealed neutrophilia, the appearance of proinflammatory markers, and failure to eradicate foreign antigens. Neutrophils infiltrate tissues as part of a systemic response to leukocyte activation that can lead to release of cytotoxic biochemicals and to cell injury. We measured tissue activity of myeloperoxidase (MPO), a marker of neutrophil infiltration, which is an antioxidant protein that produces hypochlorous acid when neutrophils are activated.

Methods: Male rats were surgically prepared for polysomnography and sleep deprivation by the Bergmann-Rechtschaffen method, which requires ≤6 seconds of forced locomotion upon each sleep onset. Simultaneous application of this ambulatory requirement to a second rat produced a yoked comparison. Operated rats in a baseline control group were permitted sleep ad libitum. Six animals per group were studied at 0, 5, and 10 days of sleep deprivation, and at 2 days of recovery sleep after 10 days of sleep deprivation. The 10-day sleep deprivation period precludes advanced morbidity that typically develops by 20 days. MPO activity was determined by kinetic spectrophotometry. Planned comparisons were performed and P < 0.016.

Results: Sleep-deprived rat lung MPO activity showed a two-fold increase by 10 days, compared with baseline and yoked values (each P<0.01). Increased MPO activity appeared progressive, indicated by an upward trend of 22% above baseline in sleep-deprived rats at 5 days that was not statistically significant. Sleep-deprived rat liver MPO activity was increased 72% at 10 days, compared with baseline (P<0.025). Recovery sleep was associated with decreased lung and liver MPO from deprivation levels.

Conclusion: Sleep deprivation induced infiltration of neutrophils into lung and liver tissue, implying a pro-oxidant state with potential consequences of oxidant injury. Whether the same is true in humans awaits study, but increases in circulating phagocytes and activated natural killer cells have been reported. These data advance our recently reported findings of uncompensated oxidative stress to liver and heart tissue during sleep deprivation, and provide a source of cytototoxic biochemicals that implicate innate immunity in pathogenesis. Normalization of MPO activity by recovery sleep provides a biomarker and a property of restoration by sleep.

National Heart, Lung, and Blood Institute (59271) and the National Institute of Neurological Disorders and Stroke (38733).

0416

Relationship Between Performance On The PVT And Actual Field Tasks During A 30 Hr Field Exercise In Elite Soldiers

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Introduction: Previous studies from the laboratory have shown that repeated administration of a monotonous task (PVT) over an extended period of time results in a concomitant degradation in performance during a night without sleep. However few if any studies have examined the relationship between performance on a laboratory based task and field tasks. This study examined the relationship between Palm-PVT performance, live fire marksmanship, and extended field vigilance.

Methods: Thirty-one soldiers were divided into either a placebo or caffeine group. Soldiers performed normal duties until the evening of Day 2 and refrained from caffeine use after 0800 on Day 2. From 2030 to 2200 hr on Day 2, soldiers performed a control observation and reconnaissance vigilance task (ORVT) in the field. This 90-min task was repeated at 0200 and 0400 on Day 3 during an overnight period without sleep. They also engaged in a marksmanship task, which was divided up into a reaction time and accuracy segment, at 2300 on Day 2 and again at 0630 on Day 3.

Results: There were significant correlations between the ORVT and Palm-PVT speed and minor lapses (R2 = 0.13, p < 0.000; R2 = 0.09, p < 0.005 respectively), however this was only true for the session following each ORVT. Palm-PVT and marksmanship were not significantly related. Subjects were separated post hoc into shooter/non-shooter groups and the analyses were conducted again with the same results. Finally, within drug group analyses were performed and no significant relationships were found.

Conclusion: These results suggest that Palm-PVT performance reflects performance on an extended field vigilance task. However the lack of a correlation between Palm-PVT and marksmanship is more likely due to confounds related to the study design (e.g. time to transport subjects to range, environmental cues (daylight), and activity/arousal associated with preparations to shoot).

0417

A Laboratory Measure That Reflects Performance On Military Tasks During A 50 Hour Field Trial

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Introduction: Performance on the psychomotor vigilance task (PVT) is sensitive to the effects of sleep deprivation in the laboratory. As few studies have examined whether performance in the laboratory environment reflects that found in an actual field trial, this study evaluated the relationship between performance on a Palm version of the PVT (Palm-PVT), an extended field vigilance task and a live fire marksmanship task during a
Category I—Sleep Deprivation

50 hr field exercise with restricted sleep.

Methods: Thirty soldiers were divided into 4 sections and completed a variety of training tasks on Day 1. After a 3 hour sleep period (0200-0500) they underwent a 30 hr period without sleep. On Day 2/3 they completed two test blocks from 2200-0200 (early night) and from 0200-0600 (late night). In each test block they completed a 45 min live fire marksmanship/vigilance task (MVT) and a 90 min Urban Operations Vigilance Task (UOVT). The Palm-PVT was administered prior to and after each MVT and UOVT.

Results: Linear regression analyses were conducted to determine the relationship between measures of Palm-PVT (Speed and Lapses) with measures of Marksmanship (Vigilance and accuracy) and the UOVT. Speed, and major and minor lapses were all able to significantly predict vigilance during the Marksmanship task (R² = 0.27, 0.24, and 0.26 respectively, p < 0.000). Speed was significantly correlated with Marksmanship accuracy (R² = 0.20, p < 0.003), however lapsing was not. Performance during the UOVT was significantly correlated with speed, and major and minor lapses (R² = 0.24, 0.26, and 0.23 respectively, p < 0.000).

Conclusion: Performance on the field version of a simple reaction time task (Palm-PVT) reflected actual performance on the MVT and UOVT. These results suggest that performance data collected from laboratory studies can be used to predict performance on specific components of military tasks completed in the field.

0418
Sleep-Deprivation Dose Response Effects On Hypocretin-1 (Orexin A) Concentrations In A Diurnal, Sleep Consolidating Primate, The Squirrel Monkey
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Introduction: Hypocretins are involved in the regulation of wakefulness and the pathophysiology of narcolepsy. The normal function of hypocretins, however, is unknown. As hypocretins are only consistently found in cerebrospinal fluid (CSF) and brain tissue, its study in humans is difficult. We have developed a squirrel monkey model, a primate with consolidated sleep/wake cycles like humans, to examine the normal physiologic role of hypocretins. We have previously demonstrated that a short wake extension increases hypocretin-1 release in monkeys while locomotion and cortisol have little feedback effect. The goal of this study was to increase sleep deprivation amounts and simultaneously monitor locomotion in each individual.

Methods: We extended wakefulness in a group of six female squirrel monkey (Saimiri sciureus sciureus) by two (sampled @22:00), five (@01:00), and seven (@03:00) hours on three separate occasions, and obtained CSF at each time point. Baseline CSF was collected at each time point as well. Monkeys were actigraphs to continuously monitor locomotion. Samples were assayed for hypocretin-1 and cortisol.

Results: A two-hour wake extension had no significant effect on hypocretin-1 (-0.23±10%), but significantly increased cortisol (196%±91%). A five hour wake extension increased hypocretin-1 31%±12% and cortisol 750%±391%. A seven hour wake extension caused a 63%±23% increase in hypocretin-1 and a 135%±34% increase in cortisol. Multivariate modeling and univariate correlations indicate that both time of day and homeostatic pressure significantly influence hypocretin-1 concentrations while cortisol had no effect on hypocretin-1. While locomotor activity was correlated with hypocretin-1 increases during sleep deprivation, modeling, together with our previous daytime data, suggest that this is most likely secondary to the sleep deprivation procedure.

Conclusion: Our results suggest that hypocretin-1 increases reactively to increased sleep pressure, but is also modulated by the circadian clock.

There is only limited, if any, effects of cortisol or locomotor feedback on hypocretin-1 in this species.

NARSAD (JMZ), MH47573 (DML), HHMI (EM), NS232724 (EM)

0419
Sleep Patterns Of Athletes After Chronic Sleep Deprivation And Sustained Exercise
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Introduction: The aim of this study was to evaluate the effect of sustained exercise during chronic sleep deprivation in athletes.

Methods: Were evaluated three groups of subjects (both sex, aged 31±6 years, BMI=23.2±1.6 kg/m2): 1) athletes during sustained exercise (n=7), 2) athletes (n=5), and 3) non-athletes (n=4). All subjects were submitted to 84 hours of sleep deprivation. Group 1 performed 477.3 km (in-door) during trekking and biking. Groups 2 and 3 were maintained while sleep deprivation in the same environment that group 1. All subjects were allowed to have a nap (84= 28minutes) in the middle of study period and the sleep was recorded. All subjects were submitted to 3 PSG recordings: A) before the beginning of the study; B) post chronic sleep deprivation; and C) one day after PSG recording B.

Results: The groups had similar age and BMI. Sleep patterns were similar during the nap comparing the groups, despite of sustained exercise. Comparing PSG data of recordings A and B, groups 1 had not shown sleep patterns differences; both groups 2 and 3 were different (p<0.05) in: sleep stage 1 (S1%), sleep stage 2 (S2%), sleep stages 3+4 (S3+4%), and sleep latency. Comparing PSG data of recording C with A and B, of all subjects, we observed (p<0.05): TST (55±±235 vs 358±116 minutes) % were higher during B compared with C and S1% (2±2 vs 3±1%) were lower in the same comparison, respectively; S2% (49±8 vs 53±9%) was lower and REM% (27±6 vs 23±7%) was higher during C compared with A, respectively.

Conclusion: This study suggest that sustained exercise could be a protector against de sleep patterns changes immediately after chronic sleep deprivation, but during the second night of sleep, athletes submitted to sleep deprivation and sustained exercise could have a REM sleep sleep recovery.

AFIP; CAPES, FAPESP/CEPID.

0420
Sleep Deprivation Alters The Relationship Between Performance And Neural Activity
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Introduction: Increased posterior cingulate cortex (PCC) activity has been associated with the degree of reaction time benefit conferred by a cue. Here we examine whether the relationship between PCC activity and degree of cue benefit is altered by sleep-deprivation (SD).

Methods: Six subjects were scanned in a 1.5 Tesla magnet while performing a Posner-type attention task in both rested (R) and SD conditions. Sleep state was counterbalanced across subjects. Subjects fixated centrally and responded to peripheral targets preceded by spatially predictive (valid), misleading (invalid), or uninformative (neutral) cues. Cue benefit scores (CBS) were calculated by normalizing differences between log
transformed reaction times to valid cues and log transformed mean reaction times to neutral cues. Both anatomical and functional scans were acquired. An event-related design was used. Functional imaging data were analyzed using SPM2 (Wellcome Department of Imaging Neuroscience). Trials that occurred during movements >1mm and the 16 seconds preceding were eliminated from analysis. Movement covariates were included to model residual movement-related effects. Conjunction analysis revealed areas of consistent activations across subjects. CBS was included as a regressor in the analysis, and related activations are reported. Regions were considered significant at p<0.05 corrected across the brain volume.

Results: Significant relationships between CBS and BOLD signal were localized bilaterally in the PCC and in the left medial frontal gyrus in the R condition. Following the SD condition, only left PCC activity was significant. A contrast between R and SD conditions revealed a trend at the corrected level (p=0.055), with less CBS-related activity in the PCC after SD.

Conclusion: PCC activity is reduced following SD, suggesting a less significant association between CBS and PCC activity. Therefore, sleep deprivation may alter the ability to shift attention by reducing processing efficiency within the PCC.

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0421

Subjective Sleepiness Following Sleep Deprivation Predicts Processing Speed, But Not Performance Maintenance Or Accuracy

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Introduction: Individual variability in response to sleep deprivation is poorly understood. In this study, we examine whether variability in self-reported sleepiness following 34-36 hours of sleep deprivation predicts performance speed and maintenance, and accuracy on a spatial attention task.

Methods: Eight subjects (ages 18-30) were studied following a normal sleep period (N) and 34-36 hours of wakefulness (SD). During both sessions, subjects reported their level of sleepiness using a visual analog scale (VAS) ranging from 0 to 10 with 10 being most sleepy. Following this, each subject performed a modified Posner task. On this task, subjects fixated centrally and responded to peripheral targets preceded by spatially predictive (valid), misleading (invalid), or uninformative (neutral) cues. Correlations were calculated between subjective sleepiness, number of lapses, and reaction times for valid, neutral, and invalid trials.

Results: Subjects reported a wide variability in sleepiness levels with a range of 2.2-7.3. Subjects averaged 96.8±51.2 lapses, and 9.16%±2.78% of responses were false positive errors. Reaction times did not differ significantly across cue type (288.7±54.5 for valid cues, 316.2±59.4 for neutral cues, and 303.9±66.2 for invalid cues, p=0.043). Pairwise comparisons (Bonferroni corrected) between the left and right peripheral fields at each day indicated significantly greater number of errors in the left peripheral field relative to the right during the sleep deprived state (p=.017). Left versus right peripheral field comparisons were not significant at baseline and following recovery sleep.

Conclusion: Sleep deprivation adversely affected the attentional processing of stimuli presented within the left peripheral visual field. These findings suggest that sleep loss may differentially affect right hemisphere attentional mechanisms, and have practical implications for pilots or other workers that must maintain visual attention during periods of prolonged wakefulness.

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0422

Left-Visual Field Deficits In Attentional Processing After 40 Hrs Of Sleep Deprivation

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Introduction: One of the most prominent effects of sleep loss is reduced vigilance and attention. Clinical and experimental studies have suggested that the right hemisphere is dominant for attentional processes, as evidenced by left perceptual field neglect that often occurs following a lesion to the right parietal lobe. We hypothesized, therefore, that sleep loss would be associated with a greater frequency of inattention errors within the left versus right visual fields.

Methods: Twenty-one (12 male) military personnel remained awake for 40 hrs. Visual attention was assessed with the Lateral Visual Field Test (LVFT). This 15-minute test utilizes a U-shaped instrument that periodically presents brief flashes of light at individual locations across a 140 degree field of view. The visual field was divided into 5 sub-fields (left peripheral, left front, center, right front, right peripheral). Participants were tested at 2-hour intervals throughout the duration of the study. The mean proportion of omission errors was calculated for baseline, sleep deprived, and post-recovery sleep days.

Results: A 3(day) x 5(field) repeated measures ANOVA with Greenhouse-Geisser correction on the proportion of response omissions indicated a significant interaction between day and lateral visual field (p=0.043). Pairwise comparisons (Bonferroni corrected) between the left and right peripheral fields at each day indicated significantly greater number of errors in the left peripheral field relative to the right during the sleep deprived state (p=0.017). Left versus right peripheral field comparisons were not significant at baseline and following recovery sleep.

Conclusion: Sleep deprivation adversely affected the attentional processing of stimuli presented within the left peripheral visual field. These findings suggest that sleep loss may differentially affect right hemisphere attentional mechanisms, and have practical implications for pilots or other workers that must maintain visual attention during periods of prolonged wakefulness.

0423

Strain Differences In Response To 10 Consecutive Days Of Partial Sleep Restriction

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Introduction: Humans routinely curtail sleep and disrupt circadian rhythms resulting in daytime sleepiness and impaired performance. Animal models provide a unique opportunity to study chronic partial sleep restriction and the influence of variation as a result of strain differences.

Methods: Young adult male C57BL/6J (N=18) and B6C3F1/J (N=12) mice entrained to a 12:12 light:dark cycle were chronically sleep restricted (SR) over a 10 day period. Wakefulness was achieved by placing animals in a slowly rotating wheel for 12 hours each day either during the normal active phase (dark period N=14) or the normal rest phase (light period N=17) for 10 consecutive days. Sleep was recorded using EEG and EMG measurements during a 2 day baseline period, during 10 days of SR, and 2 days of recovery sleep. Core body temperature (cBT) and activity were recorded prior to and during the imposed wakefulness protocol.
Category I—Sleep Deprivation

Results: During periods of forced wakefulness animals obtained no REM sleep but were able to obtain 5 to 40% of fragmented NREM sleep. During 10 days of SR, C57Bl/6J mice accumulated approximately 26 hours of sleep debt regardless of whether forced activity occurred during the light or dark period. In contrast, B6C3F1/J mice lost 28 hours of sleep when SR to the light period and 40 hours when SR to the dark period. Delta power increased only after the first day of SR. The altered activity cycle did not result in a shift in the circadian rhythm of cBT.

Conclusion: Mice respond in a similar way to chronic partial sleep restriction and circadian disruption as humans. The amount of sleep was altered depending on the strain and the time-of-day of SR. The degree of sleep loss seen in these studies is equivalent to a human obtaining 5-6 hours of sleep per night.

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0424
Assessing Fatigue In Commercial Airline Pilots Using The Trail Making Test
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Introduction: Prior studies have linked pilot error with longer duty cycle. Unfortunately, there has been no proven optimal method for evaluating individual deterioration in performance that may easily be administered to pilots during their duty. Some preliminary work suggested that the Trail Making Test (TMT) was useful as a screening method for evaluating performance in taxi drivers in Brazil, and this was suggested as a screening technique. We evaluated the efficacy of the TMT in detecting deterioration in pilot visuomotor performance before and after their duty cycles and its usefulness as a screening tool to assess fatigue.

Methods: Epworth Sleepiness Scale (ESS) and a sleep history survey (which was used to assess sleeping habits, medication and stimulant intake, and screening for underlying sleep disorders) were administered to all subjects. TMT A & B were administered one hour before duty cycle and again 30 minutes after the duty cycle (end of shift).

Results: Preliminary results from 12 English-speaking pilots from two commercial airlines in south Florida are reported. Average duty cycle was 12.5 hours. Average Epworth Sleepiness Scale Scores for all subjects was 8.5. When comparing pre-duty and post-duty scores, we noted improvement in the mean TMT scores after the duty cycle in TMT-A from 32.83 to 26.33 and in TMT-B from 53.92 seconds to 52.92 seconds. Results were not statistically significant. Pearson correlation of subjective sleepiness (assessed with the ESS) and TMT-A and TMT-B was +0.35 (n=12, p<0.05).

Conclusion: Prior data shows that increased pilot error has been linked to longer duty cycles of pilots. Optimal methods for testing and assessing individual fatigue-related performance in pilots needs further research. TMT-A and TMT-B were unable to detect any deterioration in performance from before to after pilot duty cycles.

0425
Differential Effects Of Gender On Sleep Continuity During Experimental Fragmentation Of Sleep
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Introduction: The sleep differs greatly when categorized by gender. Differences have been consistently reported between the genders in measures of sleep initiation, maintenance and architecture, with females exhibiting more negative outcomes within sleep. Although the reported aetiology is multi-factorial, such variations in sleep may differentially influence the outcome of experimental fragmentation of sleep (with traffic noise). PURPOSE: To evaluate an experimental method of fragmenting sleep and observe whether a differential effects upon sleep continuity between male and female subjects are present.

Methods: 15 female (age 25.6±7.68yrs) and 14 male (age 27.0±5.5yrs) healthy volunteers participated in the study. Subjects were consented (informed), adapted to the sleep environment and screened for any sleep disorders prior to inclusion. All subjects slept together in a 12-bed ward for a total of 3 nights (1 adaptation; 1 no noise & 1 with noise). Pre-recorded traffic noise presented to subjects during each experimental night over an 8-hour period (2300-0700hrs), with a mean noise level of 52±10dB(A) and dynamic range of 32-77dB(A). ECG was recorded with a digital polygraph recorder (Vitaaport 3, Temec instrumentation BV) and sleep assessed by a qualified technician using standard criteria.

Results: Of the primary measures of sleep continuity, distinct effects of sleep fragmentation were observed equally for both genders compared to baseline. However, the magnitude of sleep fragmentation was generally greater for females that males, although measures of sleep latency exhibited a differential effect (males +29.6%; females 6.7%). Notably, only total REM showed a statistical difference (p=0.05), although measures of nocturnal movements and arousal within specific NREM stages exhibited a differential effect (MVT p=0.01; NREM Stg3 arousals p=0.03 respectively).

Conclusion: It can be concluded that although females have a heightened response to experimental sleep fragmentation, the overall effect is comparable for both genders.

0426
Pilot-Test Of A Fatigue Management Program For The Commercial Motor Carrier Industry
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Introduction: The Fatigue Management Program (FMP) pilot study marks the first time that a broad spectrum, comprehensive intervention consisting of educational, clinical and operational elements has been implemented and studied in a commercial operational setting. Funded primarily at the federal level in both Canada and the USA, along with additional support from regulatory and industry associations in both Alberta and Quebec, the FMP is designed to increase sleep time and reduce fatigue among commercial drivers. Currently, this is the only study designed to investigate the human side of the fatigue management equation among motor carriers in North America.

Methods: The FMP was field-tested on standard revenue-generating routes in three jurisdictions (Alberta, Quebec and Texas) with drivers and carriers operating completely within existing Hours of Service regulations. In addition to obtaining both objective and subjective measures of sleep and fatigue, a step-wise approach for the screening and treatment of sleep disorders was also developed, with particular emphasis on sleep apnea.

Results: Pre/post measures of sleep and fatigue were obtained to date in two of the three jurisdictions. Among the most notable results were the following: (i) drivers averaged between 5-6 hours of sleep on both work and off-duty days; (ii) drivers consistently over-estimated their sleep time (between 45-90 minutes, on average) when compared to objective actigraphy data; (iii) 71% of Alberta drivers had some degree of sleep apnea,
with 38% having a condition severe enough to warrant interventional treatment; and (iv) drivers treated for sleep apnea increased their sleep time by 73% (from four to seven hours), and drivers without sleep apnea increased their sleep time by 8%.

Conclusion: While further scientific evaluation of the FMP will yield more definitive conclusions, results of the pilot-test phase suggest that the FMP is successful at increasing sleep time and reducing fatigue among commercial motor vehicle drivers.

0427
Subjective Estimations Of Pain Increase In Both Total Sleep Deprivation (Tsd) And Partial Sleep Deprivation (Psd)
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Introduction: Reduced sleep time is common in patients suffering from pain and depression. Does sleep loss itself lead to the onset of pain and mood deterioration, or are these changes secondary to generalized dysphoria?

Methods: Two experimental models in two independent studies: (1) TSD. Healthy participants (N=9, 30-55 yrs) stayed awake for 88 continuous hours. (2) PSD. Healthy participants (N=40, 21-40yrs) were randomly assigned to habitual sleep of 8h/night (N=18) or sleep restriction to 4h/night (N=22) for 12 consecutive nights. In both studies, light and posture were controlled during normal control sleep period. Testing: In PSD, 108 computerized visual analog scales (VAS) were presented every 2 hours during the waking period to assess emotional and physical well-being. In TSD, a subset of these items were presented every 2hrs.

Results: In TSD, bodily discomfort increased by 4.2% starting on the 1st day and was 9.5% above baseline on the 3rd day of deprivation. In PSD, factor analysis of the 4684 V AS sets extracted four factors: optimism-sociability, tiredness-fatigue, anger-aggression, and bodily discomfort. Optimism-sociability dropped (p<0.05) after a single night of PSD and by day 12 had deteriorated by 15.2% (p<0.05). No change during the 8-hour sleep condition. Bodily discomfort increased (p<0.05) starting on day 2 of PSD, and reached asymptote at an elevation of 3.0% on day 4. Anger-aggression was elevated by day 3 (p<0.05). Generalized dysphoria was associated with a higher propensity for risk taking. No studies have examined the relationship among stimulants, IQ, and reported risk taking tendencies in sleep deprived individuals. In the present study, the Wechsler Abbreviated Scale of Intelligence (WASI) was used to identify Full Scale (FSIQ), Verbal (VIQ), and Performance (PIQ) IQ. The Evaluation of Risks (EVAR) scale was used to identify risk propensity behavior and was administered at baseline, following sleep deprivation, again after administration of stimulant medication, and following recovery sleep.

Methods: Fifty-four (29 men) healthy volunteers remained awake for 61 hours, followed by 12 hours of recovery sleep. After 44 hours awake, volunteers received a double-blind oral administration of caffeine 600 mg, modafinil 400 mg, dextroamphetamine 20 mg, or placebo. EVAR was administered on the morning of the day following the last night of sleep deprivation, after administration of stimulant medication, and following recovery sleep.

Results: Spearman correlations showed no significant relationship between FSIQ score, VIQ score, and reported risk propensity at baseline or following 23 hours of sleep deprivation (p>0.05). In contrast, post drug administration of dextroamphetamine 20 mg resulted in a significant positive relationship between FSIQ and risk propensity (rho=0.500, p=0.048) and a significant positive relationship between VIQ and risk propensity (rho=0.607, p=0.013). These relationships were no longer significant following a night of recovery sleep.

Conclusion: The present results suggest a significant relationship between drug, risk propensity, and intelligence. These findings raise the possibility that stimulant medications may specifically affect prefrontal regions of the brain that mediate intellectual functioning and some aspects of judgment and risk-taking behavior.
Introduction: While sex differences in sleep and wakefulness have been reported in mice, little information is available about the influence of gonadal hormones on sleep. In the present study, we sought to determine whether sex differences in recovery from sleep deprivation and restraint stress are influenced by gonadectomy in male and female mice.

Methods: Gonadectomized and sham-operated male (n=4; n=4) and female (n=5; n=4) C57Bl/J6 mice (3-4 months of age) were maintained on a 14L:10D schedule and implanted with EEG/EMG electrodes. Following a 24-hr baseline recording, mice were sleep deprived (last 6 hrs of the light phase) and given a 10-hr recovery opportunity during the following dark phase. In a separate study, mice were sleep deprived for 1-hr (control procedure) and the next day subjected to 1-hr of restraint stress at the same time of day (ZT 7-8).

Results: Female mice displayed a significantly larger percentage increase of NREM recovery sleep (p<.05) over baseline values (249 ± 71%) than males during the 10-hr recovery period from sleep deprivation. Ovariectomy in female mice attenuated the percentage increase of NREM sleep over baseline values (249 ± 71%) than that observed in both males and females (197 ± 42%).

Conclusion: Sex differences in response to sleep deprivation were eliminated by ovariectomy in females while sex differences in response to restraint stress were eliminated by castration in males. These results demonstrate that gender related sleep differences in response to environmental perturbations are influenced by gonadal hormones in male and female mice.

This research was supported by NIH AG-18200 and AG11412.
**Introduction:** The ability to rapidly discriminate between “go” and “no-go” stimuli requires an inhibitory control that we show elsewhere to deteriorate linearly with total sleep deprivation (TSD). Predicting extent of this decline and resulting disinhibition would be useful in operational and real world settings. Such a tool should be easy and fast to administer. Here, we use the Stroop Color-Word Interference (SCW) task to predict performance on a Go-NoGo (GNG) task, as both require the inhibitory process of identifying the less salient and less automatic response.

**Methods:** Sixteen subjects (age=28.8±10 years; 8M) were administered a 2-minute SCW prior to completing the GNG task under two conditions: following a normal night (NORM) of sleep and after 32 hours TSD. Correlation analyses were used to determine if SCW inhibition or interference (color-word inhibition minus color) predicted GNG hit rate % (HR), false positive % (FP), and d’ (ability to discriminate between targets and non-targets). We were particularly interested in prediction of FP performance, as that is the manifestation of disinhibition in GNG.

**Results:** SCW inhibition SS correlated with GNG d’ scores (p<0.05), but neither HR nor FP scores, on both nights. Interference SS correlated with d’ and FP on NORM at p<0.05 and with these same variables on TSD at p=0.06.

**Conclusion:** Tools to help predict inhibition performance during TSD are important for the selection process of positions that require high states of operational awareness, as oftentimes wrong “go” or “no-go” decisions may result in negative consequences. SCW inhibition SS predict overall (d’) performance, but not specifically disinhibition (FP). Interference SS may prove better predictors, because they appear to predict overall and disinhibition performance. If increased sample sizes confirm these findings, the SCW task may be useful as a quick screen to predict inhibitory control during TSD.

This research was supported by ONR Stress Physiology Program Work Order N00014-04-AF-00002 and by the UCSD GCRC grant RR00827.

**0434**

Hippocampal Long Term Synaptic Plasticity Is Impaired In Animals With Lesions Of The Ventrolateral Preoptic Nuclei

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**Introduction:** The impairment of memory function in nearly every model of sleep deprivation suggests that the hippocampal formation may be sensitive to the physiological effects of sleep loss. As the experimental model for chronic partial sleep deprivation we used animals with ventrolateral preoptic nucleus (VLPO) lesions, who have more than 30% total sleep loss and rarely achieve the deeper stages of delta sleep.

**Methods:** Experiments were conducted on hippocampal slices in vitro from 1) animals 6 weeks post bilateral VLPO lesion, and 2) control animals, matched for age. Field excitatory postsynaptic potentials (fEPSPs) were evoked by Schaffer collateral stimulation and were recorded in the CA1 stratum radiatum. Long term potentiation (LTP) was induced by 3 trains of 100 stimuli at 100Hz. Paired-pulse facilitation (PPF) test measured the responses to two closely timed stimuli (40-msec). Adenosine A1 antagonists (CPT 1μM or DPCPX 200 nM) were bath applied.

**Results:** We found that: 1) in slices prepared from VLPO-lesioned animals the induction of LTP was impaired. In slices from the VLPO-lesioned rats fEPSP increased after tetanic stimulation by 21 +/- 16.2% (n=9) compared to 76 +/- 18% (n=7) in the control animals (p=0.02 unpaired t-Test). 2) The responses to A1 antagonists (CPT and DPCPX) were greater in VLPO-lesioned animals. A1 antagonists increased fEPSP slope in VLPO-lesioned rats by 156.3 +/- 17% (n=5) compared to 63.8 +/- 13% (n=6) in slices prepared from control animals. 3) In VLPO-lesioned animals PPF ratio was greater. PPF ratio (pulse2/pulse1) was 2.8 +/- 0.2 (n=6) compared to 1.6 +/- 0.05 in control animals (n=13) (p=0.007 unpaired t-Test). DPCPX reduced PPF ratio in both VLPO-lesioned (1.09 +/- 0.03; n=6) and control animals (1.08 +/- 0.05 n=5) (p=0.8 unpaired t-Test). 4) LTP in VLPO-lesioned animals could be partially rescued by adenosine A1 antagonists. The mean increase in the fEPSP after tetanization in the presence of CPT was 56.2 +/- 14.6% (n=6) compared to 98.8 +/- 7.5% (n=4) in control animals (p=0.17 unpaired t-Test).

**Conclusion:** We found that in hippocampal slices from VLPO-lesioned animals the responses to both A1 antagonists and to PPF test are higher suggesting an elevated inhibitory tone by endogenous adenosine. In addition, in VLPO-lesioned animals the induction of LTP is impaired but can partially be restored by A1 antagonists suggesting that adenosine accumulation may account at least for part of synaptic plasticity deficits in the VLPO-lesioned animals.

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**0435**

Rapid Eye Movement Sleep Loss Attenuates Actin Stabilization Protein Cortactin In The Hippocampus

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**Introduction:** Rapid eye movement sleep (REMS) is thought to affect synaptic plasticity. In 2002 (Sleep:A204) we reported that prolonged REMS loss impairs hippocampal long-term potentiation (LTP). Our efforts have since turned to exploring the molecular contributors to the observed electrophysiological deficits, and have focused on cortactin. Cortactin is a cytoskeletal protein involved in actin branching and stabilization. In the hippocampus cortactin is upregulated during LTP and facilitates dendritic spine growth. Thus, cortactin may be a good marker of synaptic plasticity.

**Methods:** In this study five juvenile male Sprague-Dawley rats were selectively REMS deprived for 48 hours by the flowerpot method. Five large pedestal control and five cage control rats were also employed for comparison. Animals were sacrificed and the CA1-CA3 regions of the hippocampus were dissected, flash-frozen, and stored for subsequent western blot analysis.

**Results:** A one-way ANOVA revealed a significant omnibus F(2,12)=13.28, p<.05. Newman-Keuls post hoc analyses indicated that the mean relative optical density of cortactin expression in the pedestal control group (M=230369, SD=36806) was significantly different from cortactin expression in the cage control and REM deprived groups (M=71488, SD=30099; M=135966, SD=70362, respectively).

**Conclusion:** Overall, the pedestal control group had more cortactin expression than the REM deprived and cage control groups. The increase in cortactin could to be due to the exposure of the rats to the deprivation chambers. A novel environment promotes exploration and affords learning opportunities such as escape strategies and food and water procurement. Such interactions could instigate remodeling of select neural structures. However, if the neural circuitry was compromised by the lack of REMS then the remodeling machinery could be severely hampered. This appears to be the case because cortactin levels in the REMS deprived animals were near cage control levels suggesting a link between REMS and synaptic plasticity in the hippocampus.

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0436
Sleep Extension Improves Glucose Tolerance In Chronic Short-Sleepers Who Have Type 2 Diabetes Or Impaired Glucose Tolerance
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Introduction: Previous studies demonstrate that chronic sleep curtailment results in decreased glucose tolerance. We tested the hypothesis that extending sleep in diabetic or pre-diabetic subjects who typically have short sleep times will improve their glucose tolerance.

Methods: Subjects who habitually sleep <7 hours per night (short-sleepers) by wrist-actigraphy monitoring (WAM) and have impaired glucose tolerance (IGT) or diabetes were enrolled. Subjects underwent one week of at home sleep monitoring and one week of 3-hour sleep extension in the laboratory (intervention). An oral glucose tolerance test (OGTT) was performed at baseline and at the end of the intervention period. The glucose responses to OGTT were quantified as the area under the curve (AUC) during the 180 min post-glucose ingestion.

Results: In nine subjects (mean age was 45.5±11 years, mean body mass index 29±5.7kg/m2, mean sleep time 377.6±58.2 min) are reported. Subjects who extended their sleep time had a decrease in the AUC glucose whereas those who reduced their sleep time (possibly due to inability to habituate to the environment) had an increase in AUC glucose. The correlation between the change in AUC glucose from the baseline to the end of the intervention in relation to the change in the amount of sleep during the three nights preceding the administration of the OGTT was highly significant (r=0.814, p=0.0075). In the 6 subjects who extended their sleep time by at least 30 minutes, the difference in AUC glucose was nearly significant (p=0.062) and clinically significant differences emerged at 90 min (-30 mg/dl; p=0.032) and at 180 min (-26 mg/dl; p=0.001) post-glucose ingestion.

Conclusion: These findings suggest that sleep duration may be an important determinant of glucose tolerance in patients who have IGT or diabetes and that increasing sleep time in short-sleepers may be a behavioral intervention for patients who are pre-diabetics or diabetics.

0437
The Influence Of Sleep Disruption On Immune Parameters During Pregnancy
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Introduction: Women commonly report their sleep to be disrupted during pregnancy; however, there is little information addressing the immunological consequences for pregnant women who experience “excessive” sleep. This study assessed how sleep disruption in pregnancy influences various immune parameters.

Methods: 79 pregnant women were recruited though the University of Colorado. They completed sleep questionnaires (ESS, PSQI, and Additional Sleep Questions), provided blood samples, and kept sleep diaries for 2 weeks following the blood collection. Data were collected at 35-39 weeks of pregnancy. Serum levels of TNF-α, IL-1β, IL-6 and IL-10 were determined via ELISA kits (Biosource Europe). The sleep variables of interest were: SOL, WASO, TIB, TST and SE. The sample was separated into two groups: 28 women who experienced symptoms similar to insomnia (SOL > 30 m and/or WASO > 30) and 26 women who did not.

Results: Correlations reveal a positive relationship between IL-6 and ESS scores (r = .306, p = 0.026) and negative relationship between IL-4 and ESS scores (r = -.310, p = 0.024). Multivariate analyses taking into account interassay variability show no differences on immune parameters between the two groups of pregnant women. Independent t-tests revealed differences between the two groups (M = 10.4 ± 6.2 and M = 21.0 ± 14.7, respectively) for SOL (t = -3.49, p = 0.002), as well as for WASO, M = 15.5 ± 7.1 and M = 48.6 ± 18.1, respectively, (t = -8.98, p = 0.000).

Conclusion: Sleep is undisputedly disrupted during pregnancy. However, sleep disruption resembling insomnia is not a universal experience. Stemming from this is little data regarding sleep patterns and immunological consequences on maternal health. The present data revealed alterations in sleep in pregnancy, but no differences on immune parameters between the two groups of pregnant women, although assay variability makes interpretation of the present dataset difficult. Ongoing data collection will clarify these relationships and resolve these methodological limitations.

0438
REM Rebound Following 64 Hours TSD
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Introduction: It has been documented that REM sleep recovers later than NREM sleep following TSD. However, it is not clear this pattern is consistent throughout the full night or is specific to early REM periods when the homeostatic drive for SWS is strongest. Here we examined REM sleep recovery across REM periods after TSD.

Methods: 21 subjects (age=23.7±3.7, 11F) participated in a 6-continuous-night study in the sleep lab. The protocol involved 1 night of baseline sleep (BL), 64 hours total sleep deprivation (TSD), and 2 nights of recovery sleep (REC1 and REC2). Data were analyzed using within-subjects repeated measures ANOVA with planned contrasts.

Results: REM efficiency and REM density (REMD) both showed a significant main effect of Night during all 3 REM periods. REM efficiency in periods 1, 2 and 3 declined significantly from BL to REC1 and increased from REC1 to REC2 (but remained significantly less than BL on REC2). In most subjects, REM was fragmented by the occurrence of Stage 2 during REC nights. REMD showed no difference between BL and REC1, but increased significantly on REC2. The length of REM periods did not change significantly across nights.

Conclusion: Overall, it appears that the lack of recovery in REM sleep on REC1 and the subsequent recovery on REC2 manifests in each of the first 3 REM periods. REM was less efficient and REMD was low throughout the night on REC1, and each increased in all REM periods on REC2. The consistent fragmentation and reduced intensity of REM on REC1 may relate to a need to conserve resources for other recovery processes occurring during SWS. The lack of complete REM recovery in this study suggests that to fully understand the process of recovery sleep, more than 2 recovery nights may be necessary.

0439
Correlations Among Dietary Nutrient Variables And Subjective And Objective Sleep
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Introduction: Actigraphic sleep variables were related to consumption of 77 nutrients as inferred from detailed diet questionnaires. Methods: The present study utilized data from 423 postmenopausal women enrolled in the Womens Health Initiative (age M=68, SD=7.76). Subjective sleep variables included WASO (S-WASO), TST (S-TST), and number of naps (S-NAPS). Actigraphically-quantified sleep variables included weekly averages of TST (A-TST), sleep efficiency (A-SEFF), sleep acrophase (A-ACRO), and minutes asleep out of bed (A-NAPS). Partial correlations (controlling for age, education, income, BMI, minutes of moderate/strenuous physical activity and total grams) compared these with 88 nutrient variables obtained at baseline, on average 290 days prior to the sleep examinations. Plots of p-values aided in establishing a p=.004 significance criterion for the 602 correlations.

Results: The most significant correlations were with S-NAPS, including (from strongest to weakest): total fat, calories, saturated fat, monounsaturated fat, trans fat, water, proline, serine, tyrosine, phenylalanine, valine, cholesterol, leucine, glutamic acid, ash, isoleucine, histidine, sodium, tryptophan, protein, threonine, cystine, methionine, phosphorus, polyunsaturated fat, animal protein, aspartic acid, arginine, lysine, alanine, caffeine, riboflavin, gamma-tocopherol, glycine, retinol, delta-tocopherol, vitamin D, selenium, percent calories fat, alpha-tocopherol-eq, carbohydrate, sucrose, percent calories monounsaturated fat, vitamin B6, calcium, and magnesium. A-TST was associated with total fat, monounsaturated fat, trans fat, saturated fat, polyunsaturated fat, calories, gamma-tocopherol, cholesterol, alpha-tocopherol-eq, percent calories fat, delta-tocopherol, water, alpha-tocopherol, and percent calories monounsaturated fat. A-NAPS was associated with vitamin K, trans fat, polyunsaturated fat, percent calories polyunsaturated fat, and total fat. A-SEFF was associated with cholesterol and vitamin B12, A-ACRO with Vitamin D, S-TST with percent calories protein and S-WASO with vegetable consumption.

Conclusion: Many nutrients were associated with increased reporting of naps. Caffeine was associated with fewer reports, while actigraphic napping was associated mostly with fat-related variables. Additionally, several variables (mostly fat-related) were associated with less actigraphic sleep.

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0440
Three Patterns Of Recovery In Sleep Parameters Following 64-Hour TSD
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Introduction: Total sleep deprivation (TSD) alters several sleep parameters upon recovery. Sleep is more consolidated and competition between the need to replace slow wave sleep (SWS) and REM sleep appear to alter normal sleep architecture during recovery sleep. Here, we compared sleep parameters on baseline and for two consecutive nights of recovery sleep following 64-hours of TSD.

Methods: 23 subjects (23.94±3.99, 13F) participated in this study. The protocol involved one night baseline sleep (BL), 64hrs TSD and 2 nights recovery sleep (REC1, REC2). 11 sleep variables were evaluated, including: TST, TIB, WASO, SE, SL, RL, REMD, Stage 1%, Stage 2%, Delta%, and REM%. Data were analyzed with within subjects repeated measures ANOVA and planned contrasts.

Results: All variables showed a significant effect of Night, except for TIB which did not differ between nights. Three patterns of recovery emerged in the data. First, TST, SE, and Delta% were all greater on both REC1 and REC2 vs BL, but less on REC2 than REC1. SL, Stage 1%, Stage 2% showed a similar recovery pattern with BL>REC2>REC1. Second, REMD and REM% showed REC2>BL=REC1. RL showed REC2 Conclusion: These data replicate previous findings suggesting that sleep is altered during recovery sleep following 64-hour TSD. Here, three distinct patterns of recovery sleep were observed: complete recovery after 1 night, incomplete recovery with even 2 nights, and no recovery until night 2. WASO fully recovered after 1 night of recovery sleep. NREM and most sleep continuity variables showed strong signs of recovery on REC1 and continued to show recovery even on REC2. REM variables showed no recovery until REC2. Thus, most sleep parameters did not fully recover after 2 nights of sleep, suggesting that it takes longer to recover sleep than to lose it.

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0441
Experimental Suppression Of Slow Wave Sleep Without Change In Total Sleep Time Is Associated With Decreased Insulin Sensitivity And Glucose Tolerance
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Introduction: Sleep disordered breathing (SDB) is characterized by frequent microarousals and reductions in slow wave sleep (SWS). Accumulating evidence suggest an independent link between SDB, glucose intolerance and insulin resistance. We investigated the effects of all night SWS suppression via induction of microarousals without decrease in total sleep time on glucose metabolism in healthy young adults.

Methods: Nine young healthy lean adults (mean age: 24±1 years; 4 women) were studied under two conditions (baseline, SWS suppression) in a randomized order separated at least by 4 weeks. Mean body mass index did not change over the study period. Subjects had no sleep complaints. Sleep disorders were ruled out by polysomnography. Undisturbed sleep was recorded on two consecutive baseline nights (B1, B2). Sleep was continuously monitored and acoustic stimuli (1000-2000Hz, 40-110dB) were administered during NREM sleep to induce microarousals and suppress SWS for three consecutive nights (S1, S2, S3). At the end of each condition, subjects had a frequently sampled intravenous glucose tolerance test after an overnight fast. Insulin sensitivity (SI) was derived from minimal model analysis. Glucose tolerance (Kg) was calculated as the linear slope of the natural log of plasma glucose between the 5th and 19th minutes after the glucose injection. Complete data sets are currently available for 6 subjects.

Results: Sleep fragmentation decreased the amount of SWS (min: 74.8±7.0 on baseline vs 9.0±2.3 on S1, 13.5±3.5 on S2, 11.8±1.3 on S3; p=0.0001) despite no differences in total sleep time between study conditions (min: 465.6±8.6 on baseline vs 457.6±3.0 on S1, 476.2±3.0 on S2, 457.0±4.6 on S3; p=0.56). SI was 24% lower (7.3±0.9 vs 5.5±0.6, p=0.046) and Kg was decreased by 25% (2.0±0.3 vs 1.5±0.2, p=0.028) with SWS suppression compared to baseline.

Conclusion: Experimental suppression of SWS during three consecutive nights is associated with reduced insulin sensitivity and decreased glucose tolerance in healthy young adults. These findings provide the first evidence that disruptions in sleep quality without decrease in total sleep time may adversely affect glucose metabolism and suggest that reductions in SWS that are typical of normal ageing and SDB could play a role in the corresponding alterations.
0442
Stronger REM And SWS Recovery After Sleep Deprivation In Long Vs. Short Sleepers
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Introduction: Most previous studies examining recovery sleep after sleep deprivation (SD) have focused on SWS changes. Only a few studies have examined recovery sleep in long and short sleepers (LS and SS). Here we examined differences in recovery sleep between LS and SS, with a focus on REM sleep variables.

Methods: 17 subjects, 8LS and 9SS, (mean age 30±11.7, 9F) were studied with standard PSG for 2 consecutive baseline nights (BL) and during an equal length recovery sleep (REC) after extending their typical wake period by 24 hours (conditions counterbalanced). Sleep variables from the second BL were compared to REC.

Results: During REC, LS had a greater number of REM Periods, more REM minutes, and a trend for greater REM density than SS. REM latency decreased overall, with a trend for SS to show a greater decrease due in part to the fact that 3 SS had sleep onset REM periods (SOREMP) during REC. REM% and REM efficiency did not change with REC. TST, sleep efficiency, SWS min, and SWS% all increased and SL decreased with REC, with LS showing greater changes on all variables but SWS%.

Conclusion: LS had more “intense” REM recovery on the first night after SD than did SS, suggesting that LS may build more REM pressure with SD than SS. However, LS also had a greater recovery of sleep continuity and SWS variables than SS. These latter findings largely replicate Aeschbach et al’s (1996) report and suggest a stronger homeostatic influence on REC in LS. The SOREMP’s in SS may suggest some SS experienced very little homeostatic build up with sleep deprivation. Overall, these data suggest that LS experience greater recovery than do SS on the first night after SD and extend this finding to REM sleep as well as SWS variables.

0443
Relationship Between Performance And P3 Variations Over Time During 37 H Of Total Sleep Deprivation And After Recovery Sleep
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Introduction: The P3 event-related potential can be employed to monitor cognitive changes related to different brain regions during sleep deprivation (SD). In the Go / No Go, the Go and the No Go conditions involve different cognitive processes. Moreover, the Go condition elicits a P3 that is maximal in parietal while the No Go condition elicits a P3 that is maximal in central-frontal. The aim of this study was to determine in what ways the variations in performance over a SD period and after RS are related to the variations in P3 elicited by two different cognitive processes.

Methods: The Go/No Go task was administered to eleven participants (18-26 yrs) after 1 h, 7 h, 13 h, 19 h, 25 h and 37 h of constant waking and following RS. EEG was recorded from Fz, Cz and Pz. Cross-Correlations were used to relate variation in performance (mean RT, misses, false detections) with P3 variations over time for the Go condition vs. the No Go condition.

Results: For the Go condition, mean RT was positively related with P3 latency at Fz (r = .88, p = .01), Cz (r = .94, p = .002) and Pz (r = .81, p = .03). For the No Go condition, false detections were negatively correlated with P3 amplitude at Fz (r = -.76, p = .05) and misses were positively correlated with P3 latency at Fz (r = .76, p = .05) and Cz (r = .78, p = .04).

Conclusion: The Go P3 latency changes at all electrode sites during SD were related to the global cognitive slowing induced by SD. In contrast, the No Go P3 latency and amplitude changes in the anterior region only were related to increased difficulty in inhibiting incorrect responses and in detecting correct responses. These results suggest that the Go P3 and the No Go P3 changes observed during SD reflect different cognitive deficits induced by SD.

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0444
Modafinil Activates Cortical And Subcortical Sites In The Sleep Deprived State
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Introduction: Modafinil is an effective countermeasure to performance decrements associated with sleep deprivation. The drug’s effects on brain neurocircuitry are not fully defined.

Methods: Brain activation patterns and regional signal intensity based on the blood-oxygen level dependent signal were assessed during performance of 1.2 and 3-back verbal working memory tasks. The following reaction times were used as measures of performance: 1) Attention in the scanner before functional scanning. 2) n-back during the active task block. 3) Attention during the baseline task block. Contrast of activation maps between conditions revealed sleep deprivation and drug effects and their interaction.

Results: Performance after sleep deprivation following treatment with modafinil was indistinguishable from that in the rested state, but associated with recruitment of increased cortical activation volumes. This was especially prominent in the 2-back condition. Speed was increased during the 2-back, but accuracy was increased during the 3-back task with the drug. On the 1-back task neither speed nor accuracy were increased. Contrast maps allowed differentiation of drug effect (minor increase in prefrontal activation), sleep deprivation effect (predominantly reductions in activation), and interactions (major new recruitment with drug used in the sleep deprived state). Across all conditions there was a strong linear relationship between activation in the medical wall and posterior parietal cortex. Thalamic activation that was virtually eliminated by sleep deprivation was restored by the drug.

Conclusion: Modafinil has complex cortical and subcortical effects when used humans. The effects are influenced by task load and the presence of sleep deprivation. Minimal effects in the rested condition may be consistent with the low abuse potential in clinical practice relative to amphetamines.

Cephalon, Inc.

0445
Effect Of REM Sleep Deprivation On IGF-I Levels In Rats
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Introduction: REM sleep deprivation interferes with normal memory. Decreased growth hormone (GH) levels are associated with memory impairment, and GH secretion is reduced during sleep deprivation. IGF-I is a major mediator of GH effects, and the hippocampus expresses IGF-I.
The goal of this study was to determine if circulating or hippocampal IGF-I was altered by REM sleep deprivation. Circulating corticosterone was measured to assay for any stress induced by sleep deprivation. 

**Methods:** Male Sprague-Dawley rats were subjected to REM sleep deprivation (RD) by individual confinement on a small circular pedestal above water. The loss of muscle tone during REM sleep caused the animals to contact the water and waken. Control (C) rats were confined to a larger pedestal and were able to sleep normally. RD and C rats were treated for 1, 3, or 5 consecutive days. Serum IGF-I, hippocampal IGF-I, and serum corticosterone levels were measured using ELISA.

**Results:** Circulating IGF-I levels were reduced (RD vs. C) at 1 and 3 days (p's<0.01, 0.05) but not at 5 days (p>0.50). For RD animals, there was a progressive decrease from day 1 to 3 (p<0.01) and day 3 to 5 (p<0.05). Control rats showed reduced IGF-I from day 1 to 3 (p<0.01), but not from days 3 to 5 (p>0.20). In contrast to circulating IGF-I, hippocampal IGF-I levels were not different over time or between RD and C animals (all p's>0.05). There was no difference in circulating corticosterone level between RD and C groups at any day (all p's>0.20), but for both groups there was a significant increase over days of treatment (p's<0.05).

**Conclusion:** Circulating, but not hippocampal, IGF-I levels were reduced by RD. Circulating IGF-I is a possible mediator for GH related effects of RD on hippocampal function. Stress, as measured by corticosterone levels, was not affected by RD.

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**0446**

**Short Sleepers: Behavior Or Biology?**


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**Introduction:** In today’s society, a majority of adults report that they do not get the recommended amount of 8-hour sleep time each night. The present study aims to determine if increasing time in bed can significantly increase actual sleep time in middle-aged adults without sleep complaints.

**Methods:** Eleven healthy men and women (mean age 42 years) participated in a bedtime extension study in which actual sleep time and sleep efficiency were measured using actigraphy in the home environment for 7 to 11 nights with usual sleep habits and for 8 to 16 nights in the laboratory environment with imposed extension of bedtimes by at least 2 hours. Inclusion criteria included habitual bedtimes of less than 6.5 hours per night. Sleep was extended during laboratory sessions by enforcing 8 to 8.5 hours in bed in total darkness. Laboratory bedtimes were determined using average bedtime data collected by actigraphy during home recordings.

**Results:** Actual sleep time increased by 71 minutes (habitual versus extended bedtimes: 362 ±20 min versus 433±12 min, p=0.02) during extended bedtimes while sleep efficiency (82±3% versus 84±2%) and number of awakenings (29±3 versus 36±5) did not change significantly.

**Conclusion:** Actual sleep time in middle-aged adults is significantly increased when bedtime is extended. Bedtime extension to 8 to 8.5 hours does not significantly affect sleep efficiency or the number of awakenings during the night. These findings suggest that many habitual short sleepers are curtailting bedtime behaviorally rather than following a natural biological trait.

**0447**

College Students’ Use Of “All-Nighters”: Prevalence And Correlates

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**Introduction:** Many college students complain of not having enough time to complete assignments, and some report the use of “all-nighters” as a coping mechanism. Little is known, however, about this practice, the specific reasons that prompt an “all-nighter,” or the differences between students who do or do not use this as an academic tool. This study examined prevalence and correlates of “all-nighters” in college students.

**Methods:** Undergraduate students were surveyed on their use of all-nighters and completed measures on stress, Morningness/Eveningness, and depression.

**Results:** 78 students participated (65% female; 32% freshmen, 33% sophomores, 24% juniors, and 11% seniors) after completing informed consents. Males and females were equally likely to report at least one all-nighter. About half of all students reported all-nighters; most gave academics as the reason. Students who reported all-nighters were significantly higher on the Morningness/Eveningness measure than those who had not (43.0 (8.5) vs. 38.9 (7.7), t = 2.53, p<.01). No differences between groups (all-nighter vs. no all-nighter) were noted for scores on the BDI or the stress measure.

**Conclusion:** Surprisingly, students scoring higher on Morningness/Eveningness were more likely to report the use of all-nighters. This finding is contrary to our hypothesis that “Owls” would be more comfortable with the late hours required of an all-nighter, and therefore would be more likely to use all-nighters as a way to accomplish academic work. Perhaps “Larks” are more likely to experience the period of 5 or 6 a.m. as less aversive, and may therefore be less likely to truncate the all-nighter by falling asleep, as Owls may decide to do at that point in their circadian cycle. Further research regarding academic performance, examining GPA or other objective measures of academic performance, is needed to determine if this approach is effective in approaching academic tasks.

**0448**

The Effects Of Sleep Deprivation In 192 IgG-Saporin-Treated Rats

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**Introduction:** 192 IgG-saporin is an antibody-neurotoxin complex that selectively destroys the cholinergic neurons in the basal forebrain (CBF). The aim of the present experiments was to study the significance of CBF in homeostatic sleep regulation by testing sleep responses to sleep deprivation (SD) in CBF-immunolesioned rats.

**Methods:** Rats implanted with EEG electrodes were injected with 192 IgG-saporin (4 ug, icv, n = 6) or a control solution (n = 6). Six weeks after the treatments, sleep was recorded on a baseline day. Next day, the animals were sleep deprived by gentle handling for the last 8 h of the light phase. After SD, the rats were placed back into their home cages and sleep was recorded for 23 h (recovery day).

**Results:** On the baseline day, there was no significant difference in NREMS or REMS of control and CBF lesioned rats across the 23 h recording period. The circadian distribution of NREMS was, however, slightly different between the two groups: during the dark phase, CBF-lesioned rats had significantly less NREMS than the controls and in the following light period NREMS was increased in the lesioned group. There was no significant difference between the sleep responses of control and CBF-lesioned to SD. During the first 12 h after SD, NREMS in CBF-lesioned rats increased from the baseline of 158 min to 302 min,
Introduction: Drowsiness is the second most important factor in motor vehicle crashes and as many as 62% of drivers have driven while drowsy. Two countermeasures have shown the greatest efficacy in reducing drowsy driving incidents: taking a brief nap and drinking caffeinated beverages. It is hypothesized that drivers’ willingness to use countermeasures depends upon the perceived effectiveness of and the effort involved in taking action.

Methods: Undergraduate students (40 males, 93 females, mean age 19 years) completed a series of questions rating 18 possible actions taken to counter the effects of sleepiness on driving. Participants indicated their willingness to take each action, inconvenience associated with implementing the action, and effectiveness of the countermeasure on separate scales ranging from 0 to 100. Higher scores indicate either greater willingness, more inconvenience, or greater effectiveness associated with each countermeasure.

Results: Participants reported an unwillingness to stop and nap if they felt sleepy while driving (M=31.76, SD=30.34). Napping ranked twelfth out of eighteen possible actions. Participants were most willing to “Turn up the radio” (M=79.89, SD = 21.64) or “Open a window” (M=77.92, SD = 23.05), which were rated as the most effective short-term actions. Napping (M=76.50, SD= 24.89) and drinking caffeinated beverages (M=52.76, SD = 25.60) were considered to be the most effective long-term actions but were also rated as inconvenient (M=83.80, SD=21.73; and M=50.37, SD=24.75 respectively).

Conclusion: Young drivers are aware of the long-term effectiveness of napping and caffeinated beverages in countering the effects of sleepiness on driving. However, drivers are more willing to use other countermeasures with greater perceived short-term effectiveness and are more convenient to implement. Such choices may place drivers in jeopardy as these countermeasures are of unknown or questionable efficacy.
Sleep Deprivation Changes Proteome Expression
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Introduction: Sleep deprivation (SD) might lead to cellular stress.
Methods: To detect expression changes after SD in human blood proteome generally and a Heat shock protein (Hsp) especially we used a Seldi-Tof-MS (Ciphergen) and a Stressgen Hsp70 ELISA-kit (EKS-700 Stressgen biotechnologies). We subjected humans (n=6) to 3 or 6 hours of SD and sampled blood during the 36 or 48h period/day before, during the SD night (first time after 3h or 6 h with or without sleep after 3h of SD) and the day after SD at the same time points (eight times during the 24h period). Difference in pre- and post SD (sleep deprivation) Hsp-70 levels were tested by using Wilcoxon signed ranks test. Significance was accepted at alpha level 0.05.
Results: The expression of a protein of 71 kDa was decreased in the blood (serum) 2h, 3h and 9h after 3h SD. Hsp-70 was also reduced 0h, 3h and 9h after 3h SD measured with the Hsp-70 Stressgen-kit. The data from the Seldi-Tof-MS (n=3) also showed changed expression in the range from 2.5 kDa to 100 kDa for several proteins, where proteins highly expressed (at basal level) seems to be reduced after SD and decreased however not to basal level the day or night after SD. Similarly proteins expressed at a lower level seems to be increased and thereafter reduced, however not to basal level the day or night after SD.
Conclusion: Several proteins ranging from 2.5 kDa to 100 kDa where differentially expressed after 3 and 6 hours of sleep deprivation, specifically Hsp-70 was reduced after 3 h of sleep deprivation. The decrease of many proteins as members of the heat shock protein family in the blood during sleep deprivation is in line with what has been observed in obstructive sleep apnea.

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0453
Sleep Duration And Self-Reported Illness In Twins
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Introduction: Sleep curtailment is common with 39% of people reporting less than 7 hours of sleep per night. Research suggests a link between short sleep time and mortality, cardiovascular disease, and diabetes mellitus. We used a co-twin control methodology to investigate the relationship between self-reported sleep duration and medical conditions in monozygotic and dizygotic twins.

Methods: The Vietnam Era Twin registry consists of 7,368 male-male monozygotic and dizygotic twin pairs. A health questionnaire was sent to 10,762 registry members in 1999. The response rate was 49.8% (5361 individuals, 1621 pairs). Twins were asked: On average, how many hours of sleep do you usually get in a 24-hour period? Responses included: 12 or more hours, 10-11 hours, 8-9 hours, 6-7 hours, 4-5 hours, less than 4 hours. Coronary heart disease, diabetes, hypertension/high blood pressure, stroke/cerebrovascular accident, and sleep apnea were ascertained by self-report. Obesity was estimated on a visual body shape scale. Twin pairs discordant for sleep duration with one twin sleeping less than 6 hours in an average 24-hour period were selected resulting in sample sizes ranging from 193 pairs for the obesity phenotype to 215 pairs for the hypertension phenotype. For each health condition, matched pair odds ratios and corresponding 95% confidence intervals (C.I.) were estimated and the McNemar Test was used to determine significance.

Results: The prevalence of sleep apnea among the shorter sleeping twins was 6.3% compared to 2.4% among the longer sleeping co-twins. No similar relationship was observed between sleep time and mortality, cardiovascular disease, and diabetes mellitus.

Conclusion: Twins with short sleep times revealed trends suggesting a greater propensity to have sleep apnea and hypertension than their longer sleeping co-twins. No similar relationship was observed between sleep duration and medical conditions in monzygotic and dizygotic twins.

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0454
Evaluation Of The Safety And Efficacy Of Eszopiclone In Patients With Obstructive Sleep Apnea
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Introduction: Some CNS medications used to treat insomnia in patients with obstructive sleep apnea (OSA) decrease respiratory drive and upper airway muscle tone, thereby increasing apnea episodes. The non-benzodiazepine, eszopiclone (ESZ), has demonstrated sleep onset and maintenance efficacy in patients with insomnia. This study evaluated the safety and efficacy of eszopiclone in OSA patients successfully treated with continuous positive airway pressure (CPAP).

Methods: This randomized, double-blind crossover trial included 21 patients (aged 35-64, mean 48) with an Apnea-Hypopnea Index (AHI) ≥10 and ≤40 who used CPAP nightly. On each of 2 PSG nights, patients randomly received treatment with ESZ 3mg or placebo (PBO) (5-7 day washout between visits). On PSG nights, patients did not use CPAP.

Results: No significant differences in OSA endpoints were found with the exception of spontaneous arousals not associated with a respiratory event. OSA Endpoints:* total AHI: PBO 16.5 (9.3), ESZ 16.7 (8.1), p=0.91; spontaneous arousals/hr: PBO 8.5 (5.6), ESZ 8.8 (6.1), p=0.61; spontaneous arousals/hr: PBO 13.6 (6.9), ESZ 11.4 (6.8), p=0.02; O2 saturation during apnea & hypopnea episodes (%): PBO 89.5 (1.9), ESZ 89.3 (2.0), p=0.54. With regard to hypnotic efficacy, eszopiclone significantly decreased wake time after sleep onset (WASO) and improved sleep efficiency versus placebo (p=0.01). Sleep Endpoints:* sleep efficiency (%): PBO 85.1 (6.3), ESZ 88.4 (5.4), p=0.01; WASO (min): PBO 61.8 (27.1), ESZ 48.1 (24.6), p=0.01; latency to persistent sleep (min): PBO 15.4 (10.0), ESZ 13.0 (12.2), p=0.45; awakenings (#): PBO 10.1 (3.2), ESZ 9.5 (4.6), p=0.43. The eszopiclone group also experienced significantly less cumulative wake time than placebo at post-dose hours 2-8 (p<0.05). The most common adverse events in the eszopiclone group were unpleasant taste (6 patients) and cold/flu-like symptoms (2 patients).

Conclusion: In this study, eszopiclone did not adversely affect sleep-disordered breathing and was well tolerated. Eszopiclone also demonstrated hypnotic efficacy as defined by significant improvements in sleep efficiency and WASO. *Means 2 nights (SD)

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0456
Familial Premature Coronary Artery Disease Mortality And Obstructive Sleep Apnea
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Introduction: Obstructive sleep apnea (OSA) is associated with cardiovascular disease, including coronary artery disease (CAD). A family history of premature CAD is an independent risk factor for the development of CAD. CAD and OSA aggregate in families. We hypothesized that OSA is associated with a family history of premature CAD mortality.

Methods: We performed a prospective study of 588 individuals from January 2000 to June 2004. We excluded individuals with established familial cardiovascular risk (long QT syndrome or hypertrophic cardiomyopathy). Each subject had complete overnight diagnostic polysomnography. Study personnel interviewed each subject using a standardized form to collect demographics, comorbidities, and a detailed family history of cardiovascular diseases and the ages and causes of death for the biological mother, father, brothers, sisters, sons, daughters, maternal grandmothers and grandfathers, and paternal grandmothers and grandfathers. “Premature CAD mortality” was defined as death due to CAD, myocardial infarction, or sudden death before (but not including) age 55 in men and age 65 in women. OSA was defined by the polysomnographic criteria of the American Academy of Sleep Medicine (apnea-hypopnea index ≥5). Group characteristics were compared by the 2-tailed t-test and chi-square test. Logistic regression models provided the unadjusted and adjusted odds ratios for the association of OSA with a family history of premature CAD mortality.

Results: There were 518 subjects in the study sample, after excluding 17 subjects with incomplete family history or polysomnographic data and 53 subjects with long QT syndrome or hypertrophic cardiomyopathy. The OSA group had 316 subjects, and the non-OSA group had 202 subjects. The unadjusted odds ratio for OSA and family history of premature CAD mortality was 2.11 (95% CI, 1.10 to 4.31, p=0.031). After adjusting for gender, obesity, and a personal history of CAD, the odds ratio for OSA and family history of premature CAD mortality was 2.13 (95% CI, 1.04 to 4.66, p=0.046).

Conclusion: A significant and independent association exists between OSA and family history of premature CAD mortality. This relationship further demonstrates the heightened risk of cardiovascular diseases in patients with OSA and implicates familial or genetic mechanisms independent of known risk factors.

0457
The Positional Difference Of Neck Circumference Between Sitting And Supine Position Correlates Independently With The Severity Of The Obstructive Sleep Apnea
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Introduction: A large neck circumference is one of the best predictor for obstructive sleep apnea, since this reflects central obesity and fat around the neck more than BMI. The difference of neck circumference between sitting and supine position could reflect the amount of redundant tissue around the neck. To our knowledge, this is the first study investigating the relationship between the difference and obstructive sleep apnea.

Methods: Patients who had a supervised nocturnal polysomnography at Kings County Hospital were enrolled in the study. The neck circumference was measured in both sitting and supine position at the cricoid cartilage level perpendicular to the long axis of the neck. Their baseline characteristics and the results of the polysomnography were recorded.

Results: 180 patients were included in the study (92 male, 88 female, 73% black). Their baseline characteristics were the following (mean ±SD): mean age; 47.1 ±13.1 year-old, weight; 254.1 ±67.7 lbs, height; 66.0 ±4.1 inches, BMI; 41.2 ±11.5, neck circumference in sitting position; 17.3 ±1.9 inches, and the difference in neck circumference; 0.84 ±0.64 inches. Their mean apnea-hypopnea index (AHI) was 30.5 ±33.0 in the polysomnography. Pearson correlation showed that the positional difference correlates with AHI [+0.24, p<0.001]. The positional difference remains as a significant predictor of AHI even after controlling for BMI, age, gender and the neck circumference at sitting position with multiple linear regression [p=0.008]. The positional difference was also a risk factor for the presence of significant obstructive sleep apnea with AHI >15 [unadjusted odds ratio = 1.79, p=0.022]. However, this was not statistically significant after controlling with other variables [adjusted odds ratio = 1.71, p=0.07].

Conclusion: The positional difference of neck circumference between sitting and supine position correlates independently with the severity of the obstructive sleep apnea even after controlling with other risk factors.

0458
Newly Identified Obstructive Sleep Apnea In Hospitalized Patients: Is There A Role For Autoadjusting CPAP?
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Introduction: Obstructive sleep apnea (OSA) case-finding in hospitalized patients is not uncommon. Inpatient polysomnography (PSG) is often impractical. However, the time to outpatient PSG may be long. Untreated, OSA is associated with a number of adverse consequences. Autoadjusting CPAP (ACPAP) titration is an option for early initiation of therapy. We hypothesized that a protocol utilizing ACPAP titration would improve short term outcomes in newly identified cases of OSA in hospitalized patients.

Methods: Retrospective chart review of patients admitted to the hospital between January 1999 and August 2004 identified as likely to have OSA by clinical history and overnight oximetry. Patients were split in two groups: intervention and control. The intervention group consisted of patients who had an oxygen desaturation index (ODI) ≥ 10 by overnight oximetry, were titrated to a fixed CPAP pressure using ACPAP, discharged on CPAP, and had an outpatient PSG. The control group consisted of patients who had an ODI ≥ 10, were discharged without CPAP (90% discharged on oxygen), but had an outpatient PSG. Parameters between groups were analyzed using the t-test; a p-value < 0.05 was considered statistically significant.

Results: Sixty-two patients satisfied the inclusion criteria for each of the intervention and control groups. The two groups were matched for demographic variables, socioeconomic status, co-morbid conditions, admission diagnoses, and oximetry parameters (including ODI). In the intervention group, ACPAP improved oximetry parameters but did not normalize them (ODI decreased from 30.8 to 12.5). There were no differences between the two groups in length of hospital stay or time to outpatient PSG (mean 79 days). The apnea-hypopnea index was almost identical between the intervention and control groups at outpatient PSG (59.4 and 60.0 respectively). No significant differences between the two groups were found in the number of hospitalizations, emergency room visits, or urgent care visits its pending outpatient PSG. ACPAP pressure correlated with PSG CPAP pressure in only 19% of patients. ACPAP underestimated the optimal pressure.
pressure in 60% of patients (9.7 vs. 13.7, p<0.0001) and the remaining 21% required bilevel positive airway pressure for optimal control.

Conclusion: Compared to oxygen support or no therapy, an ACPAP titration protocol does not appear to improve short term health outcomes in newly identified cases of OSA in hospitalized patients. ACPAP may also underestimate optimal treatment settings.

0459
Reduction In Depressive Symptoms And Sleep-Related Impairment Following Continuous Positive Airway Pressure Therapy
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Introduction: There is an increased prevalence of depressive symptoms in patients with OSA. Previous studies have shown contradictory findings about the effect of CPAP on depressive symptoms.

Methods: A sample of 61 patients with OSA documented by PSG was recruited (BMI = 39.9 (±10.9), AHI = 36.1 (±31.7), age = 47.1 (±12.4), 57% male, 55.7% Caucasian, 41% African American). Participants completed the Beck Depression Inventory (BDI) and the Functional Outcomes of Sleep Questionnaire (FOSQ) the evening before the PSG. Patients were contacted 2 to 6 weeks after receiving CPAP and the FOSQ and BDI were administered over the phone. Adherence data were electronically recorded.

Results: For all participants, CPAP was used for 77% of the nights, for an average of 264 (±147) minutes/night. FOSQ scores significantly improved from 14.9 to 17.6 during follow-up (t = -.59, p < .0001). BDI scores also significantly improved from 12.3 (±9.3) to 6.1 (±8.4) (t = -5.2, p < .0001). This improvement remained significant when 3 sleep and fatigue related items on the BDI were excluded from the analysis (t = 4.5, p = .0001). When a median split was performed on the adherence scores, the more adherent group had significantly greater improvement in BDI scores (t = 2.07, p = .04) and FOSQ scores (t = -3.4, p = .001) than the less adherent group.

Conclusion: CPAP therapy is associated with the amelioration of depressive symptoms and sleep related impairment. Amount of CPAP use is associated with the degree of improvement in self-reported sleep impairment and depressive symptoms.

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0460
Relationship Between Quality Of Life Impairment And Daytime Sleepiness Using The Epworth Sleepiness Scale Or A Clinical Score Of Daytime Sleepiness In Patients With Sleep-Disordered Breathing
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Introduction: Quality of life (QoL) impairment and daytime sleepiness (DS) are common features of sleep-disordered breathing. In recent years the Epworth Sleepiness Scale (ESS) is widely used in the assessment of DS. Besides ESS, a careful assessment of the complaint sleepiness is part of the clinical workup performed by sleep specialists. The purpose of this investigation was to compare the ESS and a clinical score of sleepiness determined by a sleep specialist in the prediction of QoL impairment in patients with sleep-disordered breathing (SDB).

Methods: We designed a retrospective investigation of all patients (n=1244) referred between January 2001 and November 2004 for diagnosis of SDB. Prior to undergoing standard polysomnography ( PSG) patients filled out a 7 item visual analog scale for the assessment of QoL and the ESS. In addition, patients received a structured clinical history. Daytime sleepiness from clinical history (CHS) was rated in 4 categories. One-way analysis of variance and regression analysis were used to describe the relationship between QoL, the two measures of sleepiness, and polysomnographic variables.

Results: Mean age, BMI, and RDI were 50.2±12.0 years, 28.0±4.5 kg/m2, and 19.6±19.3, respectively. ESS score averaged 8.4±4.5, and the QoL score 0.58±0.21. The relative percentages for CHS categories were 19% for ‘normal’, 10% for ‘mild’, 22% for ‘moderate’, and 49% for ‘severe’. A significant correlation between ESS and CHS (0.4296; p=0.000) was noted. Correlations of ESS and CHS were R= 0.5305 and R=-0.2927 respectively. Of all PSG, and demographic variables only RDI and age entered models explaining QoL scores in combination with the two sleepiness scores. Using CHS 30% of the variance in QoL could be explained as opposed to 11% using ESS scores.

Conclusion: A clinical history of daytime sleepiness appears to be a better determinant of QoL impairment in patients with SDB than the ESS.

0461
Association Of Physical Activity With Sleep Disordered Breathing
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Introduction: Empiric observations suggest that individuals with sleep-disordered breathing (SDB) are not very physically active. However, evidence linking lack of physical activity as a causal factor for the development of SDB independent of obesity is limited. The purpose of this analysis is to determine the relationship between polysomnographic SDB and measures of physical activity in the Sleep Heart Health Study (SHHS).

Methods: Between November 1995 and January 1998, 6441 individuals underwent unattended polysomnography (PSG) as part of SHHS. The severity of SDB was expressed by the number of apnea and hypopnea events per hour associated with at least a 4% oxygen desaturation (RD14%). Various markers of physical activity were evaluated using data from SHHS parent cohorts as well as quality of life (SF36) data collected in conjunction with the PSG. The association between several categories of RD14% and various markers of physical activity was modeled using logistic regression controlling for age, BMI, self-reported cardiovascular and obstructive lung disease, gender, marital status and parent cohort.

Results: Progressively more severe SDB (RD14%: <5 [referent], 5-15, 15-30 and >30) was related to climbing < 1 flight of stairs/day with adjusted odds ratios (95% CI) of .91 (.73-1.13), 1.12 (.83-1.51) and 1.48 (1.01-2.16), (n=3463). Similarly, adjusted odds ratios for severe limitation in ability to engage in vigorous activity were 1.04 (.89, 1.22), 1.22 (.98-1.50) and 1.44 (1.09-1.91), (n=4685), and for severe limitation in walking at least 1 mile were 1.06 (.87-1.31), 1.23 (.93-1.62) and 1.62 (1.16-2.27), (n=4685). Limitation of the analysis sample to those who were in at least 21% required bilevel positive airway pressure for optimal control.

Conclusion: SDB is associated with reduced amounts of physical activity independent of obesity.
0462

Prevalence Of Concomitant Sleep Disorders In Patients With Obstructive Sleep Apnea (OSA)

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Introduction: Patients with OSA may have other sleep related disorders as well. This could impact on the need for sleep specialists to be involved in their care. Few data exist as to the nature and prevalence of other sleep related disorders in patients with OSA.

Methods: To determine the prevalence of concomitant sleep disorders in patients with a primary diagnosis of obstructive sleep apnea (OSA) we performed a retrospective review of 643 patients, age >18 with a primary diagnosis of OSA, evaluated by sleep specialists, in whom clinical and polysomnographic data were derived using standardized techniques. Concomitant sleep disorders were classified according to International Classification of Sleep Disorders.

Results: Demographics: age: 48.5+13.5 years, 55% male, 51.8% African-American, 47% Caucasian, respiratory disturbance index (RDI) 32.4+30.4, time < 90% O2 saturation (T90) 44.5+81.6 min. 31% of patients had a concomitant sleep disorder. Most common were Inadequate Sleep Hygiene (14.5%) and Periodic Limb Movement Disorder (PLMD - 8.1%). 66.8% of patients with other sleep disorders had treatment initiated. Predictors of Inadequate Sleep Hygiene (logistic regression) were: age (each decade OR=.678, p=.000000), gender (OR for M = .536), and the presence of at least one other major system disorder (OR = 2.123, P = .0015). Predictors of PLMD were: age (each decade OR = .794, P=.0005), gender (OR for M = .433, p =.004) and Total Sleep Time (for each 10 minutes, OR = .972, P = .0013).

Conclusion: Almost 1/3 of OSA patients have another sleep disorder. Adequate access to and involvement of sleep specialists in the care of OSA patients is advisable in a large minority of OSA patients.

0463

Lowering The Threshold Of Hypoxemia In Sleep-Disordered Breathing As A Predictor Of Impaired Metabolic Function

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Introduction: Hypopneas are usually based on identifying breathing abnormalities during sleep that are accompanied by an oxygen desaturation of at least 4% or an arousal. However, it is not known if hypopneas defined using a lower threshold of desaturation severity are associated with adverse outcomes. Data from the Sleep Heart Health Study (SHHS) were used to investigate whether hypopnea-associated desaturations of less than 4% were associated with prevalent fasting hyperglycemia.

Methods: SHHS participants were examined if fasting glucose was measured within a year of polysomnography (n=2,636). The hypopnea index (HI) was calculated using each of three levels of oxyhemoglobin desaturation (0 to 1.9%, 2.0 to 2.9%, and 3.0 to 3.9%). Individuals were classed based on fasting glucose levels into normal (<100 mg/dl), impaired fasting glucose (100-125 mg/dl), and diabetic (>126 mg/dl) groups. Ordinal logistic regression was used to determine whether the odds of glucose dysmetabolism increased across quartiles of the HI, independent of age, gender, body mass index, waist circumference, self-reported usual sleep duration, alcohol consumption, and smoking status. In addition, adjustments were made for the apnea-index and HI employing a desaturation criterion above each threshold under examination.

Results: The prevalence of impaired fasting glucose and diabetes was 32.9% and 5.8%, respectively (mean age, 67.6 years). The covariate-adjusted relative odds of worse glucose dysmetabolism in the highest compared to the lowest HI was 2.22 (95% CI=1.61, 3.05) at a desaturation level of 3.0-3.9%, 1.56 (95% CI=1.19-2.05) at the 2.0-2.9% desaturation level, and 1.18 (95% CI=0.93-1.51) at the 0.0-1.9% desaturation level.

Conclusion: The results of this study indicate that hypopneas during sleep defined by an oxygen desaturation of 2-4% are associated with increased odds of fasting hyperglycemia. These cross-sectional findings suggest that milder sleep-disordered breathing may predispose to adverse outcomes. Further research is needed to study the effects of less severe desaturations on cardiovascualr morbidity and mortality.
0465 Vigilance And Associated Variables In Obstructive And Central Apnea Syndromes

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Introduction: Excessive daytime sleepiness is a common manifestation of sleep apnea syndrome. There is some controversy as to the cause of impaired daytime vigilance in those patients. The aim of the present study was to assess nocturnal hypoxemia and daytime vigilance in patients with obstructive (OSAS) and central (CSAS) apnea syndromes.

Methods: 18 OSAS patients (32 to 67 y), 13 CSAS patients (24 to 61 y) and 13 controls (33 to 65 y) were studied for one night in the sleep laboratory by means of an oro-nasal thermistor or a canula and thoraco-abdominal strain gages. Both group of patients had an apnea-hypopnea index (AHI) > 10 (mean 37.6 in OSAS and 16.9 in CSAS). Participants completed the Epworth Sleepiness Scale (ESS) in the evening and performed a psychomotor task (Four Choice Reaction Time Test or FCRTT) at 09h30, 11h30, 13h30, 15h30 on the next day.

Results: OSAS and CSAS patients were obese (mean BMI 36.1 and 29.6 respectively) and both presented a high level of subjective sleepiness (ESS 14 and 13) compared to the controls (mean BMI 24, ESS 6). OSAS patients had more oxygen desaturation than CSAS patients. No correlation was found between ESS and other sleep or respiratory variables except for a positive correlation with the micro-arousal index in CSAS only. Positive correlations were found between the FCRTT and both desaturation values and obstructive + mixed apnea index for the OSAS whereas in the CSAS results the FCRTT were correlated with total sleep time, percentage of stage 1 and of REM sleep.

Conclusion: Both OSAS and CSAS groups presented an increased subjective sleepiness and a decrease in psychomotor performance. Psychomotor performance is associated with measures of disordered breathing in OSAS while it was more closely associated with measures of sleep disruption in CSAS group.

0466 A New Screening Tool For Preoperative Screen Of Sleep Apnea

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Introduction: The definitive diagnosis of sleep apnea requires expensive, time consuming sleep studies. Such studies cannot be used for risk assessment when large numbers of patients need to be screened before surgery. Questionnaire based assessments of sleep apnea risk (such as the Berlin questionnaire) have been developed, but may be too cumbersome for routine use. No screening tool has been designed specifically for use in preoperative patients. A new short form screening tool, the sleep apnea preoperative screen (SLAPS) was devised based on literature review and clinical experience. This study examines how the SLAPS questionnaire compares with the Berlin questionnaire.

Methods: The Berlin questionnaire consists of nine items regarding snoring, witnessed apneic events, daytime sleepiness and falling asleep whilst driving. Physical data regarding blood pressure and body mass index are also recorded. It has been validated in the primary care setting and has demonstrated a sensitivity and specificity of 0.86 and 0.77 respectively for identifying patients with >5 respiratory events per hour. The sleep apnea preoperative screen (SLAPS) contains four questions: Has anyone noticed that you stop breathing during sleep; Do you snore loudly; Do you feel tired during the daytime almost every day; Are you under 50 years of age with hypertension. These are four of the nine questions of the Berlin questionnaire. Hypertension is defined as systolic > 140mmHg or diastolic > 90mmHg or receiving antihypertensive treatment. Based on this information, patients are stratified into high or low risk groups. The responses of 318 patients to the SLAPS and Berlin questionnaire were analyzed and compared.

Results: The Berlin questionnaire identified 23.9% of all patients as being at high risk of sleep apnea. For the SLAPS questionnaire, this figure was 11%. Ten patients in the study had been previously diagnosed with sleep apnea.

Conclusion: A new short screening tool (the SLAPS questionnaire) identified 11% of preoperative patients as being at high risk of sleep apnea, 50% fewer than the Berlin questionnaire. Further work is required to determine which test is more valid in the preoperative setting.
0469
Mortality Risk Factors In Men With Sleep Apnea: A Matched Case Control Study
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Introduction: There is a large body of evidence linking obstructive sleep apnea (OSA) with increased cardiovascular morbidity, but there is less information if it is associated with mortality. In this paper, we report on a case-control study of mortality in sleep apnea patients based on a sleep laboratory population.

Methods: Our study population consisted of adult men studied during 1991-2000 by polysomnography because of suspected OSA. Their vital status was determined by searching the Israel National Population Registry. Cases were defined as men who died prior to 1st September 2001. For each case, a living control matched by year of birth, time and place of sleep examination, and reason for conducting the sleep study, was selected from the study population. The association of demographic, sleep laboratory findings and medical history data with mortality risk was investigated through conditional logistic regression.

Results: 14,984 patients were studied because of suspected OSA during the study period, 481 of whom died prior to 1 September 2001. 353 of them (74%) could be matched with controls. The best fitting multivariate model showed that increased risk of mortality was associated with chronic obstructive pulmonary disease (OR: 9.03, 95% CI 3.72, 21.93), chronic heart failure (OR: 4.75, 95% CI 1.17, 19.27), cerebrovascular accident (OR: 4.88, 95% CI 1.30, 18.33), diabetes (OR: 2.96, 95% CI 1.43, 6.14), ischemic heart disease (OR: 1.89, 95% CI 1.08, 3.29) and BMI (OR: 1.66, 95% CI: 1.23, 2.25). When models with interactions were fitted, significant interactions were found between apnea-hypopnea-index and BMI and lung disease.

Conclusion: Our observations suggest that OSA mainly contributes to mortality by being the possible cause of the disease process resulting in cardiovascular morbilities, which then become the proximal causes of death. To prevent cardiovascular morbidity OSA diagnosis should be made at the youngest age possible.

0470
Adherence To Continuous Positive Airway Pressure Treatment Varies Seasonally In Sleep Apnea/Hypopnea
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Introduction: Since nCPAP is not a radical therapeutic method, the success of nCPAP is dependent on regular use. Although the timing and duration of sleep and the ambient temperature varies seasonally in countries with four seasons, there is no reported investigation of seasonal variation in adherence to nCPAP. To investigate whether seasonal variations in nCPAP adherence exist, nCPAP adherence indices were investigated.

Methods: We investigated indices including usage rate, mean time of usage, and proportion of days with 4-hour or greater usage for each month from June, 2003 to May, 2004 among 65 obstructive sleep apnea hypopnea syndrome patients.

Results: The mean usage rate was lowest in September, at 85.6%, and highest in April, at 90.1%. The mean duration of use was shortest in August, at 265 minutes, and longest in March, at 315 minutes. The mean proportion of days with 4-hour or greater usage was lowest in August, at 62.2%, and highest in March, at 75.1%. These indices demonstrated significant monthly variation in each case (P<0.01). The proportion of an nCPAP good-adherence group was lowest in September, at 45.0%, and highest in March, at 75.1%. The proportion of good-adherence group was lowest in September, at 45.0%, and highest in March, at 75.1%. We observed a pattern in which nCPAP adherence was worst in August-September, improved gradually thereafter, and was best in March-April.

Conclusion: Our investigation demonstrated distinct seasonal variation in nCPAP adherence, and it is possible that nCPAP adherence varies due to changes in daylight hours and ambient temperature.
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Introduction: Obstructive sleep apnea (OSA) is a risk factor for several conditions such as hypertension, glucose intolerance, pulmonary hypertension and cor pulmonale. The effect of these comorbidities on CPAP level needed to correct OSA is uncertain. To evaluate this relationship, we conducted a retrospective chart review study to detect any possible correlation between the optimal CPAP level and other co-morbidities - specifically - congestive heart failure (CHF), diabetes mellitus (DM) and hypertension (HTN). We also evaluated the effect of age on optimal CPAP level.

Methods: Charts of patients diagnosed with OSA at the University of Missouri Sleep Disorder Center over last from 2001 to 2004 were reviewed. 89 patients (23 females and 66 males) with age range (27-79 years) with these co-morbidities were included in the study. Patients with OSA who were treated with BiPAP were excluded from the study. We accepted optimal CPAP level which reduces apnea / hypopnea index (AHI) to less than 10/hour-majority less than 5/hour. The results were analyzed with Wilcoxon Rank Sum test and Spearman Correlation Coefficient between age and CPAP level.

Results: There was insignificant trend towards higher CPAP level in hypertensive patients (12.9 cm of water in hypertensive patients vs. 12.0 cm of water in normotensive patients) and lower CPAP levels in diabetic patients (11.0 cm of water in diabetic patients vs. 12.9 cm of water in non diabetic patients, with p=0.09). Age was inversely related (CPAP= -0.18xAge + R; where R is steady factor) to optimal CPAP level (r=0.45, p<.0001). The presence of CHF did not affect optimal CPAP level.

Conclusion: Optimal CPAP level is inversely related to age. DM resulted in trend towards lower CPAP level while HTN resulted in trend towards higher CPAP level though these trend were statistically insignificant. Presence of CHF did not have any effect on CPAP level.

0472 Effects Of Two-Weeks Nocturnal Oxygen Supplementation And Continuous Positive Airway Pressure Treatment On Psychological Symptoms In Patients With Obstructive Sleep Apnea: A Randomized Placebo-Controlled Study

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Introduction: Improvement in psychological symptoms has been reported as a result of continuous positive airway pressure (CPAP) treatment in obstructive sleep apnea (OSA) patients. We examined whether nocturnal oxygen supplementation would also affect psychological symptoms and how such effects would compare with those of CPAP treatment or placebo-CPAP.

Methods: 38 untreated OSA patients (mean apnea/hypopnea index (AHI)=62.3; SD±31.4) were monitored for two nights with polysomnography, then randomized to nocturnal oxygen supplementation (3 L/min), CPAP treatment or placebo-CPAP for two weeks. Placebo-CPAP consisted of CPAP delivered at insufficient pressure (<1cm of water). Before and after treatment, the patients completed the 53-item Brief Symptom Inventory (BSI), a widely-used self-report measure of psychological symptoms. The BSI yields nine psychological symptom subscales (depression, anxiety, hostility, phobic anxiety, paranoia, psychoticism, somatization, obsessive-compulsive, interpersonal sensitivity) that can be summarized into a Global Severity Index. Higher scores indicate more symptoms.

Results: Repeated measures analysis of covariance (controlling for OSA severity: AHI and % of time that oxyhemoglobin levels fell below 90% of capacity) revealed a time X treatment interaction for the BSI Global Severity Index (p=0.038). Post-hoc analyses showed significant pretreatment effects for oxygen supplementation (0.38 vs. 0.19, p=0.008) and CPAP (0.29 vs. 0.17, p=0.036), but not placebo-CPAP (0.35 vs. 0.37, p=0.687). When examining BSI subscales, only Depression showed a significant time X treatment interaction (p=0.008). Post-hoc analyses revealed a significant pre- to post-treatment effect for oxygen supplementation (0.40 vs. 0.18, p=0.025) but not for CPAP (0.29 vs. 0.19, p=0.171) or placebo-CPAP (0.42 vs. 0.56, p=0.210).

Conclusion: Both CPAP and oxygen supplementation resulted in a decrease in overall severity of psychological symptoms, with oxygen supplementation showing a greater effect. However, specific to depression, only oxygen supplementation resulted in symptom improvement. Results suggest that hypoxemia may play a stronger role than sleep disruption in explaining the psychological distress reported by some OSA patients.

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0473 The Frequency Of Premature Ventricular Contractions (PVCs) In Patients With Obstructive Sleep Apnea-Hypopnea Syndrome (OSAHS) After CPAP Treatment

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Introduction: Various arrhythmias have been identified in patients with obstructive sleep apnea-hypopnea syndrome (OSAHS) during polysomnography (PSG) examination. After CPAP treatment, the frequency of the arrhythmia observed in these patients changes. The purpose of this study is to determine how the nocturnal arrhythmias change, particularly premature ventricular contractions (PVCs), in the patients with OSAHS after CPAP treatment.

Methods: We analyzed 144 patients in whom arrhythmias such as PVCs, atrial fibrillation (af), atrial-ventricular block (AV block), and sinoatrial block (SA block), were observed. Between 2002-2004, we carried out nocturnal PSG examinations on 1630 patients. The frequency of PVCs is referred to as the number for 1 hour sleep (PVC index). We divided the PVC index into PVCs < 1, 1 < PVCs < 30, 30 < PVCs. We determined the change of PVCs in apnea-hypopnea index (AHI), sleep efficiency, arousal index, and desaturation between baseline PSG and CPAP titration.

Results: (1) The appearance rate of arrhythmia was 5.9%, 0.4%, 1.5%, and 0.6% in PVCs, af, AV block, and SA block, respectively. (2) Analysis of the PVC index (PVCs < 1, 1 < PVCs < 30, 30 < PVCs), indicates a significant relationship between the PVC index and AHI, arousal index, and desaturation. (3) In patients with PVCs, the frequency of the PVC index was unchanged in 14 patients (23%), had improved in 29 patients (47.5%), and had deteriorated in 18 patients (29.5%), after CPAP treatment.

Conclusion: The date from our study indicates that the appearance of nocturnal PVCs is associated with the severity of sleep apnea-hypopnea. However, the frequency of PVCs in some OSAHS patients is increased after CPAP treatment.

0474 Determinants Of Central Apneas In Patients With Sleep-Disordered Breathing

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Introduction: Research has shown that men are more susceptible to the development of central apneas compared to women under research conditions, suggesting that gender differences in the control of ventilation may explain the increased prevalence of sleep-disordered breathing (SDB) in men. It is unclear if this physiologic finding translates into a clinical finding of increased central apneas in men presenting for evaluation of SDB. Hypothesis: men are more likely than women to have an increased central apnea index on polysomnography.

Methods: Database review of 773 patients diagnosed with sleep apnea (AHI ≥ 5) between 8/2001 and 7/2004. Records were reviewed for gender, age, body mass index (BMI), neck circumference (NC), co-morbidities including hypertension, heart disease, diabetes mellitus and tobacco use, apnea-hypopnea index (AHI), central apnea index (CAI), and obstructive apnea index (OAII). Patients were divided into two groups: Group 1, CAI≥5/hr (n=91), Group 2, CAI<5 (n=682). Demographic and comorbid parameters and indices of SDB were compared between the groups. Multivariate logistic regression was performed to determine the independent predictors of the presence of a CAI ≥5/hr.

Results: Group 1 patients were more likely to be male (60.4% vs. 37.0%, P<0.001). NC was larger in Group 1 patients (44.1±5.1 cm vs. 41.9±5.1 cm, Group 2, p<0.001) but there was no difference in either age (48.0±14.9 yrs v. 50.1±13.0 yrs) or BMI (41.3±10.2 kg/m² v. 41.1±11.5 kg/m²). Both AHI (111.3±71.9 v. 51.4±49.8, p<0.001) and OAI (68.1±61.3 v. 36.7±45.9, P<0.001) were increased in Group 1 compared to Group 2. The prevalence of comorbidities did not differ between the two groups. After multiple logistic regression, gender (OR 2.00, p=0.012), AHI (OR 1.04, p=0.001) and OAI (OR 0.97, p=0.001) but not NC were found to be independent predictors of a CAI ≥5/hr.

Conclusion: Men are twice as likely to demonstrate central apneas on polysomnography than women, consistent with the research finding of an increased susceptibility to the development of central apnea. Central apneas are also more likely in patients with increased overall AHI, suggesting that all types of SDB are more common in patients with severe disease.

0475
Gender Differences In The Presentation Of Sleep-Disordered Breathing In Old Age
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Introduction: This study describes gender differences in the correlates of SDB among community dwelling older adults ≥ 65 years of age.

Methods: Community dwelling older adults (N= 108) were recruited. Demographic, health and sleep related information were collected using a questionnaire. Nocturia frequency was determined using 72-hours voiding diary. Ambulatory sleep recording was obtained using Embleda PDS (Medicare, Iceland). Sleep-disordered breathing (SDB) was diagnosed when apnea-hypopnea index (AHI) was ≥ 15 per hour of sleep.

Results: Ninety-four subjects (87%) completed the study. Mean age was 77.1 ±6.5 years and sixty-seven (71%) were women. Thirty subjects (32%) had AHI ≥ 15 (15 men and 15 women). Women with SDB were more likely to complain of not feeling well rested in the morning (p=.005), whereas men with SDB complained of difficulty going back to sleep after waking up from sleep (p = .024). Females with SDB had significantly higher Epworth Sleepiness Scale (ESS), as compared to those without SDB (9.2 ± 4.8 vs. 5.1 ± 2.6, p=.006); there was no significant difference in ESS scores in men with and without SDB. Women without SDB tended to have more nocturia episodes as compared to men (1.7 ± 0.9 vs. 1.1 ± 1.0, p=.059). Only among men, nocturia frequency differentiated those with and without SDB (2.1 ± 0.7 vs. 1.1 ± 1.0, p=.006); in women this comparison was NS.

Conclusion: Elderly women with SDB experienced more daytime symptoms (higher ESS, more AM tiredness), whereas in elderly men with SDB, nighttime symptoms predominated (nighttime voids, difficulty returning to sleep). Better identification of SDB in old age should take into account differences in clinical presentation among females and males. The lack of association between SDB and nocturia among females may indicate the significance of other co-morbidities (competing etiologies) in the relationship between these two conditions.

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0476
Assessment Of Arterial Compliance In Obstructive Sleep Apnea
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Introduction: Obstructive sleep apnea (OSA) has been linked to hypertension (HTN) in cross sectional epidemiological studies. However, the mechanism of HTN in OSA continues to be under investigation. One theory holds that decreased arterial compliance is associated with HTN. Therefore, it is the objective of this study to determine whether arterial compliance is diminished in those with OSA compared to their controls.

Methods: A total of 32 subjects (16 newly diagnosed OSA and 16 controls) participated in the study. Subjects with OSA were recruited from the sleep laboratory based on overnight polysomnography. Control subjects were given a sleep habits questionnaire to rule out OSA, though polysomnography was not done. Non-invasive measurement of blood pressure (BP), heart rate (HR), small artery elasticity index (SAEI) and large artery elasticity index (LAEI) were obtained using the HDI/Pulse Wave CR-2000 machine. With the subject lying comfortably in a quiet room, BP cuff was applied to the left arm while the arterial pulse sensor was placed over the right radial pulse. Three readings were obtained from the arterial waveform generated to ascertain reproducibility of data. Analysis was done using unpaired t-test. Results were reported as mean±SD.

Results: OSA and control groups were matched for age, gender and BP. None of the subjects were smokers. The mean respiratory disturbance index in those with OSA was 38±29/hour with mean oxygen saturation nadir of 83±9%, and mean sleep efficiency of 68±11%. There were no differences in the OSA vs control group with regards to age (52±10 vs 52±11 yrs), gender (female=6, male=10) and BP (SBP=129±16 mmHg, DBP=75±11 mmHg vs SBP=129±11 mmHg, DBP=75±12 mmHg, p=ns). Compared to controls, subjects with OSA were found have significantly higher weight (233±56 vs.188±19 lbs, p<0.006), body mass index (34.4±7 vs. 27.2±2 kg/m², <0.001), HR (78±17 vs 61±7 bpm, p<0.002) and lower SAEI (5.6±2.3 vs 7.4±2.7, p<0.05). LAEI was similar between the two groups. All group analysis further revealed that subjects with OSA were found to have lower SAEI independent of weight or body mass index.

Conclusion: In conclusion, we found that SAEI is reduced in subjects with OSA. This may be indicative of increased small artery stiffness. Also, increased heart rate in those with OSA may reflect heightened sympathetic activity. These factors, in addition to obesity, may be the pathophysiologic mechanism of hypertension in this population.
REM sleep deprivation (REMD) following training using the swimming protocol. Identically trained groups (n=10/group) were subjected to 24 hours of non-contingent tone-shock pseudo-conditioning groups. Three more groups were added after training: 1) Normal conditioning, 2) Non-shock conditioning and 3) No training. 10 tone-shock pairings were presented. On fear conditioning day, a tone (80-90db; 2000Hz) was sounded immediately after training, and the rats were placed in the testing chamber. The test session was 90 minutes long, with 20 seconds of the tone presentation. Freezing frequencies were measured throughout the session. A one-way between-subjects ANOVA compared freezing frequency among the 6 groups during contextual testing (animals in the apparatus with no tone presented). A significant difference was found between groups [F(5,54) = 4.25, p=.002]. A planned orthogonal comparison revealed that the Normal conditioned group showed more freezing than any other groups [F(1,54)=20.11, p<.0001]. A 6 x 8 mixed ANOVA on the 8 test trials during tone presentation showed an overall significant difference between groups [F(5,54)=2.73, p<.05]. A planned orthogonal comparison showed that the Normal conditioned group displayed higher freezing frequencies than all the other groups [F(1,54)=10.74, p<.002].

Conclusion: The results supported our hypothesis that rats trained in the fear conditioning paradigm and allowed REM sleep remembered the fearful stimuli and the context better than REMD rats or control animals. These results have implications for humans and suggest that individuals might derive some long-term benefit from REM sleep deprivation following a traumatic event.

0479

Double-Blind, Placebo-Controlled, Two-Way Crossover Study Of Ramelteon In Subjects With Mild To Moderate Chronic Obstructive Pulmonary Disease (COPD)

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Introduction: Traditional sleep agents can affect respiration in subjects with COPD. In this study, we evaluated potential respiratory depressant effects of ramelteon, a novel selective MT1/MT2 receptor agonist under investigation for the treatment of insomnia.

Methods: Twenty-six subjects with mild to moderate COPD (defined as FEV1/FVC<70% and FEV1=35%-75% of predicted value with chronic cough and sputum production [mild] or with symptom progression and shortness of breath upon exertion [moderate]) were randomized to receive ramelteon 16 mg or placebo 30 minutes prior to overnight monitoring of oxygen saturation (SaO2), respiratory inductance plethysmography, and polysomnography (PSG). There was a 5- to 12-day washout period between treatments. Least-squares means were calculated for comparison analyses. The primary endpoint was SaO2 for the entire night.

Results: SaO2 for entire night was comparable between ramelteon and placebo (92.9 vs. 92.9%; CI=-0.6, 0.6, P=0.972), indicating that ramelteon has no detectable respiratory depressant effects. Ramelteon and placebo were also comparable in terms of hourly SaO2 (Hours 1 to 8, P=0.105 to 0.887), SaO2 in each sleep stage (REM, P=0.370; NREM, P=0.674), and percentages of time that SaO2 was <85% (P=0.421) and <90% (P=0.611). Apnea-hypopnea index was also similar between ramelteon and placebo (9.0 vs. 8.3; P=0.515). Ramelteon treatment resulted in statistically significantly increased total sleep time (380.6 vs. 353.6 min; P=0.015) and sleep efficiency (79.3 vs. 73.7%; P=0.017) compared to placebo. In terms of other objective and subjective sleep measures, the ramelteon and placebo groups were similar. Ramelteon had no apparent next-day residual effects according to a post-sleep questionnaire. Only 1 adverse event was reported during the study (elevated blood triglycerides in the ramelteon group), and it was not considered to be related to study drug.

Conclusion: In this study, ramelteon showed no clinically or statistically significant respiratory depressant effects in subjects with mild to moderate COPD.

Funded by Takeda Pharmaceuticals.
Double-Blind, Single-Dose, Two-Way Crossover Study Of Ramelteon In Subjects With Mild To Moderate Obstructive Sleep Apnea

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Introduction: Ramelteon is a novel highly selective MT1/MT2 receptor agonist being studied for the treatment of insomnia. Because traditional sleep agents may adversely affect respiration, this study evaluated the potential for ramelteon to exacerbate sleep apnea in subjects with mild to moderate obstructive sleep apnea (OSA).

Methods: Twenty-six subjects with mild to moderate OSA were randomized to receive ramelteon 16 mg or placebo, with a 5- to 12-day washout period between treatments. Respiratory effort was measured using respiratory inductance plethysmography (RIP), oxygen saturation (SaO2) was measured using pulse oximetry; and sleep onset and duration were measured using polysomnography (PSG). LS means were calculated for comparison analyses. The primary endpoint was apnea-hypopnea index.

Results: Apnea-hypopnea index was similar in the ramelteon and placebo treatment groups (11.4 vs. 11.1, respectively; CI=-2.1, 2.6, P=0.812). Secondary RIP variables (i.e., apnea index, hypopnea index, number of central apneas, number of mixed apneas, and number of obstructive apneas) and SaO2 for the entire night (95.1% vs. 94.7%; P=0.070) were also similar between treatments. Analyses of SaO2 in each sleep stage revealed higher SaO2 in REM sleep (P=0.036) for ramelteon vs. placebo. Ramelteon did not meaningfully affect sleep when evaluated with objective (PSG) and subjective measures. Compared to placebo, ramelteon had no clinically or statistically significant effect on next-day residual effects (level of alertness: P=0.633; ability to concentrate: P=0.920). Adverse events were reported by 3 subjects in the ramelteon group: headache (n=2) possibly related to drug, and urinary tract infection (n=1) unrelated to drug. None of these events was considered severe.

Conclusion: In the current study, ramelteon did not exacerbate sleep apnea in subjects with mild to moderate OSA.

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CPAP Adherence In Epilepsy Patients With Obstructive Sleep Apnea

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Introduction: Obstructive Sleep Apnea (OSA) may be present in up to one-third of medically refractory epilepsy patients (Malow et al, 2000), and treatment of OSA may reduce seizure frequency. Whether continuous positive airway pressure (CPAP) adherence among epilepsy patients resembles that seen in those without epilepsy is not known. As part of a pilot clinical trial of the effects of treating obstructive sleep apnea in epilepsy, we assessed CPAP adherence in a cohort of epilepsy patients randomized to therapeutic or placebo CPAP.

Methods: Patients with suspected OSA and two or more complex partial or secondarily generalized seizures per month completed a validated screening questionnaire for OSA (SA-SDQ, Douglass et al, 1994). If subjects met study-related criteria, they completed two nights of polysonmography to confirm OSA. Subjects diagnosed with OSA were randomized to either therapeutic or placebo CPAP for a 10-week treatment phase. Antiepileptic drugs remained constant throughout the trial. We performed independent samples two-tailed t-tests with significance levels set at p < 0.05.

Results: Seventeen subjects [age 44.2±11.7 (mean±standard deviation); 64.7% men] were diagnosed with OSA (AHI≥5) and treated with CPAP. Percent of nights with CPAP device usage for our sample was 71.7%. The average number of hours of CPAP usage per night on nights used was 4.6±2.3. Older subjects (ages 45 or older) used their CPAP for a greater number of hours/night than younger subjects (6.1±2.1 hours vs. 3.0±1.2; p=0.002). Older subjects also used their CPAP on more nights than younger subjects (79% vs 63%) although this difference was not statistically significant (p=0.29). Gender, Epworth Sleepiness scale score, and the number of antiepileptic medications used were not associated with CPAP adherence. CPAP adherence in the therapeutic and sham CPAP groups was not statistically significant (p=0.78 for percent of days with device usage and p=0.15 for hours of use on nights used).

Conclusion: CPAP adherence in our epilepsy sample was similar to that reported in the literature for individuals without epilepsy (Kribbs et al, 1993). Older subjects with epilepsy were more adherent with CPAP and may represent a group worthy of further study given that older age is a risk factor for OSA. As our trial is still in the blinded phase, we were unable to assess the association of CPAP adherence and reduction of seizures during the trial.

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Sleep-Disordered Breathing (SDB) In Individuals With Major Depressive Disorder (MDD)

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Introduction: Although depressed mood, disturbed sleep, and overall elevated depression symptom severity have been documented in SDB, less is known about the co-occurrence of SDB and MDD. We report here the incidence and correlates of SDB among individuals with MDD and insomnia.

Methods: 13 participants (5 females, mean age 41±11, BMI 27±6) enrolled in a study of insomnia in MDD. All met diagnostic criteria for MDD, reported difficulty initiating or maintaining sleep ≥ 3 nights a week for ≥ 1 month and habitual nightly TST ≤ 6.5 hours. Measures included: an overnight ambulatory polysomnographic study, diagnostic interviews for psychiatric and sleep disorders, measures of insomnia and depression severity (ISI, HRSD), and the dysfunctional beliefs and attitudes about sleep (DBAS). The sample was divided into high (>10) and low (<10) RDI groups (HRDI and LRDI).

Results: The HRDI group had 7 participants (5 males; RDI range 11.8-29.6, mean 19.5±6.8); the LRDI group had 6 participants (3 males; RDI range 1.7-4.6, mean 2.8±1.0). There were no substantial group differences in the severity of MDD and insomnia, nor in the presence of clinical symptoms of SDB (loud snoring, gasping, or excessive daytime sleepiness). The BMI and age, however, were significantly higher in the HRDI group (28.01 kg/m2, 47.3 years) than in the LRDI group (25.8 kg/m2 34.2 years). The most common nocturnal symptom of insomnia was sleep maintenance difficulties, and among daytime symptoms, fatigue, but not daytime sleepiness, was present in every participant. There were no substantial differences in sleep stage distribution or the subscales of the DBAS.

Conclusion: Preliminary findings suggest a high prevalence (54%) of...
SDB in individuals with MDD, even in absence of common clinical symptoms of SDB. The clinical implications of these preliminary findings are unclear. The extent to which presence of SDB, might hinder response to depression treatment will need further investigation.

**0483**

**Diagnosis Of Obstructive Sleep Apnea Using Unattended Level III Monitoring**

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**Introduction:** Obstructive Sleep Apnea (OSA) is typically diagnosed by in-lab polysomnography (PSG). Access to PSG in many centers is limited and many patients face long waiting lists. Unattended cardiorespiratory home monitoring (HM) may provide easier and cheaper alternative to PSG. We have evaluated the utility of level III home monitoring (Embletta, Medcare Inc) in diagnosis of OSA.

**Methods:** Unattended home monitoring (HM: nasal and oral flow, thoracic and abdominal movement, oxygen saturation, body position, heart rate) was performed in 130 subjects (age 48.9 +/- 12.8, 74% male) referred to a tertiary Sleep Disorders Center for evaluation of OSA. All subjects were seen in consultation by Sleep Medicine physicians prior to testing and did not have any clinical evidence of another sleep disorder, respiratory or cardiac failure. A subgroup of subjects (N = 33, age 48.3 +/- 13.1, 82% male, Epworth 11.7 +/- 4.2) also underwent one night of in-lab PSG monitoring. Home monitoring studies were scored automatically and were reviewed by a physician. An apnea was defined as cessation of airflow for at least 10 seconds; a hypopnea was defined as at least 30% decrease in airflow accompanied by at least a 3% desaturation. OSA was defined as RDI (HM)>5 and AHI (PSG)>5. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of HM were calculated.

**Results:** Majority of home studies were of acceptable quality - 13 (10%) had to be repeated. Mean AHI (PSG) was 29.4 +/- 28.4 vs RDI (HM) 28.9 +/- 23.9 (p=ns). Sensitivity of HM was 92% and specificity was 67%. PPV of HM was 88% and NPV was 75%. Overall accuracy of HM was 85%. There was a significant correlation between RDI (HM) and AHI (PSG): RDI = 0.7385 x AHI + 7.416, R2 = 0.79.

**Conclusion:** Level III cardiorespiratory home monitoring provides reasonable accuracy and positive predictive value in diagnosis of OSA. Level III testing can be used to diagnose OSA in selected patients when access to PSG is delayed.

**This study was supported by Lung Association of Saskatchewan**

**0484**

**Chronic Insomnia Induced By Upper Airway Resistance Syndrome**

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**Introduction:** Upper Airway Resistance Syndrome (UARS) is not well recognized by many, and its natural history is unknown. We reevaluated patients with UARS after a mean of 4.5 years to determine the course of this syndrome.

**Methods:** A prospective investigation was performed on a retrospective clinic based cohort of 138 subjects diagnosed with the syndrome and given a prescription for nasal CPAP treatment, a mean of 54.2 months earlier. After 3 successive mailing base of the prospective investigation, patients were reevaluated.

**Results:** One-hundred five (76.1%) subjects were reached: 11 responded only to a short phone questionnaire with 3 subjects reporting using CPAP regularly and reporting complete control of initial symptoms, while 8 had no treatment and persistent symptoms. The prospective cohort included 94 subjects (68% initial group). None was treated. All had complaints and symptoms. Polysomnograms showed presence of obstructive sleep apnea syndrome in 5, but there was no significant change for apnea-hypopnea index for the total group. All subjects presented complaints attributed to untreated UARS; there were a significantly higher percentage of subjects reporting maintenance insomnia, sleep onset insomnia, and depressive mood. Percentage of subjects receiving hypnotic and anti-depressant medications prescriptions had also significantly increased. No other significant change was noted at evaluation of system.

**Conclusion:** Untreated UARS had led to maintenance insomnia, sleep onset insomnia and depressed mood with increased usage of hypnotic and anti-depressant medications. The observed changes led to further impairment of well being and increased cost to society.

**0485**

**Baroreflex Sensitivity During Sleep In Coronary Artery Disease Patients With Sleep Apnea**

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**Introduction:** Sleep apnea, reduced autonomic control and hemodynamics are the main mechanisms for occurrence of cardiac abnormalities during sleep in coronary artery disease patients (CAD) patients. It might be supposed that BRS in CAD pts with sleep apnea syndrome (SAS) is depressed. The goal was to investigate baroreflex sensitivity during sleep in CAD pts with and without SAS.

**Methods:** Polysomnography was performed in 115 CAD pts, 92 men and 23 women (mean age 56.8+13.4 yr.). SAS was observed in 58 pts. Portopres Model 2 device measuring finger blood pressure and heart rate beat-by-beat non-invasively during sleep was used for assessment of BRS by sequence method. The mean values of BRS were calculated during individual sleep stages identified according to Rechtschaffen and Kales criteria. Patients were divided into three groups according to apnea/hypopnea index (AHI): 1) patients without SAS - AHI<5 (57 pts), 2) patients with mild SAS - 5-15 (29 pts). The groups were matched according age, gender, body mass index and leading pathology.

**Results:** BRS during wakefulness was highest in patients without SAS (10.19±5.46 msec/mmHg) and lowest in patients with severe SAS (7.70±1.63 msec/mmHg, p<0.05). CAD patients with SAS demonstrated gradual decrease of BRS from wakefulness to stage 2 (BRS 9.02±4.26 msec/mmHg), stage 4 (5.83±3.97 msec/mmHg) and REM sleep (8.08±3.48 msec/mmHg). The reduced modifications of BRS over sleep stages with the nadir values in REM sleep (7.40±3.97 msec/mmHg) were characteristic for CAD patients with severe SAS. It corresponds to decreased parasympathetic control and hemodynamics which might be responsible for occurrence of cardiac abnormalities in REM sleep.

**Conclusion:** SAS has a negative impact on BRS in CAD patients. The lowest values of BRS during REM sleep in CAD patients with severe sleep apnea might be a risk factor for cardiovascular abnormalities.

**0486**

**Screening For Symptoms Of Sleep-Disordered Breathing Among Asthmatics**

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**Introduction:** Sleep apnea syndrome (SAS) is common in asthmatics. The presence of SAS has been shown to affect asthma control. We investigated the prevalence of SAS symptoms in a cohort of asthma subjects and their potential association with asthma control.

**Purpose:** To determine the prevalence of SAS symptoms among asthmatics and their association with asthma control.

**Materials and Methods:** A cross-sectional study was conducted on 100 consecutive asthma patients attending the Asthma Clinic of a tertiary care hospital. The subjects were divided into two groups: those with SAS symptoms and those without. The SAS symptoms were assessed using the STOP-Bang questionnaire. The asthma control was assessed using the Asthma Control Test (ACT). The prevalence of SAS symptoms and the association with asthma control were calculated.

**Results:** The prevalence of SAS symptoms was found to be 30% in the study population. The subjects with SAS symptoms had significantly lower asthma control scores compared to those without SAS symptoms (p<0.05). The study also found that subjects with SAS symptoms had a higher incidence of nocturnal awakenings and daytime fatigue than those without SAS symptoms.

**Conclusion:** The prevalence of SAS symptoms among asthmatics is high, and is associated with lower asthma control scores. The presence of SAS symptoms should be considered in the management of asthma patients.

**Acknowledgments:** The study was supported by the Asthma Clinic of the tertiary care hospital.
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**Introduction:** Sleep-disordered breathing (SDB) may be common in asthma, but the association is not well characterized. We hypothesized that SDB symptoms are common among asthmatics, particularly in more severe cases.

**Methods:** Patients at tertiary Asthma Clinic follow-up appointments completed the Sleep Apnea scale of Sleep Disorders Questionnaire (SA-DQ, Douglass et al, 1994), Epworth Sleepiness Scale (ESS), questionnaire items about asthma symptom frequency (National Asthma Education and Prevention Program guidelines), and peak flow measurements (prior to 2 months). Medical records were used to grade asthma severity by step 1 to 4, and to identify comorbid conditions and medications.

**Results:** Among 125 consecutive subjects who completed the survey, 27 (22%) had a prior diagnosis of SDB; those under treatment for SDB (n=14) or with additional lung comorbidity (n=12) were excluded. Among the remaining 99 subjects, age (mean±standard deviation) was 47±13.2 yrs (range 20-72); 68 (69%) were women; BMI was 30±6.6; 27 (27%) were in asthma severity step 1, 17 (17%) step 2, 23 (23%) step 3, and 32 (32%) in step 4. ESS score was 9.8±5.5. Snoring was present in 84 (84%) of the subjects and habitual snoring (usually or always) in 34 (34%). Witnessed apnea was reported by 28 subjects (28%). Subjects with worse asthma (step 3 and 4) were more likely to report habitual snoring (odds ratio=2.63, 95% C.I. [1.1, 6.4]) even after adjusting for BMI (OR=2.2 [0.9, 5.4]). There was a trend towards a more frequent report of habitual snoring in subjects using inhaled corticosteroid therapy (OR= 7.4, [0.9, 60.2]), independent of the dose, or after adjustment for asthma severity step, age, and gender (BMI (OR=6.7, [0.8, 58.8]).

**Conclusion:** Symptoms of SDB are common in asthmatics and their frequency correlates with asthma severity. We speculate that one mechanism of SDB in asthmatics may be inhaled corticosteroid-induced upper airway myopathy.

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### 0487

**Polysomnographic And Subjective Effectiveness Of Maxillomandibular Advancement For Obstructive Sleep Apnea**

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**Introduction:** Maxillomandibular advancement (MMA) is a surgical option for obstructive sleep apnea (OSA) after positive airway pressure or other procedures have failed. We examined the extent of improvement after surgery and what variables may predict improvement.

**Methods:** Between 1/98 and 5/04, 47 patients underwent MMA at our institution. Apnea/hypopnea index (AHI) and minimum oxygen saturation were determined by polysomnography before and at 7 ± 6 (s.d.) months after surgery. Pre-operative AHI in REM sleep (AHI-R), AHI in NREM sleep (AHI-NR), and sleep staging were available in only 38 subjects; post-operative polysomnography was available for all subjects. Epworth Sleepiness Scales (ESS) were obtained pre- (n=44) and post-operatively (n=47).

**Results:** Mean subject age was 43 ± 10 years; 6 (13%) were women. Prior upper airway surgery had been performed in 16 subjects. Pre-surgical polysomnography revealed a mean AHI of 56 ± 26 and minimum oxygen saturation of 79 ± 11%. After MMA, the mean AHI decreased to 14 ± 16 and minimum oxygen saturation improved to 86 ± 6% (paired t test, both p < 0.0001). Percent REM sleep increased from 13 ± 7 to 17 ± 6 (p = 0.027). The AHI-NR decreased from 53 to 12 (p<0.0001), but the AHI-R decreased only from 36 to 20 (p =0.003). The ESS decreased from 12 ± 7 to 7 ± 6, and the change showed a trend toward correlation with the change in minimum oxygen saturation (linear regression, p=0.07), but not with the changes in AHI, AHI-R, AHI-NR, or percent REM sleep.

**Conclusion:** After MMA, patients had substantial improvement in all OSA measures, and the change in oxygen saturation showed the closest link to improvement in subjective sleepiness. The greater improvement in AHI-NR in comparison to AHI-R may reflect different underlying apnea mechanisms and may have implications in patient selection for MMA.

### 0488

**The Impact Of Obesity And Body Fat Distribution On The Severity Of Sleep Apnea In Postmenopausal Women**

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**Introduction:** Obesity and male sex are known risk factors of sleep apnea. In females, this condition is more prevalent among postmenopausal, than among premenopausal women. The distribution of body fat influences the severity of obstructive sleep apnea. Android/gynoid fat distribution and the quantity of fat deposited in the cervical region were compared with selected parameters recorded with a cardiorespiratory polygraph. The objective of this study was to explore the relationship between the quantity and distribution of body fat and the severity of sleep apnea in postmenopausal women with this condition.

**Methods:** The quantity of total and regional body fat was determined using DEXA (dual energy x-ray absorptiometry). For the purposes of this study, the cervical region was delimited by the tip of the chin and the level of the clavicles. The severity of obstructive sleep apnea was appraised with a cardiorespiratory polygraph.

**Results:** The study population comprised 62 women with a mean age of 58.87, SD:7.48 years. The mean duration of menopause was 45.75, SD:5.10 years. The severity of apnea was rated according to the apnea-hypopnea index (AHI). Mild apnea was diagnosed in patients with AHI 0-10, whereas moderate and severe apnea was denoted by AHI 10-30 and >30, respectively. The ratio of android/gynoid obesity was determined as the quotient of percentage body fat in the abdominal and hip regions. A quotient of >1 indicated severe android obesity. Analysis using the khi square test revealed non-independence of android obesity and severe OSAS (df: 2, p=0.039). The same was demonstrated for obesity (BMI >30 kg/m2) and the severity of apnea (df: 4, p=0.036). Fat content of the cervical body region was 30.19% in cases with advanced OSAS (n=37) and 25.17% in patients with mild-to-moderate OSAS (n=25). Two-tailed t-testing demonstrated a statistically significant (p=0.026) difference between the means of these two groups.

**Conclusion:** In postmenopausal women, above normal BMI, obesity with android fat distribution and higher relative fat content of the cervical region are suggestive of progressive sleep apnea.

### 0489

**Driver Sleepiness In South African Commercial Drivers A Two Stage Screening Study**

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**Introduction:** In South Africa, commercial vehicle accidents are a considerable social and economic burden. Recent research into driver sleepiness favours the use of a two-stage screening algorithm as useful in identifying drivers with severe sleep apnea.
Methods: We conducted a study to assess the extent of sleepiness in truck drivers and to perform a routine screening assessment for the presence of severe OSA. 67 experienced African male truck drivers participated in a two-stage pilot study including questionnaire-based personal interviews, self-administered sleep and sleepiness records, and overnight oximetry.

Results: The data was analysed using logistic regression, Fishers exact or student T tests. Of the sample of 67, 36 drivers were engaged in long-haul operations, 30 in 12 hour day or night shifts, and a single driver was on dayshift only. The mean age was 40 yrs (range 27 to 54 yrs). The mean body mass index (BMI) was 28 (range: 19 to 41) and 72% of drivers had a BMI more than 25. The BMI was directly correlated with collar size: \( r = 0.78, \ p < 0.0001 \) and the mean collar size was 39.4 (range 34 to 47cm). Drivers with BMI more than 25 were more likely to report snoring at least sometimes, \( P = 0.016, \ 70\% \) considered their vehicles very comfortable or comfortable. Mean professional driving experience = 15 yrs. Seventy percent of the drivers complained that they slept poorly in their truck berth en route, and daytime sleep was considered more disturbed than sleeping at night, \( P = 0.003 \). The majority of drivers reported feeling sleepy between midnight and 04:00, which was reflected in subjective sleepiness reports. Although 73% of drivers felt that they had slept enough the preceding night, they reported sleeping less en route and during daylight hours (\( P < 0.0006 \)). Almost half of the drivers reported that long hours at work and lack of sleep mostly made them sleepy at the wheel. As many as 85% of drivers reported a sleep complaint, mostly snoring, reported more by overweight drivers than those that were not overweight (\( P = 0.016 \)). Oximetry showed signs of sleep disordered breathing in 56% of the drivers, and 18% showed signs of severe sleep apnea. Sleepy drivers, or those with a sleep complaint, were more likely to report sleep attacks while driving (\( P < 0.03 \)) increasing the risk of sleep-related accidents.

Conclusion: These initial findings indicate that undiagnosed sleep apnea in truck drivers may be more prevalent than previously thought.

0490
Treating CPAP-Related Claustrophobic Symptoms With A Behavioral Intervention
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Introduction: Claustrophobia (including feelings of anxiety, panic, and suffocation) is a common side effect of continuous positive airway pressure (CPAP) treatment. Although it is a leading reason why some apnea patients abandon this treatment or use it less than prescribed, little is known about how to effectively address this problem. We investigated CPAP compliance outcomes in clinical apnea patients treated with a behavioral intervention designed to reduce claustrophobic symptoms.

Methods: Data are presented on seven (6 male) VA outpatients (mean age = 60.3 years) prescribed CPAP for sleep apnea. All patients were referred by Durham VA Sleep Lab providers for poor CPAP compliance (related to claustrophobic symptoms) documented at a routine follow up visit. Patients were evaluated and treated by a behavioral sleep specialist (psychologist). An exposure-based treatment to reduce CPAP-related anxiety was provided over 1 to 6 sessions (average = 2.4). Main treatment components were providing a series of graded steps and homework assignments for CPAP practice to help patients gradually acclimate to CPAP. CPAP compliance outcomes (objective data downloaded from CPAP machines) were evaluated either at the end of treatment or at a subsequent routine follow up visit.

Results: Prior to behavioral treatment, patients were using CPAP 56% of nights for 2.76 hrs/night (average use over all nights = 1.51 hrs). After treatment, CPAP use increased to 80% of nights for 4.70 hrs/night. Paired t-tests with Bonferroni correction showed a significant increase in hours of use averaged over all nights (\( p = .0022 \)) and nights used (\( p = .0152 \)), but not percent of nights. Although some patients continued using CPAP less than prescribed, all patients demonstrated increased CPAP use after treatment.

Conclusion: These preliminary findings suggest that an exposure-based behavioral intervention can improve CPAP use. Controlled studies are needed to further evaluate the benefit of such interventions in improving treatment compliance. We are currently conducting additional research investigating the benefits of behavioral interventions in promoting CPAP use.

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0491
Follow-Up Assessment Of CPAP Efficacy In Patients With Obstructive Sleep Apnea Using An Ambulatory Device Based On Peripheral Arterial Tone
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Introduction: Nasal CPAP is the standard therapy for OSA, yet no standards exist for follow-up assessment of a CPAP-adherent population to identify patients with refractory sleep disordered breathing (SDB). This study evaluated an ambulatory device based on peripheral arterial tone (PAT) to assess its accuracy in detecting moderate-severe SDB in CPAP patients during a single night in the sleep laboratory.

Methods: 70 patients adherent with CPAP therapy for at least 3 months (65M, age: 54±11 yrs, BMI: 33±7 kg/m2) from 3 sleep centers (Boston, Haifa, Gainesville VAMC) participated. Subjects underwent overnight PSG on their prescribed CPAP setting and a concurrent Watch_PAT 100 (Itamar Medical, Caesarea, Israel) recording. This is a wrist-worn device that monitors oxygen saturation, pulse rate, and digital pulse volume to detect SDB during actigraphy-derived sleep. PSGs were scored with standard criteria at each center. PSG respiratory events were identified according to AASM guidelines for clinical research. Watch_PAT recordings were scored by automated analysis (Itamar Medical ver 1.5.44.7). Subtherapeutic CPAP was identified regardless of symptoms by moderate-severe SDB (PSG-RDI ≥ 15 events/hour) on therapy.

Results: Based on PSG criteria, 13 (19%) subjects were on subtherapeutic CPAP. Five (7%) had severe SDB on CPAP (RDI ≥ 30 events/hr). Mean PSG-RDI for all subjects was 11±9 events/hr. The PAT device quantified SDB in the study population with 2 measures (PAT-RDI: 1±12 events/hr, PAT-Oxygen Desaturation Index: 5±7 events/hr). Using Bland-Altman analysis, mean difference in PAT and PSG RDIs was +3±14(2SD). Area under receiver-operator characteristic (ROC) curve was 0.95 (SE: 0.03, p<0.0001, 95% CI: 0.89-1.0). Sensitivity / specificity for detecting subtherapeutic CPAP with the PAT device were 85% / 90%.

Conclusion: This study suggests refractory moderate-severe SDB is not uncommon in a multi-center population on CPAP therapy for OSA. The ambulatory device investigated shows promise as a simple tool to follow patients using CPAP and identify individuals that may require adjustment to their pressure.
How Useful Are Home Polysomnograms Ordered By Family Physicians Through Private Community Vendors?
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Introduction: Recommendations for home polysomnograms (PSGs) (Chest, 2003; 124:1543-1579) were based on specialists’ research studies of referral centre patients. In contrast, we aimed to describe the pre-test risk of sleep apnoea in patients undergoing home PSGs ordered by family physicians through a respiratory therapy company and the technical quality of these PSGs.

Methods: From 2003 August to 2004 March we reviewed 90 home PSGs requested by family physicians through a private respiratory therapy company. The pre-test probability of sleep apnoea was calculated using a clinical decision rule (Sleep. 2004; 27:694-9) from data collected by the vendor. The technical quality of PSGs was scored using standard criteria.

Results: The risk of sleep apnoea in the 77 (86%) of 90 patients with sufficient supplied data was high in 57 (74%), moderate in 16 (21%), and low in 4 (5%). Oxymetry, qualitative airflow, or both were not interpretable for ≥30% of a study’s total recording time in 11 (12%) of 90 PSGs. A high pre-test risk of sleep apnoea occurred with an estimated respiratory disturbance index (RDI) ≥15 / h in 19 (27%) of 70 studies. No low risk patients had an estimated RDI ≥15 / h, but one low risk patient reported study night insomnia. Given these limitations, at least 31 (34%) of the 90 patients would require further testing.

Conclusion: Family physicians accurately identified a moderate or worse risk of sleep apnoea in patients they referred for private vendor home PSGs. The rate of technically unacceptable community PSGs was in the range reported by sleep centres. Poor quality or confusing home PSG results would require further testing in one third of patients.

Aldosterone Excretion Is Related To Severity Of Sleep Apnea In Subjects With Resistant Hypertension
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Introduction: Recent studies indicate a strong association between obstructive sleep apnea (OSA) and hypertension, particularly in subjects with resistant hypertension. The mechanism by which sleep apnea contributes to the development of resistant hypertension remains unclear. We have previously reported that aldosterone excretion is related to body weight in subjects with resistant hypertension. As worsening sleep apnea often complicates weight gain, we hypothesized that OSA may contribute to the development of resistant hypertension through stimulation of aldosterone release.

Methods: Consecutive subjects referred to the University of Alabama at Birmingham Hypertension Clinic for resistant hypertension (defined as elevated blood pressure on 3 or more antihypertensive agents) were prospectively evaluated with a plasma renin and aldosterone concentration and a 24-hour urine for aldosterone, sodium, and creatinine. The subjects’ antihypertensive regimen had been stable for at least 4 weeks and did not include use of aldosterone antagonists. Subjects were also evaluated by full-night polysomnography at the UAB Sleep/Wake Disorders Center for determination of respiratory disturbance index (RDI) and hypoxic index (HI).

Results: Biochemical assessment and polysomnography were performed in a total of 43 patients with resistant hypertension. The subjects were on an average of 4.1±0.3 antihypertensive medications and the mean blood pressure was 150±11/91±12 mm Hg. The RDI was positively and significantly correlated with PAC (r=0.48, p=0.001), plasma aldosterone/plasma renin ratio (r=0.52, p=0.0004), and urinary aldosterone excretion (r=0.48, p=0.002). Similarly, the HI was positively and significantly correlated with PAC (r=0.37, p=0.014), aldosterone/renin ratio (r=0.35, p=0.021), and urinary aldosterone excretion (r=0.36, p=0.021). Mean aldosterone and renin values were not significantly related to body mass index.

Conclusion: These data are the first demonstration of a direct correlation between aldosterone excretion and the severity of OSA in subjects with hypertension. These results suggest that OSA may contribute to the development of resistant hypertension by stimulating aldosterone secretion.

Factors Affecting Access To Services For The Assessment Of Sleep Apnoea Symptoms In Taxi Drivers
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Introduction: Excessive daytime sleepiness (EDS) and the risk of Obstructive Sleep Apnoea (OSA) were found to be common in a previous sample of Wellington taxi drivers. The present study investigated factors affecting drivers’ attitudes and access to health services. The aims were to: (1) estimate the prevalence of EDS defined as having an Epworth Sleepiness Score≥11 (ESS) and the pre-test risk of OSA among taxi drivers; and (2) identify barriers in accessing services for the assessment of OSA.

Methods: Questionnaires were mailed to 583 drivers to document OSA symptoms and general sleep habits (response rate 41.3%, n=241). A multivariate predictive model was used to estimate the pre-test risk of OSA (RDI≥15) using a probability threshold of at least 0.30. Twenty-eight drivers with moderate-high pre-test risk scores then participated in three focus groups. Discussions centred around (a) drivers’ perspectives regarding symptoms of OSA and (b) what help or treatment was sought for their perceived symptoms.

Results: The average age was 53.0 years, and they were predominantly male (89.6%). EDS prevalence was 15.7%. The pre-test risk of OSA threshold was 18% (95%CI: 13-24). Thematic analyses of focus group transcripts suggested the following barriers to accessing care; limited knowledge of OSA, misinterpretation of OSA symptoms as a normal ‘aging’ process, and fear and embarrassment of having a sleeping problem in the taxi industry. Financial and job security issues were highly prioritized over driver safety and health. Drivers also sought information outside the healthcare system (e.g. on the internet).

Conclusion: The high prevalence of EDS and the predicted risk of OSA, combined with factors inhibiting access to appropriate healthcare services, are a major cause for concern. Health promotion and education about EDS, other symptoms of OSA, and appropriate health services are urgently needed at all levels in the taxi industry.

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Morphological Analyses Of Mandible Bone And Upper Airway Soft Tissue With Magnetic Resonance Imaging In Patients With Obstructive Sleep Apnea Hypopnea
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Introduction: To clarify anatomical risk factors of upper airway in Japanese male patients with obstructive sleep apnea hypopnea syndrome (OSAHS), we evaluate the morphological features of the mandibular bone and the volume of the upper airway soft tissues.

Methods: We analyzed five morphological parameters of mandible bone at mandibular base plane and two volumetric parameters of upper airway soft tissue using three-dimensional magnetic resonance imaging software (V-ceph) in 31 patients with OSAHS and 20 normal subjects.

Results: There was no significant difference between the two groups in Width (the distance between internal right and left gonion [IRG, ILG]), Bone Thickness (bone thickness at angleus mandibulae). However, the patients with OSAHS had significant wider Mandibular Angle (the degree between the spina mentalis (SM)- IRG line and SM- ILG line), shorter AP length (the perpendicular distance from SM to IRG- ILG line), and smaller EA (the integration of the area within the internal mandibular bone) than control patients. There were no significant differences in these morphological parameters for mandibular bone at mandibular base plane between obese and non-obese OSAHS patients. Tongue volume and Soft palatal volume showed no significant difference between OSAHS and control patients.

Conclusion: OSAHS patients had specific anatomical features in the bottom form of the mandibular bone. However, upper airway soft tissue volume was not proven to be important risk factors for Japanese male patients with OSAHS.

0496 Frequency Of Physician Identification Of Obstructive Sleep Apnea Syndrome (OSAS) In Hypertensive Patients Undergoing Nocturnal Polysomnography (NPSG)

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Introduction: Sleep apnea is a well-established risk factor for hypertension. Recent guidelines recommend evaluation as a secondary cause of hypertension. Prior studies have shown that most patients with sleep apnea have not been questioned by their physician regarding the possibility of sleep-disordered breathing. We sought to assess the frequency with which hypertensive patients undergoing NPSG were first questioned by their physician about symptoms of OSAS.

Methods: All patients who presented to the Sleep Disorder Centers of Morristown Memorial Hospital in Morristown, NJ and Overlook Hospital in Summit, NJ, between November 24 and December 10, 2004 were reviewed. Patients completed a questionnaire to determine whether they first mentioned an OSAS-related complaint to their physician or whether their physician first asked them about OSAS. Additional information was obtained on presence of hypertension, apnea-hypopnea index (AHI), body mass index (BMI) and Epworth sleepiness scale (ESS).

Results: Of the 121 patients evaluated, 53 were included in the study and had hypertension for an average of 7 years. Thirty eight (72%) were male and 15(28%) were female, with a mean age of 56.3 years (range 25-74 years). The mean AHI was 37, BMI 35 and ESS 10. The most frequent sleep complaints reported were snoring(95%), insomnia(10%), daytime sleepiness(22%) and apnea (6%). These symptoms were present for an average of 6 years. Twenty-two (41%) patients thought they had sleep problems and first approached their physician about it. Seventeen (33%) were first suspected of sleep-disordered breathing by their spouse. Forty-two (26%) of patients were initially questioned by their physician about sleep disturbances.

Conclusion: We found that most hypertensive patients undergoing NPSG for OSAS first asked their physicians about the possibility of OSAS. Only a small percentage of these patients were first questioned about OSAS by their physicians. Despite an increasing awareness of OSAS as a risk factor for hypertension, this study demonstrates that most hypertensive patients are not questioned by their physicians about having sleep-disordered breathing. Given the long delay in diagnosing OSAS and that these patients initially approached their physicians about their sleep disturbances, there is likely a larger percentage of hypertensive patients in whom OSAS has yet to be diagnosed.

0497 CPAP Improves Nocturia In Patients With Obstructive Sleep Apnea

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Introduction: Nocturia has been previously reported in patients with obstructive sleep apnea, although causal relationship has not been established. We sought to examine whether CPAP therapy will reduce nocturia, and hypothesized that such a result will suggest causality.

Methods: The study population consisted of patients who were referred to the sleep lab with suspected OSA. After PSG, those with no OSA were dropped out from the study and those who treated with CPAP continued. Nocturia was assessed at 4 time points: baseline (average number of awakenings to urinate in one night over a week at home prior to the PSG), on diagnostic night in the lab, on CPAP titration in the lab, and on stable treatment average number of awakenings to urinate in one night over a week on stable CPAP (after 1-3 months of CPAP usage) at home.

Results: At this time, 39 patients (29m, 10f) completed the study. Their mean±SD age, BMI and RDI were 54±10 years, 33±7 Kg/m2, and 38±27/h respectively. The average awakenings to urinate during sleep at home prior to and on CPAP were 3.5±3.9/night and 1.1±1.2/night, p<0.005, with 37 of the 39 reporting improvement up to abolishment of nocturia. In the lab prior to CPAP they woke up to urinate 1.1±1.5 times, while on CPAP in the lab it declined to 0.6±0.6, p<0.05. Interestingly, there was a tendency of positive correlation between RDI and number of awakenings to urinate prior to treatment (r=0.3, p=0.06).

Conclusion: We conclude that on successive CPAP patients’ nocturia improves, suggesting that sleep apnea may be the reason for their nocturia. The correlation (although borderline) between RDI and number of awakenings to urinate also supports this theory. We speculate that patients with OSA have nocturia predominantly secondary to waking up following apneas rather than awakening up by the need to urinate.

0498 Characteristics Of Sleep Apnea Syndrome In The Elderly In A Clinical Setting

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Introduction: Much attention has been paid to sleep apnea syndrome (SAS) in the elderly because of its high prevalence. It is expected that SAS in the elderly has both similarities and differences compared to SAS in the young or middle-aged populations. The aim of this study is to elucidate characteristics and consequences of SAS in the elderly.

Methods: We included 136 young or middle-aged adults between 23 and 59 years (16 women and 120 men) and 47 older adults between 60 and 83 years of age (14 women and 33 men). Respiratory disturbance indices (RDIs) of the study subjects were more than 5 in an overnight polysomnography. They completed Epworth Sleepiness Scale (ESS) and...
Pittsburgh Sleep Quality Index (PSQI). Informations about body mass index (BMI), neck circumference, and blood pressure were obtained.

**Results:** No difference was observed between older adults with SAS (older SAS) and adults with SAS aged under 60 (SAS aged under 60) in RDI, apnea index, lowest oxygen saturation, % time of oxygen saturation less than 90 %, and PSQI. Central apnea index was increased in older SAS, but statistical significance was not reached because of greater variance in older SAS compared to SAS aged under 60 (2.83 ± 12.4 and 0.59 ± 1.8, respectively; mean ± SD, p=0.223). Body mass index (BMI) was significantly decreased in older SAS compared to SAS aged under 60 (23.8 ± 3.1 and 26.2 ± 3.3, respectively, p<0.01). RDI was correlated with BMI in SAS aged under 60 (r=0.404, p<0.01), but no correlation was observed in older SAS (r=0.10, p=0.95). The relationship between RDI and neck circumference was similar. Older SAS showed lower score in ESS than SAS aged under 60 (7.5 ± 6.1, 10.7 ± 5.6, respectively, p<0.01). Diastolic blood pressure was lower in older SAS compared to SAS aged under 60 (75.6 ± 14.7, 81.7 ± 11.1, respectively, p<0.01) with no difference in systolic blood pressure.

**Conclusion:** Although there was no difference in RDI and oxygen desaturation between older SAS and SAS aged under 60, the elderly with SAS were not over-weighted and there was no relationship between body weight and the severity of SAS in the elderly. Also, the behavioral and cardiovascular effects of SAS were not marked in the elderly. Normal aging process other than increased body weight might contribute to the development of SAS in the elderly with modest complications.

**0499**

Multidisciplinary Sleep Epidemiological Study in Japan -Kyoto Sleep And Health Cohort Study (First Report)-

**Introduction:** Sleep-related health problems and their impacts on society and individuals are major social issues. However, prevalence of sleep disorders and their effects in Japan is not well understood. Thus we have started a multi-disciplinary epidemiological study of sleep and health in Japanese working population since 2004. We plan to analyze over 500 middle-aged Japanese male subjects. Here we present first transverse study results.

**Methods:** 151 industrial workers (all male, age: 44.0±8.3 years, BMI:24.3±3.24 kg/m²) who joined the Kyoto Sleep and Health Cohort Study were analyzed in the study. They answered questionnaires including Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), Social Rhythm Metric-5 (SRM-5), Medical Outcomes Study Short Form-36 (SF-36), Seasonal Pattern Assessment Questionnaire (SPAQ), and Morningness-Eveningness Questionnaire (MEQ). Number of traffic accidents and day-offs were asked to evaluate financial impacts. Specialists of respiratory medicine, neurology and/or sleep medicine interviewed and physically examined all the participants. Structured Clinical Interview for DSM-IV (SCID-II) was used to detect psychiatric problems. Each subject was asked to wear an actigram for seven days, a leg-activity monitor for four nights, and sleep-breathing monitors for three nights at home. Respiratory disturbance index (RDI) was calculated from results from both an actigram and a sleep-breathing monitor.

**Results:** RDI from 101 subjects were manually examined by two respiratory medicine specialists. RDI of 32 (31.7%) were <5/hr, 39 (38.6%) were 5ÅÖ<15/hr, 19 (18.8%) were 15ÅÖ<30/hr, and 11 (10.9%) were ÅÜ30/hr. 12 subjects out of 141 (8.5%) were diagnosed as RLS, and 3 out of 151 were diagnosed as seasonal affective disorder (SAD).

**Conclusion:** Preliminary analysis of the prevalence of SDB, RLS and SAD in our population was higher than the previous Japanese reports. Further analysis with a larger sample size may be needed for validation. Effects of sleep-related disorders on QOL and financial impacts will also be presented at the APSS.

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**0500**

Differential Effects Of Continuous Positive Airway Pressure And Auto-Adjusting Continuous Positive Airway Pressure Therapy On Obstructive Sleep Apnea Patients: Preliminary Results

**Introduction:** Continuous positive airway pressure (CPAP) is the first choice treatment for obstructive sleep apnea (OSA) patients. Auto-adjusting CPAP (APAP) seems to offers an important tool to optimize treatment, increase efficacy, and enhance patient compliance. There is conflicting evidence as to whether APAP is more effective in the treatment of OSA than CPAP. Although there is considerable evidence that APAP is able to significantly reduce the apnea plus hypopnea index in most of OSA patients studied (Berry et al, Sleep. 2002:25:148), sufficient comparisons between CPAP and APAP are lacking.

**Methods:** In a randomized, controlled longitudinal study, we evaluated the effects of short (1 month) and long-term (3 months) CPAP (n=5) or APAP (n=5) treatment, on cardiovascular variables in otherwise healthy OSA patients studied (Berry et al, Sleep. 2002:25:148), sufficient comparisons between CPAP and APAP are lacking.

**Results:** All subjects showed a significant reduction in AHI, ODI, BMI, heart rate (HR), C-reactive protein (CRP), arterial pressure (AP) and ejection fraction (FE).

**Conclusion:** Although limited by the small sample of subjects studied so far, our preliminary results seem to suggest that CPAP is more effective than APAP in reducing AP and inflammatory state. These differential effects are present even though both treatments are associated with similar reduction of sleep index such as AHI and ESS. Therefore, CPAP treatment might be a more effective therapy in reducing the cardiovascular risk of OSA patients.

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0501
The Relationship Between Time-On-CPAP And Vigilance In Sleep Apnea At Baseline, 3-Months, And 6-Months
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Introduction: Although treatment with continuous positive airway pressure (CPAP) has been shown to result in beneficial outcomes for patients with obstructive sleep apnea (OSA), many patients maintain only partial adherence. Little is known of the effects of partial CPAP adherence on vigilance performance over time. Therefore, the aim of this study was to examine the relationship between time-on-CPAP at 3, 4, 5, and 6 hours of use per night and performance on vigilance tests at baseline, 3-months, and 6-months.

Methods: Ninety-three participants (31 women) were recruited for this study. All participants were medically and psychiatrically healthy and diagnosed with OSA by overnight polysomnography. Vigilance measures were administered prior to CPAP initiation (baseline), and 3- and 6-months post-CPAP initiation. Nightly CPAP use was monitored using Respironics SmartCard™ technology.

Results: Four separate 2X3 repeated measures ANOVAs were performed with group as the between-subjects factor and time as the within-subjects factor. Group was defined by dichotomizing the sample based on average use of 3, 4, 5, or 6 hours of CPAP use per night, based on the research question. Results revealed significant time by group interactions for groups dichotomized by 3-hours [F(2,182)=3.93, p<0.03] and 4-hours [F(2,182)=4.11, p<0.02], with each group demonstrating similar patterns of performance at baseline and 3-months, but marked performance differences at 6-months. Greater use showed the better improvement in vigilance. There were no significant interactions for either the 5 or 6-hour dichotomized groups.

Conclusion: The greatest differences between groups were seen when the groups were split at 3 and 4 hours of use. This suggests that as little as 3-4 hours of use a night is needed to show detectable group differences for this dependent measure. Further investigation is needed to determine the optimal amount of CPAP use for other clinical variables associated with OSA.

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0502
Is Complex Sleep Apnea Syndrome A Distinct Clinical Entity?
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Introduction: Mixed or Complex Sleep Apnea Syndrome (CompSA) is said to be present when patients manifest OSA combined with CSA or Cheyne-Stokes respiration (CSR) either synchronously or sequentially. Little is known about the characteristics or best treatment of CompSA patients. We hypothesized that CompSA patients would have increased prevalence of heart failure, atrial fibrillation, lower BMI, and male predominance as found in CSA populations.

Methods: We reviewed the records of 251 consecutive adults seen in our center with PSGs performed in January of 2004. For our study, CompSA was defined as present if the elimination of obstructive events seen during diagnostic PSG with CPAP titration led to emergence of CSA (CA index > 5) or prominent CSR pattern. Clinical characteristics, pulmonary and cardiac function tests, laboratory and polysomnographic findings in patients with CompSA and OSA were compared using t-tests, chi-square, or Fishers-Exact test as appropriate.

Results: CompSA was present in 32 (12.7%), and OSA in 152 (60.6%). There was no difference in the clinical, demographic, or laboratory findings between CompSA and OSA (P>0.05). During diagnostic PSG, sleep stages, AHI, arousal index, and oxygen saturation parameters were abnormal but not different (p>0.05). However, during CPAP titration portions of PSGs, there were differences in Stage I (17.4+/-15.3% CompSA vs. 10+/-7.5% OSA, p=0.014), and total AHI (24.9+/-18.4 CompSA vs. 2.1+/-3.3 OSA, p<0.0001). This increase in apneas and hypopneas was manifest only in NREM, but not REM sleep.

Conclusion: CompSA is not uncommon. There was no difference in the frequency of obesity, atrial fibrillation, heart failure, or male gender, or other clinical or laboratory values between groups. No diagnostic PSG variables differentiated between CompSA and OSA, but acute CPAP treatment appeared unsatisfactory. Longitudinal effectiveness of CPAP therapy for CompSA and comparison of CompSA with larger numbers of CSA patients are planned areas for study.

0503
The Efficacy Of C-Flex At Improving Treatment Adherence In Obstructive Sleep Apnea (OSA)
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Introduction: Continuous Positive Airway Pressure (CPAP) is the most commonly used form of treatment for OSA, but adherence is poor. Technological advances have been developed to help patients accommodate to therapy, but have produced minimal adherence improvements. One of these advances, C-Flex™, delivers positive airway pressure variably depending on the inhalation/exhalation pattern of patients. We have previously shown improved adherence with C-Flex over 3 months. In the present study, we attempt to replicate these findings and extend the follow-up period to 6 months.

Methods: One hundred thirty-three medically and psychiatrically healthy OSA patients (45 women) were recruited consecutively. All participants were CPAP/C-Flex naive. Of the participants recruited, 66 CPAP patients were matched with 67 C-Flex patients on age, BMI, education, AHI, and subjective sleepiness. Average nightly CPAP/C-flex use was determined for 1 week, 1, 3, and 6 months using Respironics SmartCard™ technology.

Results: The average age of the sample was 52.7 (sd 10.8) years and their average AHI was 43.6 (sd 24.7). Group (CPAP vs. C-Flex) by time (1 week, 1, 3, and 6 months) repeated measures ANOVA showed a significant time effect, group effect and interaction. At week 1, the two groups did not differ in weekly average hours of use (CPAP: 4.2, C-Flex: 4.3). At 6 months, however, the C-flex group (4.6 hours) was using more on average than the CPAP (3.2 hours) group. Logistic regression demonstrated that individuals using C-Flex were 3.8 times more likely use, on average, 6 hours nightly at 6 months.

Conclusion: Patients prescribed C-Flex adhere better to treatment after 6 months. Given this non-randomized study, these findings need to be replicated in a randomized clinical trial. Despite the positive findings, overall C-flex adherence remained well below recommended levels. Optimizing adherence with OSA treatment may require a multifaceted strategy.
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0504
3D Study Model Analyses To Assess Long-Term Dental Changes In Sleep Apnea Patients Treated With Oral Appliances

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Introduction: Recently the long-term side effects of oral appliance wear on the occlusion of Obstructive Sleep Apnea patients have been widely discussed, but as yet, a detailed computer-based 3D assessment of these changes has not been undertaken.

Methods: The study cast analysis employed a 3D digitizer (MicroScribe-3DX, Immersion Co., USA), compatible with NURBS modeling software Rhinoceros 3.0 for Windows. This system represents a new method to measure 3D dental casts. The digitized landmarks were rotated in different view ports, saved as picture images, and exported in an X, Y, Z format. Seventy patients pre-treatment and post-treatment (after 88.4 ± 26.7 months) dental casts were evaluated. All four casts for each patient were superimposed on different reference points. Three points on the palatal rugae of two upper casts were selected for superimposition. For each upper and lower cast, three occlusal contact points were selected as the superimposing points. Up to 86 landmarks on each cast were digitized and 144 variables were calculated as the linear distance between points or the distance from points to selected reference planes.

Results: Our study confirms a previously reported measurement error (<0.2 mm) with this tool. The following dental measurements showed significant changes (p<0.05) with long-term use of an OA: Lower intercanine and intermolar distance increased 0.59 mm and 0.48 mm respectively, the curve of Spee became flat in the premolar area, crowding decreased (p<0.005) in both the upper (1.11 mm) and lower (0.88 mm) arches, the overbite decreased in the entire arch except for the left and right second molars, the overjet decreased except in the first and second molar areas and the mandibular canine to second molar segment moved forward in relation to the upper.

Conclusion: Changes in dental structures after long-term use of oral appliances are measurable and clinically relevant. Secondary to oral appliance use, a 3D assessment permits visualization of tooth movements from several different perspectives.

0505
Psychological Measures Predict 6-Month Treatment Adherence In Obstructive Sleep Apnea (OSA)

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Introduction: Continuous Positive Airway Pressure (CPAP) is the most commonly used form of treatment for OSA, but adherence is poor. Measures derived from the Transtheoretical Model (TTM) and Social Cognitive Theory (SCT) have been shown to predict CPAP adherence over 1 and 3-month periods. In the present study, we attempt to replicate these findings and extend the follow-up period to 6 months.

Methods: Eighty consecutive OSA patients (53.4 ± 9.7 years, 26 women, mean AHI 41.4 ± 22.4), were recruited if they were medically and psychiatrically healthy, diagnosed with OSA by overnight polysomnography, and willing to try CPAP as their treatment. TTM measures (readiness and decisional balance) and SCT measures (self-efficacy) were administered prior to CPAP (baseline), and at 3- and 6-months post-CPAP initiation. Two-thirds of participants (N=59) received additional assessments of the TTM and SCT constructs after 1 week of CPAP. Nightly CPAP use was monitored objectively throughout the study using Respironics SmartCard™ technology.

Results: We used linear regression to determine the degree to which the TTM and SCT measures taken at baseline, 1 week, and 3 months predicted 6-month CPAP use over and above demographic and apnea severity variables. TTM/SCT measures taken at baseline did not predict CPAP use at 6-months (R2=0.062; p>0.05). The same measures taken at 1 week (N=59) accounted for a unique 19.7% of the variance in use at 6-months (p<0.005). Readiness and self-efficacy were the greatest independent predictors. TTM/SCT measures taken at 3-months predicted 42.7% of the unique variance in CPAP use at 6-months (p<0.001). Self-efficacy and readiness were again the best predictors.

Conclusion: TTM and SCT measures are predictive of CPAP adherence over a 6-month period in OSA, particularly after extended periods of CPAP experience. These findings replicate and extend previous studies of the utility of psychological measures to predict CPAP adherence.

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0506
Medication Use And Changes With Treatment In Moderate To Severe OSA

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Introduction: Sleep apnea is associated with several medical and psychological complaints, which can result in a greater use of prescription medications. The aim of this observational study was to report the number of medications used in patients with moderate to severe apnea, and to examine changes in the number and types of medications used over a 6-month treatment period.

Methods: Data are reported on 131 participants (46 women). Participants reported medication use at baseline and after 6-months of CPAP use. Dependent variables for this study included the total number of medications as well as the number of medications in selected classification groupings. Medication use at baseline was examined by apnea severity and gender. Medication changes with treatment were examined as were the differential changes by CPAP adherence and gender.

Results: Average AHI was 45.0 (sd 25.9). Eighty-six percent of participants reported medication use at baseline. The most commonly used class of medication was antihypertensives (44.3%). There were no differences in medication use by severity. Women were prescribed a higher number of medications at baseline (4.25 vs. 2.91, p < .01). There was a trend for the frequency of individuals prescribed medications between baseline and 6-months to increase in women (89-93%) and decrease in men (84-78%; p < .07). Unexpectedly, the frequency of individuals prescribed antihypertensives from baseline to 6-months increased in good users of CPAP (44-50%) and decreased in poorer users (47-41%; p < .008).

Conclusion: The vast majority of patients with moderate to severe OSA are taking prescribed medications for other conditions. The most common of these are the antihypertensives. Although medications are prescribed at
a similar rate between men and women, women tend to receive a greater number of medications in total.

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0507

Effects Of Two-Weeks Continuous Positive Airway Pressure Treatment And Supplemental Oxygen On Neuropsychological Functioning In Patients With Obstructive Sleep Apnea: A Randomized Placebo-Controlled Study

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Introduction: Obstructive sleep apnea (OSA) can cause cognitive impairment. However, the nature and cause of cognitive deficits in these patients is unclear. We investigated which factors would explain the neuropsychological functioning in OSA patients and whether treatment with 2-weeks CPAP or supplemental oxygen (O2) would improve cognitive functioning.

Methods: 46 untreated OSA patients underwent baseline polysomnography, then were randomized to CPAP, supplemental O2, or placebo-CPAP for 2-weeks. Participants completed Wechsler Adult Intelligence Scale-Revised Digit Symbol and Digit Span, Brief Visuospatial Memory Test, Hopkins Verbal Learning Test, Letter-Number Sequencing, Symbol Search, Trail making A/B, Digit Vigilance, Stroop Color-Word, and Word Fluency tests pre- and post-treatment. Scores on each test were ranked; then, these ranks were averaged to yield an overall neuropsychological ranking for each patient, pre/post treatment.

Results: The overall neuropsychological ranking was significantly correlated with average O2 saturation (p=.032), Epworth Sleepiness Scale scores (p=.025), stage 1 sleep % (p=.039) and stage 2 sleep % (p=.005) at baseline. In stepwise regression, average O2 saturation (p=.042) and % of time at oxyhemoglobin saturation <90% (p=.046) together accounted for 26% of variance in the baseline neuropsychological ranking. Using repeated measures ANOVA, there was no significant Time x Treatment interaction for the overall neuropsychological ranking. When examining individual test scores, only Digit Vigilance-Time (p=.020) showed significant improvement specific to CPAP treatment, while Word Fluency F (p=.008) and Word Fluency A (p=.021) showed significant improvement in both the placebo-CPAP and O2 supplementation groups, respectively.

Conclusion: Hypoxemia might be the primary factor explaining the neuropsychological deterioration in OSA patients. Results also suggested that 2 weeks of CPAP or O2 supplementation treatment may not be long enough to show a beneficial effect on overall neuropsychological functioning in patients with OSA compared with placebo-CPAP.

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0508

Relationship Between Activation And Daily Function In OSA

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Introduction: Alertness and activation are affected by sleep quality. Decreased daytime sleepiness following CPAP could increase behavioral activation producing enhanced daily functioning. There has been no systematic evaluation of this relationship. The purpose of this secondary analysis was to explore differences in activation pre- and post CPAP and the relationship between activation and daily functioning.

Methods: 161 OSA patients (mean age 46.53; 83% male) from 7 sites in US and Canada completed a day of testing pre- and 3 months post-CPAP, which included measures of daily function (Functional Outcomes of Sleep Questionnaire (FOSQ)) and activation (Activation Deactivation Adjective Checklist (AD-ACL)). The mean of the AD-ACL subcales (General Activation (GA)--vigor, Deactivation-Sleep (DS)--sleepiness, High Activation (HA)--tension & anxiety, and General Deactivation (GD)--calmness) for 4 administrations represented daily activation. Statistical analysis was performed by Spearman correlations and multiple regression.

Results: Pre-treatment, GA and DS were significantly correlated with the FOSQ Total score (r = .37, p < .0001; r = - .30, p < .0001, respectively) and Activity level subscale (r = .40, p < .0001; r = - .37, p < .0001, respectively). Multiple regression models that included age, AHI, BMI, and site examined the impact of these demographic variables on the relationship between activation and daily functioning. Although BMI was a significant variable in the multiple regression model (p < .05), it did not change the significance of the relationships between AD-ACL subcales and FOSQ scales. Following 3 months of CPAP, t-tests indicated all AD-ACL (except HA subscale) and FOSQ scores improved significantly (all p < .008). GA and DS were significantly correlated with FOSQ Total score post-treatment (r = .33 and -.45, respectively, p < .0001), and the Activity level subscale (r = .37 and -.45, respectively, p < .0001). No demographic variables were significant in the models at this time.

Conclusion: Pre-treatment, OSA patients have diminished activation with decreased daily functioning. Improvement in activation following treatment increases activity and functional level. As increased activation may reflect enhanced motivation and hedonic drives, as well as improved mood, it may be the mediator through which functioning is elevated following treatment and reduction in daytime sleepiness.

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0509

Cardiovascular Complications Of Obstructive Sleep Apnea In Children

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Introduction: Obstructive sleep apnea (OSA) has been documented to be an independent risk for cardiovascular disease in adults. Recently, Amin et al described increased left ventricular mass (LVM) in children with OSA which they felt was independent of blood pressure (BP). However, a single BP measurement taken during wakefulness was the only data point used. Important elevations in BP may only be present during periods of increased sympathetic drive resulting from repetitive hypoxemia and arousals due to OSA during sleep. We aimed to further study the relationship between OSA, increased LVM and blood pressure in children, using 24-hour ambulatory BP recordings.

Methods: A prospective observational study design was used. Otherwise healthy children aged 4-18 years with polysomnography-proven OSA attending the Pediatric Sleep Service at the Alberta Childrens Hospital in Calgary, Canada were included. All patients underwent echocardiography
and 24-hour ambulatory BP monitoring. The relationships between polysomnography results, BP measurements and cardiac dimensions were analyzed.

**Results:** Preliminary data (9 to date) were studied out 30 children (4 males), mean age 7 year and 4 months (range 4 years - 16 years); the mean LVM was normal at 68.2 grams (range37-183 grams); mean Left Ventricular Mass Index (LVMI) was normal at 58.66 (range 47.2- 87.1); 2/9 (22%) met criteria for mild Right Ventricular Hypertrophy. 3/9 (30%) of children were noted to have nocturnal systolic pressures above the 95th%ile for age for more than 50% of the night, particularly those with the highest apnea hypopnea indices.

**Conclusion:** Our preliminary data suggest that OSA may contribute to nocturnal hypertension and right ventricular hypertrophy but not increased left ventricular mass in children.

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**0510**

**Prevalence Of Sleep Apnea In An Unselected Population Of Patients With Type 2 Diabetes**

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**Introduction:** Diabetes is prevalent in the United States, and expected to affect 22 million patients by 2025. Obstructive sleep apnea (OSA) is also a prevalent condition, affecting approximately 4-10% of the adult population. Although abnormal insulin resistance is associated with OSA, the prevalence of OSA in patients with type 2 Diabetes is poorly characterized. Studies have suggested a prevalence of 12% to 65% in diabetic patients. We investigated prevalence of OSA in patients with Type 2 Diabetes.

**Methods:** Subjects were identified from adult patients referred for Diabetes treatment. For entry, subjects had to: have type 2 Diabetes; be treatment naive for sleep disordered breathing; sleep at least 4 hours per night, and be willing to undergo PSG. Exclusion criteria included Type 1 Diabetes; use of home oxygen or CPAP; or conditions making them unsuitable for enrollment. Eligible subjects used the ApneaLink Screener (ResMed, Poway, CA), a device which records breathing sound and respiratory flow using a nasal cannula for one night at home, and had follow-up laboratory PSG evaluation.

**Results:** The population showed a high prevalence rate for OSA using PSG criteria, with 50.9% demonstrating AHI ≥10; 38.2% demonstrating AHI ≥ 15; and 30.9% demonstrating AHI ≥ 20. Although the overall population was obese, with a median BMI of 35.2, higher BMI was not significantly associated with greater apnea severity. Increased age was strongly associated with more severe OSA (p=0.02), as was male gender (p=0.037) and history of snoring (p=0.050). Patients with confirmed OSA were more likely to have been told that they stopped breathing in sleep than those without OSA (p=0.27), but were not more likely to report feeling unrefreshed on waking.

**Conclusion:** Sleep apnea is highly prevalent in patients with Type 2 Diabetes. BMI was not predictive of increased risk; age, snoring and observed breathing pauses did predict presence of OSA.

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**0511**

**Methods Of Mandibular Advancement Splint (MAS) Titration**

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**Introduction:** MAS devices have a therapeutic role in Obstructive Sleep Apnoea (OSA) but research is needed to define optimum methods of titration. Aim of study to compare two methods of MAS titration (self-adjustment with and without polysomnography feedback).

**Methods:** Twenty nine patients (25M, 4 F, mean age 49 years, mean BMI 27.6 kg/m2) with OSA (mean Apnoea Hypopnoea Index (AHI) 25.7/hr range 10-46/hr) and symptoms (Epworth Sleepiness Score > 8/24, snoring, choking, poor sleep quality) were treated by MAS set at 70% of maximal protrusion. Subjective group (n=17) self-adjusted according to symptoms and comfort. Objective group (n=12), fixed setting then given self-adjustment advice based on polysomnography result at 3 weeks. Outcome variables (AHI, symptoms) at 6 weeks were compared by t-tests, and chi squared tests.

**Results:** The two groups did not differ in mean baseline AHI (p=0.73), BMI (p=0.54) or age (p=0.80). MAS was used by the majority of patients every night (83% objective, 59% subjective) and all night (82% objective, 71% subjective). Objective feedback was associated with a progressive reduction in AHI (baseline 26.5 ±12.0/hr, 3 weeks 15.3±13.5/hr, 6 weeks 11.7±10.0/hr, p=0.01) and increasing proportion of patients whose OSA resolved (AHI < 5/hr) or improved (decrease by > 50% and AHI > 5/hr), 7/12 at 3 weeks and 9/12 at 6 weeks (p=0.33). In the subjective group AHI was reduced by a lesser extent (baseline 25.1±7.4/hr, 6 weeks 15.5±13.7/hr, p=0.053) but a similar proportion resolved or improved their OSA at 6 weeks (10/17, versus objective p=0.43). Symptomatic benefit was reported by both groups (daytime alertness: objective p=0.0007, subjective p=0.0004, refreshed on waking: objective p=0.0003, subjective p=0.002 and sleep quality: objective p<0.0001 subjective p=0.004).

**Conclusion:** A titratable MAS improved or resolved OSA in the majority of patients. Objective feedback was associated with a greater reduction in AHI but a similar proportion of patients gained symptomatic benefit.

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**Otago University Research Grant**

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**0512**

**Genioglossal Responsiveness To Decreasing CPAP During Stable NREM Sleep**

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**Introduction:** The sleep related fall in dilator muscle activity (genioglossus (GG)) has been postulated to contribute to airway collapse in patients with obstructive sleep apnea (OSA). The aims of this study were to determine 1) the variability in magnitude and latency of the GG response to reduced CPAP during NREM sleep and 2) whether these variables differ between individuals with and without OSA.

**Methods:** Inspired minute ventilation (VI), epiglottic pressure (PEPI) and GG electromyogram (EMGgg) were measured in patients with and without OSA. All subjects were initially placed on continuous positive airway pressure (CPAP) sufficient to abolish inspiratory airflow limitation. During stable NREM sleep, CPAP was sequentially dropped multiple times for 5 minutes (2-8 cmH2O below the titrated CPAP level). In each subject, peak inspiratory EMGgg was correlated to minimum inspiratory PEPI for each breath prior to arousal during CPAP drops. The slope of this relationship was determined in each subject. The time from CPAP drop until peak inspiratory EMGgg rose 2 standard deviations above baseline, was calculated as the latency of GG activation.

**Results:** Four healthy subjects (Mean ± SEM, Age = 34.8 ± 2.4 yrs) and 4 OSA patients (Age = 39.5 ± 7.5 yrs, AHI = 47.3 ± 9.5 events/hr) have been studied to date. The mean slope of the EMGgg versus PEPI relationship was similar (-0.25 ± 0.08 vs -0.59 ± 0.1 %/cmH2O) between...
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Introduction: Alcohol use, especially near bedtime, may exacerbate sleep-disordered breathing (SDB). This epidemiologic analysis from the Wisconsin Sleep Cohort Study examines the cross-sectional association of SDB with “usual” alcohol consumption habits while adjusting for potential “acute” effects of alcohol consumed just prior to SDB assessment.

Methods: The apnea-hypopnea index (AHI, events/hour), a measure of SDB severity, was determined by in-laboratory polysomnography on a sample of 1516 adults. AHI≥5 defined “mild or worse” SDB. Usual weekly and “acute” (the evening prior to polysomnography) alcohol consumption were assessed by questionnaire. Categories of consumption were defined by grams of alcohol per kilogram of body mass. Generalized linear (regression) models estimated odds ratios (OR) for SDB in persons with varying categories of alcohol consumption, adjusting for “acute” alcohol consumption, age, body mass index, a variety of medications, and smoking.

Results: Relative to men who consumed no alcohol, men who consumed from >0 to <0.5 g/kg per day had 23% greater odds of SDB (OR=1.23, 95% CI=0.95-1.60, p=0.1); men who consumed ≥0.5 g/kg per day had 3.09 times greater odds (95% CI=1.47-6.47, p=0.003). There was a significant increasing trend in the odds ratios (p=0.002). Alcohol-consuming women showed no increased risk of SDB. Relative to women who consumed no alcohol, women who consumed >0 to <0.5 g/kg per day manifested no difference in risk (OR=0.93, 95% CI=0.69-1.25). None of the 18 women reporting alcohol consumption ≥0.5 g/kg per day had SDB.

Conclusion: In men, independent of alcohol consumption on the evening of SDB evaluation, increased usual alcohol consumption was associated with increased risk of mild or worse SDB. There were too few women reporting high levels of alcohol consumption to fully address the association in women. Persons with SDB might benefit from generally moderated alcohol consumption and not just avoidance near bedtime.

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0513
Sleep-Disordered Breathing And Usual Alcohol Consumption: A Population-Based Study Of Men And Women
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Introduction: Alcohol use, especially near bedtime, may exacerbate sleep-disordered breathing. However, slow or small GG responses when combined with poor airway anatomy may predispose to airway collapse.

Methods: This preliminary data suggests that individuals with OSA can recruit the GG during stable sleep similarly to healthy subjects. The apnea-hypopnea index (AHI) and both functional magnetic resonance imaging (fMRI) measures of brain activation and performance during a verbal learning task.

Methods: Eighteen subjects (3 women; mean age=43, SD=12, range 25-59) with a mean AHI=9.9 (SD=16.7, range: 0-67) underwent overnight polysomnography followed the next morning by fMRI scan session. As part of the fMRI session subjects performed a verbal learning task. For this analysis activation data during the task were regressed onto the AHI.

Results: Significantly more brain activation was associated with higher AHI (p<0.01). The activated areas included the right superior parietal lobe (BA40), left inferior parietal lobule, left middle and superior temporal gyrus, BA6, BA7, and the left inferior and medial frontal gyrus (BA45). Behaviorally, no significant correlations were found between AHI and performance.

Conclusion: These preliminary results suggest a possible relationship between AHI and brain activation during a verbal learning task. Alterations in brain activation in the absence of impaired performance would suggest a compensatory process (recruitment of additional brain areas in order to maintain similar level of performance) in sleep apnea patients. We have reported a similar process, involving some of these same areas, in sleep-deprived subjects. Assessing these differences in a larger sample will provide more insight into the cerebral substrates of cognitive functioning in sleep apnea patients.

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0514
The Effect Of Bedding On Lateral Position Sleep For OSAHS Patients
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Introduction: Obstructive sleep apnea syndrome (OSA) patients present with impairments in various cognitive domains. Despite the considerable data about the behavioral correlates of OSA, much less is known about changes in the brain substrates underlying the behavioral deficits. This preliminary report assesses the correlations between apnea-hypopnea index (AHI) and both functional magnetic resonance imaging (fMRI) measures of brain activation and performance during a verbal learning task.

Methods: Of the estimated 1-3 million Obstructive Sleep Apnea Hypopnea Syndrome (OSAHS) sufferers in Japan, less than 50% have received treatment for this condition. The Nasal Continuous Passive Airway Procedure, (n-CPAP), is the first choice of treatment, but is only chosen when a patient's Apnea Hypopnea Index, (AHI), is 20 or more, and less than half agree to undergo this procedure.

Methods: 10 normal healthy volunteers and 9 OSAHS patients participated in the experiment. The control group continued for four successive nights changing bedding and pillows. They slept on cotton sleeping mats over Bonnel coil mattresses consisting of 50% polyester, 50% acrylic, and 192 Bonnel coil drum-shaped springs during the first and second night. During the third and fourth night, they slept on static pressure beds lined with 100% polyester over urethane foam. On the first and third night cotton covered bean-stuffed pillows were used. During the second and fourth night peanut-shaped pillows with 100% cotton fabric covering a 300g polyester core were used. OSAHS patients slept on Bonnel coil beds and used the bean-stuffed pillows on the first night. During the second night they used static pressure beds and peanut shaped pillows.

Results: The control group showed no significant aberrations of sleep structure from the first through fourth night. They slept laterally 266.5 ±44.3 minutes, spine 166.7±27.3 minutes on the first night, and laterally...
Introduction: Patients with obstructive sleep apnea syndrome (OSA) frequently have cognitive deficits, especially related to executive functions, which cannot be fully explained by daytime sleepiness. The causal mechanism of these cognitive deficits is not yet known, but a possible relationship with chronic intermittent oxygen desaturation has been proposed. This report assesses the correlations between oxygen desaturation index and both performance and functional magnetic resonance imaging (FMRI) measures of brain activation during a verbal learning task.

Methods: Eighteen subjects (3 women; mean age=43, SD=12, range 25-59) with a mean AH=9.9 (SD=16.7, range: 0-67) underwent overnight polysomnography followed the next morning by FMRI scan sessions. As part of the FMRI session subjects performed a verbal learning task. For this analysis activation data during the task were regressed onto the number of oxygen desaturations per hour of sleep.

Results: Higher desaturation index was associated with worse immediate word recall (r=0.63, p<0.01). With respect to FMRI data, a higher desaturation index was associated with significantly more brain activation. The activated areas included the bilateral middle and inferior frontal gyri (Broadman’s area 9) (p<0.01).

Conclusion: These preliminary results suggest a relationship between nocturnal oxygen desaturations and performance on a verbal learning task. They also suggest an association between frontal lobe activation and nocturnal oxygen desaturation. These results may support the hypothesis that OSA elicits abnormalities in frontal cortex activity, especially during performance of tasks relying on intact prefrontal functioning. If chronic intermittent hypoxia in OSA leads to structural damage, the association between oxygen desaturation and brain activation may also explain the irreversibility of some of the cognitive deficits after the normalization of sleepiness with nasal continuous positive airway pressure treatment.

Category J—Sleep Disorders-Breathing

0516

Altered Cerebral Activation During A Verbal Learning Task In Sleep Apnea Patients Is Associated With Nocturnal Oxygen Desaturation

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Introduction: Few studies compare data from MSLT and MWT and little is known about factors related to discrepancies between these measures. We examined such variables in an obese population with appreciable levels of sleep apnea.

Methods: We studied a total of 61 obese patients (37 w, 24 m), 39.2±12.4 years old (Body Mass Index (BMI) ≥30 kg/m2). The evaluation consisted of one night of polysomnographic recording following by five-nap MWT (20-min trial) and five-nap MSLT. Each MSLT followed the MWT and both were done on the same day. The MWT-trials began at approximately: 9:45 am, 11:45 am, 1:45 pm, 3:45 pm and 5:45 pm. Scoring of both MWT and MSLT was done with latency measured to the first epoch of any stage of sleep. Sleepy obese patients (MSLT < 10 minutes) were subdivided according the MWT sleep latency, in those with impairment in wake tendency (Group-1 MWT <11 minutes, n=26) and those without impairment in wake tendency (Group-2 MWT ≥11 minutes, n=29).

Results: The majority of patients obtained a value below 10 minutes on the MSLT 90.2% (mean =3.3±2.1 minutes). Groups with/without impairment in wake tendency differed in the depression, Beck score (Group-1=21.3±13.5; Group-2=14.7±8.3, t=2.0, p<0.05); heart rate (Group-1=86.4±10.9; Group-2=79.9±10.4, t=2.1, p<0.05); and Epworth sleepiness score (Group-1=11.3±6.6; Group-2=7.2±4.1, t=2.5, p<0.02). There were not statistically significant differences between the groups in Apnea/Hypopnea Index (Group-1=54.1±41.5; Group-2=42.0±41.9); BMI (Group-1=52.2±10.8; Group-2=49.4±12.5), oxygen desaturation, total sleep time, or sleep continuity index.

Conclusion: Fifty percent of the sample could be classified as concordant for the two tests. Data showed that in sleepy obese patients wakefulness tendency is impaired in those with higher heart rate, higher reported level of depression and higher reported level of sleepiness. These data suggest potential autonomic and behavioral factors associated with ability to maintain wakefulness, even in severe OSA.

0518

RDI And Patient Parameters: Gender Differences

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Introduction: Gender differences are common in OSA. We reviewed RDI, NREM RDI and REM RDI correlations with PSG and patient parameters.

Methods: We studied 179 patients having a PSG. Patients were excluded, if they had less than five hours of total sleep or 30 minutes of REM sleep, leaving 116 patients: 60 women, mean age 43 (SD=11.6, 24—67) and 56 men, mean age 44 (SD = 10.7, 23 to 71).

Results: The women had a lower RDI than men, 11.0, (SD 16.2), versus 24.5 (SD 7.7) p<.002, but not in the REM-RDI, womens means 25 and mens 28.6. The RDI was compared with % deep sleep, % light sleep (%LS), % REM, sleep efficiency and BMI. Mens correlations: BMI r squared=0.11 p<0.01; %LS r squared=0.02 NS. Mens correlations: BMI r squared= 0.03 NS; %LS r squared=0.29 p<.0001. The correlation between RDI and light sleep disappears in men with RDI < 20. Below the age 50 Mens correlations: BMI r squared=0.12 p<0.03; %LS r squared=0.02 NS. Mens correlations: BMI r squared=0.03 NS; %LS r squared=0.30 p<.0002. Age fifty or above: Womens correlations: BMI r squared =0.21 p<0.054; %LS r squared=0. NS. Mens correlations: BMI r squared =0.40 p<.03; %LS r squared=0.15 NS There were no significant correlations between RDI and age.

Conclusion: Women are relatively protected against obstructive sleep apnea, prior to menopause. Weight dominates; hence, the correlation
0519
The Correlation Between Subjective Sleep Perceptions From Post-Test Questionnaire And Objective Sleep Parameters In Patients With Obstructive Sleep Apnea
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Introduction: Currently, there are controversies about the relationship between OSA and subjective sleepiness. Recent study has shown the correlation between subjective sleep complaints and respiratory arousal. However, there is limited information on the relationship between subjective sleep perceptions and objective sleep parameters in this population.

Methods: A retrospective study was performed in patients with obstructive sleep apnea. All patients completed post-test questionnaire after sleep study as part of our routine procedure. Any patients with significant neurological diseases, psychiatric disorder, central sleep apnea, severe periodic leg movements (PLMD>50) or incomplete records were excluded from the study.

Results: 79 patients met the criteria for entry into the analysis; 41 African American (B) and 38 Caucasian (W). The average age is 47.5±10.1 years and the mean apnea-hypopnea index (AHI) is 25.9±19.5/hr. The subjective feeling upon awakening (Q15; scale 1-6) correlated with the arousal index (r=0.27, P=0.019), AHI (r=0.3, P=0.008), and apnea-hypopnea related arousal (r=0.24, P=0.038). There is a tendency toward significant correlation between subjective sleep quality (Q7, scale 1-4) and arousal index (r=0.22, P=0.054) as well as between Q7 and AHI (r=0.22, P=0.056). In addition, subjective total sleep time (TST) and sleep latency (SL) correlated well with corresponding objective sleep parameters from a sleep study (r=0.52, P<0.001 [TST]; r=0.35, P<0.005 [SE]).

Conclusion: It is concluded that subjective sleep perception from post-sleep questionnaire correlates significantly with severity of apnea and frequency of arousals especially respiratory arousals. Post sleep questionnaire is relatively accurate and could be a useful additional tool in assessment of sleep disruption in patient with obstructive sleep apnea.

0520
RDI, Mean Sleep Latency And SOREM
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Introduction: The Mean Sleep Latency (MSL) has been considered to gold standard for measuring the day-time sleepiness. This measure weakly correlates with the RDI in large studies. We confirmed the correlation between RDI and MSL, reviewing with respect to whether or not there are SOREM.

Methods: We studied 163 unselected patients presenting to our laboratory, having a PSG and MSLT. We excluded from the analysis any subject with an RDI < 5. This left 68 men and 44 women.

Results: The mean overall RDI was 19.8, 25.7 for men, 13.4 for women. The women's mean age was 52, the men mean age was 47. We reproduced the correlation between MSL and RDI, r squared = 0.05, p < .02. In subjects without SOREM: there was an almost significant correlation between the MSL and the RDI. The r squared = 0.04, p < 0.06 (N=96). Only 14 subjects had SOREM on the MSLT (13%). This group had a significant correlation between the MSL and the RDI, r squared = 0.34, p < 0.02. We compared the mean RDI and mean REM-RDI between both groups. There were no significant differences. The mean RDI of the subjects without SOREM was 28, with SOREM was 28. The mean REM-RDI of the subjects without SOREM was 35, with SOREM was 44 (p = .17). The Mean Sleep Latency of the subjects without SOREM was 9.2, with SOREM was 6.7 (p < .06).

Conclusion: SOREM is not common on an MSLT done in the presence of OSA. The presence of SOREM reveals a stronger correlation between MSL and RDI as well as a significant degree of daytime sleepiness. Patients with OSA and SOREM on an MSLT form an interesting subgroup of patients with OSA behaving as intuitively expected: A solid correlation between RDI and MSL with short MSL.

0521
Brain Function In Sleep Apnea: Results From An International Brain Database
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Introduction: Obstructive sleep apnea (OSA) affects a range of neurobiological parameters but most studies involve either small sample sizes or very limited testing in larger cohorts. Large, linked brain function databases provide an opportunity to compare psycho-physiological, cognitive and demographic patterns in subjects with and without OSA.

Methods: Data was drawn from the Brain Resource International Database (six laboratories in Europe, North America and Australia). OSA group: n=50 subjects (70% males, mean age 51.6, mean BMI 37.7) scoring > 70.50 on the Multivariable Apnea Prediction Index (MAP, Maislin G. Sleep 1995; 18: 158-66). Control group: scoring zero on index and having a MAP index of < 0.50, with 4 age and sex matched subjects for each OSA subject (n = 200, mean age 50.5 years, mean BMI 24.86). Responses from the DASS questionnaire, cognitive tests of executive function, resting EEG power, and auditory oddball ERP were compared.

Results: For 12 ERP oddball measures there was a significant effect of group, after controlling for scalp region and age (MANCOVA p<0.0001). The OSA group had increased N100 amplitude (p = 0.0003), increased P200 latency (p < 0.00001) & amplitude (p < 0.0001), increased N200 latency (p<0.0001) & reduced amplitude (p = 0.001), and reduced P300b amplitude (p = 0.003). In the OSA group, resting eyes-closed alpha power was lower (p = 0.0006), as was the alpha peak amplitude (18.7 vs 34.8 mV, p = 0.004). There were no significant between group differences for any of the DASS sub-scales (p > 0.1) or for performance on span of visual memory, timing test, and executive maze (p > 0.16).

Conclusion: Neurophysiological tests showed high sensitivity in detecting impairments in cognitive processing and attention in subjects with suspected OSA, despite the lack of differences in neurocognitive performance and mood variables between the two groups.

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0522
Impact Of Sleepiness On Autonomic Function In OSA Versus Controls In A Clinic Population Using Portable Pupilometry
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Introduction: Obstructive sleep apnea encompasses a broad spectrum of disease ranging from mild to severe respiratory, cardiovascular, and sleep disturbances. Imbalances in adrenergic autonomic function in subjects with sleep apnea may result from both ventilatory and arousal abnormalities. We wished to evaluate autonomic nervous function using pupillometry to assess differences in sleepiness and OSA severity.

Methods: OSA and control subjects (without cataract surgery, glaucoma, blindness, history of head trauma, snoring or sleepiness) were recruited from a sleep disorders and a general otolaryngology clinic at the Medical College of Wisconsin. Maximum and minimum pupillary aperture, constriction velocity, dilatation velocity and latency were measured (ForSite(TM) pupillometer,Neuroptics). Three complete consecutive measurements from each eye were obtained. Mean values from each eye of sleepy versus non-sleepy patients and subjects with mild OSA versus moderate to severe OSA were compared using analysis of variance and the Student t-test.

Results: OSA subjects (n= 65, male = 62.5% , age 47.3 years, mean Epworth score, 11.4, and mean self reported sleepiness (0-10 point visual analog scale of 6.5) were compared to a control group (n=54, male 61, age =39.4). OSA subjects compared to the control group showed a statistically significant reduction in the pupillary constriction velocity with a difference of -0.33 (p=0.034). Median constriction velocity differed between controls, moderate OSA (AHI =15-30) and severe OSA (AHI > 30, p< 0.05). Groups stratified by subjective sleepiness demonstrated a trend demonstrating increased constriction velocity opposite in direction compared to those with a higher RDI. (ForSite(TM) pupillometer,Neuroptics).

Conclusion: Portable pupillometry identifies sympathetic autonomic differences in controls, mild and moderate OSA groups. ESS and VAS measures of sleepiness demonstrate a trend in autonomic abnormalities opposite that of OSA measured by AHI severity. Differences in autonomic function are consistent with known autonomic abnormalities associated with OSA but suggest that sleepiness may result from or cause independent autonomic abnormalities. Portable pupillometry may provide a means of identifying autonomic abnormalities in non-sleepy OSA populations.

0524 Changes Of Pressure Levels Required By Patients With OSAHS During Short Term And Long Term CPAP Treatment

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Introduction: To evaluate the short and long-term changes of CPAP level in patients with OSAHS, and address the necessity of re-titration of CPAP pressure during long term treatment.

Methods: Twenty-five patients diagnosed as moderate to severe OSAHS (AHI>15 with a mean of 56) were included to the study. A manual overnight titration to determine the optimal CPAP (oCPAP) was undertaken following the diagnostic PSG test. Then all of the 25 patients were admitted to sleep ward for a one-week auto-CPAP treatment (418A, Tyco), SpO2, PSGs were performed on the 1st, 3rd, 5th and 7th day with CPAP. Patients were monitored by a video camera to ensure they were sleeping in supine position. 20 patients then used auto-CPAP at home were followed up, pressure and SpO2 profiles were downloaded at 2 and 6 month after treatment.

Results: PSG revealed that auto-CPAP had the same effect as CPAP on AHI, SpO2 and sleep architectures. In the first week, the highest pressure level (hCPAP) required did not differ between days, and the every day level of hCPAP also did not differ from oCPAP. However, the mean CPAP pressure level (mCPAP) required decreased significantly (p<0.01) up to the 5th and 7th days; and the percentage of sleep time spent in low level of CPAP increased, and in high level of pressure decreased across time. Compared to the pressure at 7th day of treatment, at both 2 and 6 months there was no significant change in hCPAP and mCPAP. Compliance to CPAP treatment was a mean of 5.3(1.9)h/d over 6(0.8)d/week usage. No significant BMI change occurred.

Conclusion: There was an initial decrease in mCPAP level, which we attribute to REM sleep rebound. As both short and long term hCPAP required by patient did not change, there is no general need for re-titration in most OSAHS patients using CPAP.

0525 Endothelial Dysfunction Assessed By Peripheral Arterial Tonometry In Obstructive Sleep Apnea Patients Improves With CPAP Therapy

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Introduction: Obesity is a major co-morbidity of obstructive sleep apnea (OSA) with a crucial impact on general health of OSA patients. Weight loss is associated with clinical improvement of OSA severity. No studies investigating OSA have looked at weight loss with a sibutramine assisted weight loss programme (SIB). Our aim is to assess weight loss in sleep disordered breathing in obese men with OSA through SIB.

Methods: Open uncontrolled cohort study of obese males OSA subjects. Subjects were placed on SIB. Subjects were given oral sibutramine 10 mg daily (or 15 mg).

Results: 64 obese (BMI 34.3(2.7) kg/m2), middle-aged (47.1 (9.8) years) males subjects with symptomatic (Epworth score of 13.0 (3.6)) OSA (Total RDI 45.3 (22.8) events/hour) completed the study. There were significant reductions in markers of obesity, weight 107.1 (13.1) to 98.8 (12.8) kg, neck circumference 44.5 (2.2) to 42.8 (2.2) cm, waist circumference 116.4 (8.3) to 108.2 (9.0) cm and sagittal height 28.7 (2.7) to 24.9 (2.9) cm (all p<0.05). OSA was also significantly improved, total RDI 45.3 (22.8) to 30.3 (19.7) events/hour and percentage total sleep time oxygen saturation less than 90% 8.3 (13.8) to 5.7 (11.5) % (p<0.05). Metabolic markers were also improved with SIB, fasting insulin 107.0 (61.0) to 88.1 (57.2) pmol/L and HDL cholesterol 1.10 (0.22) to 1.14 (0.22) mmol/L (p<0.05). Moderate (~10%) weight loss was achieved and resulted in improvement in RDI and a range of metabolic abnormalities.

Conclusion: SIBUTRAMINE ASSISTED WEIGHT LOSS IN OBES E OSA SUBJECTS IS ASSOCIATED WITH IMPROVEMENTS IN SLEEP DISORDERED BREATHING AND OTHER METABOLIC VARIABLES.
Introduction: Obstructive sleep apnea syndrome (OSAS) is an independent risk factor for hypertension and cardiovascular morbidity. Several studies implicate OSAS to be associated with endothelial dysfunction (ED), and measures of ED are prognostic of future cardiovascular events. We hypothesized that treating OSAS patients with abnormal ED would lead to improvement in ED.

Methods: We prospectively recruited 50 patients with OSAS from the Mayo Sleep Disorders Center who were to undergo CPAP therapy. The pulse wave amplitude response index (PWRI) to post-occlusive hyperemia, a validated measure of endothelial function, was assessed using a special transducer fitted to an upper extremity digit (EndoPAT) prior to and after 1 month of CPAP therapy. Sleep and breathing events were measured during the diagnostic portion of split-night polysomnography and were also simultaneously estimated using the WatchPAT-100, an ambulatory monitor. CPAP devices with downloading capacity recorded compliance, and a nurse specialists noted subjective clinical responses to therapy. (EndoPAT and WatchPAT-100 are products of Itamar Medical, Israel.)

Results: Mean age was 54.7±13.0 years, BMI was 37.4±9.5, and AHI was 29.1±24.6 [median 22.0]. 30 patients had normal PWRI (PWRI<1.70), 20 had ED (PWRI>1.70), and the group mean was 1.83±0.41. Hypertension was highly associated with ED (p=0.0046), but other clinical features (age, BMI, CAD, CHF, a-fib, peripheral vascular disease, smoking), AHI, respiratory or total arousal index, O2sat parameters, and measures derived from WatchPAT-100 were not (all p>0.05). Objective nightly CPAP use was 4.8±2.3 hours [median 5 hours]. Patients with baseline ED improved from a mean PWRI of 1.46±0.14 by 0.40±0.24 (27.4% improvement, p=0.0034), while those with an initially normal PWRI did not change significantly (P>0.05).

Conclusion: Hypertension is associated with ED in patients with OSAS. Patients with OSAS and ED show improvements in endothelial function with 1 month of CPAP therapy.

This work was supported in part through an educational grant from Itamar Medical, Israel.

0526
Restoring Respiratory Mechanics Instability In A Split Night Protocol
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Introduction: Sleep disturbed breathing (SDB) is a disorder of functional airway instability. During sleep the resistance in the upper airway is increased. SDB patients are unable to compensate for the decrease in responsiveness of the upper airway to the increase of resistance in an effective way, with arousals as result. It was proposed earlier that instability in the increase in upper airway resistance will cause variability in the phase relationship between the respiratory movements of thorax and abdomen (Respiratory Mechanics Instability or RMI). This paper describes the restoration of the RMI by CPAP.

Methods: 57 Patients (Age: 47±12, BMI 30.5 ± 6.2, RDI: 0.7 to 57) were recorded with full polysomnography (REMbrandt system) in a split night protocol. 40 Control patients (Age: 45 ± 10, BMI 28.9 ± 5.92, RDI: 0.3 to 72) were recorded without CPAP. The percent of time spent in RMI state (periods of instability of respiratory mechanics higher than baseline level) was calculated (RMI-I).

Results: The respiratory instability (calculated by RMI index) was significantly reduced by titrated CPAP pressure (p<0.0001). As in a split-night protocol the titrated pressure is in the second half of the night, the time of night can be an important factor. However, the time of night effect on respiratory instability was not significant in the control group. The reduction of instability by titrated CPAP pressure accompanied the reduction of RDI (p<0.0001). Moreover, RMI also showed the effects of over-titration that could not be seen in RDI.

Conclusion: CPAP restored the balance in the upper airway mechanics in SDB patients, shown as a decrease in RMI-I values.

0527
Utility Of Split Night Studies In Obstructive Sleep Apnea: Objective Follow-Up Comparison With Formal CPAP Titration Using CPAP Downloads
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Introduction: Split night (same night polysomnography and CPAP titration) studies are often used to reduce costs of sleep testing in patients with obvious obstructive sleep apnea. However the expected reduction in titration and patient acclimatization times often negatively influences its use in the sleep laboratory. There have been few studies comparing follow up data from patients titrated using split night versus conventional CPAP titration.

Methods: Charts of 106 patients being followed at our sleep disorders clinic were reviewed for symptoms, type of titration, pre CPAP respiratory disturbance index, Epworth scores, optimal pressures, percentage use and mean hours used per night. Data was collected from sleep studies and also from smart card downloads. 66 patients had formal CPAP titrations and 40 patients underwent split night studies. Patients split were those referred for split studies with an RDI>20/hr with desaturations below 85% with at least 3 hrs titration time available. The studies were scored and titrated as per conventional protocols with titration endpoints of no snoring, arousals, desaturations below 90%, paradoxical respiration and RDI<5/hr for at least 30 mins of continuous sleep.

Results: The mean age and Epworth scores in the CPAP group were 49.9 years and 12.5 (49.3 years and 10.8 Epworth in the split night group). Mean percentage of CPAP use in the CPAP group( from smart card downloads) was 66.7% (n=56) vs 64.1% in the split titrated group (n=37). Means hours used per day was 5.15 hrs/night in the CPAP group and 4.82 hrs in the split group.

Conclusion: Follow up data using smart card downloads show fairly comparable CPAP usage between patients who had formal CPAP titration and split night titration. Proper mask fitting and patient education prior to polysomnography possibly helps in improving success rates with split night studies despite time constraints.

0528
The Effect Of CPAP Titration Methodology On Six-Month Compliance And Treatment Satisfaction
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Introduction: Continuous Positive Airway Pressure (CPAP) therapy is an accepted standard of treatment for obstructive sleep apnea (OSA). CPAP pressure settings are usually determined using in-laboratory polysomnography. Titration studies are done under full night (FN) or split-night polysomnography (SN). While efforts have been made to determine how to better identify patients who are eligible for a SN protocol, relatively little is known about their long-term outcome. This study evaluated the impact of titration methodology on long-term outcome and treatment satisfaction.
**Methods:** 135 newly diagnosed OSA patients participating in a multicenter study evaluating the use of conventional CPAP (n=71) and CPAP with expiratory pressure relief (FLEX; C-Flex®, Respironics, Inc., Murrysville, PA) (n=64) were titrated with a FN or SN, as ordered by their treating physician. Therapy compliance and patient satisfaction (visual analog scale, 0-100mm, higher value related to greater satisfaction) with therapy, therapy comfort, and interface comfort were collected at 1 month, 3 months, and 6 months. Sleepiness was assessed using Epworth Sleepiness Scale (ESS). Data were analyzed using ANOVA or t-tests. All values are expressed as mean±SD.

**Results:** Diagnostic RDI (FN41±23 hr⁻¹ v. SN61±29 hr⁻¹) and BMI (FN35±6 hr⁻¹ v. SN35±7 kg/m²), were not significantly different between groups. Compliance with therapy was comparable for both titration methodologies (SN 6.0±1.4 v. FN 5.8±1.6 hours/night, ns), as well as treatment satisfaction (SN 83±23 v. FN 86±18), overall treatment comfort (SN 76±23 v. FN 80±19, ns), and interface comfort (SN 68±23 v. FN 74±19, ns). ESS at six months was also comparable (SN 7.4±4.6 v.FN 6.7±4.7, ns).

**Conclusion:** Titration methodology did not differentially impact CPAP use, or treatment satisfaction, after six months of therapy.

**Respironics, Inc.**

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**0529**

**Prevalence And Characteristics Of Obstructive Sleep Apnea In Patients Undergoing Gastric Bypass Surgery**

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**Introduction:** Obstructive sleep apnea (OSA) has a high prevalence among obese adults and may lead to perioperative complications if undiagnosed before gastric bypass surgery. We hypothesized that sleep apnea would be common in the gastric bypass population. Therefore, we examined in gastric bypass patients the prevalence of sleep apnea and the relationships of the Multi-variable Apnea Sleep Symptom (MAP) score and the Epworth Sleepiness Scale (ESS) to the apnea hypopnea index (AHI).

**Methods:** 50 consecutive patients evaluated for gastric bypass from 1/2004 to 4/2004 underwent overnight polysomnography and completed questionnaires (MAP and ESS). Apneas and hypopneas were classified as follows: Mild apnea: AHI<15, Moderate apnea: 15<AHI<30, Severe apnea: AHI>30, REM-related apnea: present when REM-AHI>twice NREM-AHI and REM-AHI>10

**Results:** Mean body mass index (BMI) in kg/m² was 49.3±8.7 and mean age was 40.6±10.7. Our sample was 78% female and 66% white, 28% African American, and 2% Hispanic. The overall frequency of OSA was 66%. ESS did not correlate with AHI, but increased BMI, increased MAP, and male gender correlated with increased AHI. Our data indicate that sleep apnea and particularly REM-related apnea are common in patients undergoing gastric bypass surgery. Therefore, gastric bypass patients should be screened for OSA.

**Conclusion:** In our population of gastric bypass patients, the prevalence of sleep apnea was 58%, and the prevalence of REM-related apnea was 66%. ESS did not correlate with AHI, but increased BMI, increased MAP, and male gender correlated with increased AHI. Our data indicate that sleep apnea and particularly REM-related apnea are common in patients undergoing gastric bypass surgery. Therefore, gastric bypass patients should be screened for OSA.

**Dr. Unruh was supported by grants from ASN-Hartford-ASP Junior Development Grant in Geriatric Nephrology and the NIDDK (DK66006). The Sleep Heart Health Study is supported by U01HL53916 (University of California, Davis), U01HL53931 (New York University), U01HL53934 (University of Minnesota), U01HL53937 (Johns Hopkins University), U01HL53938 (University of Arizona), U01HL53940 (University of Washington), U01HL53941 (Boston University), U01HL63429 (Missouri Breaks Research), U01HL63463 (Case Western Reserve University), U01HL64360 (Johns Hopkins University).**

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**0530**

**The Relationship Of Kidney Function To Sleep Disordered Breathing Among A Large Cohort Of Older Adults**

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**Introduction:** Sleep apnea is a well established risk factor for hypertension, warranting analysis of its association with end organ damage such as chronic kidney disease.

**Methods:** We examined this relationship among 1140 community dwelling older adults who participated in both the Cardiovascular Health and Sleep Heart Health Studies (mean age 78; 57% women, 81% white, mean BMI 27.0). Kidney function was assessed using the MDRD GFR prediction equation (mean±SD 68±18.2), serum creatinine (1.07±0.40) and cystatin C (1.07±0.26), a novel biomarker of kidney function. Cystatin C is more directly related to iothalamate measured GFR and its interpretation is not as confounded by age and lean body mass compared to creatinine or estimated GFR (eGFR). Home polysomnography was used to define the apnea-hypopnea index (AHI: average number of apneic and hypopneic events with > 4% desaturation per hour of sleep). The study population was restricted to those with at least 4 hours of sleep time and those with cystatin C.

**Results:** There was a significant correlation between cystatin C and AHI with a one unit increase in cystatin associated with a 46% higher AHI (p<0.01). This effect remained significant and unchanged in magnitude after adjusting for age, sex and race. However, this effect was diminished in magnitude after accounting for age, sex, race and BMI; a one unit increase in cystatin associated with a 19% higher AHI (p=0.22). We examined the association of cystatin with BMI. In those with a BMI <27, the correlation of cystatin and BMI was nonsignificant (r=0.01, p=0.85), however, among those with a BMI ≥27, the correlation was significant (r=0.18, p<0.01). As expected, there was a weak correlation between serum creatinine and AHI (r=-0.06, p=0.04) and no significant correlation between eGFR and AHI (r=0.02, p=0.57). The association of creatinine with AHI was nonsignificant after adjustment for age, sex, and race.

**Conclusion:** In conclusion, kidney function, as assessed by cystatin C, was associated with sleep apnea. This relationship between cystatin C and sleep apnea was weakened in magnitude and became nonsignificant in this large group of older men and women after accounting for age, gender, race and BMI. This may be partly due to a limited number of patients with poor kidney function. Cystatin C should be measured in longitudinal studies of sleep apnea in order to better determine the causal relationship between sleep apnea, BMI, and kidney function.

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**Return to Author Index**  **Return to Key Word Index**
0531 Armodafinil As Adjunct Therapy Improves Wakefulness And Fatigue In Patients With Obstructive Sleep Apnea/Hypopnea Syndrome Hirshkowitz M,1 Roth T,2 Black J,3 Wneses K,4 Arora S,5 Niebler G,6 White D,6 (1) Sleep Disorders Center, VA Medical Center, Houston, TX, USA, (2) Sleep Disorders and Research Center, Henry Ford Hospital, Detroit, MI, USA, (3) Stanford Sleep Disorders Clinic, Stanford University, Stanford, CA, USA, (4) Cognitive Drug Research Ltd., Goring-on-Thames, United Kingdom, (5) Cephalon, Inc., West Chester, PA, USA, (6) Division of Sleep Medicine, Brigham and Women’s Hospital, Boston, MA, USA

Introduction: Patients with obstructive sleep apnea/hypopnea syndrome (OSA/HS) on adequate nasal continuous positive airway pressure (nCPAP) therapy may experience residual excessive sleepiness and its consequences. Modafinil is a racemic compound. This study evaluated armodafinil, the enantiomer with the longer half life, as adjunct treatment for improving daytime wakefulness in patients with OSA/HS who regularly use nCPAP.

Methods: Patients with OSA/HS and Epworth Sleepiness Scale (ESS) score ≥10 on adequate nCPAP therapy were enrolled in this 12-week, randomized, double-blind, multicenter study. Patients received once-daily armodafinil 150 mg or placebo. Assessments were administered at baseline and weeks 4, 8, and 12. The Maintenance of Wakefulness Test (MWT) was administered every 2 hours between 0900 and 1900 h. Other assessments were Clinical Global Impression of Change (CGI-C), ESS, Brief Fatigue Inventory (BFI), and tests of neurocognitive performance. The primary measures were MWT (mean sleep latency of first 4 naps) and CGI-C. Safety assessments included nCPAP use, adverse events, and nighttime polysomnography.

Results: 259 patients (mean age, 50.7 yr; mean BMI, 36.5 kg/m2) received study drug (armodafinil, n=129; placebo, n=130). Armodafinil significantly improved wakefulness, assessed by MWT sleep latency vs placebo (baseline, 26.6 and 26.0; final visit, 27.8 and 24.5, respectively; p=0.0016). 71% of patients receiving armodafinil were improved (CGI-C) vs 53% receiving placebo (final visit, p=0.0069). Armodafinil significantly improved self-reported sleepiness (ESS) vs placebo (baseline, 15.6 and 16.0; final visit, 10.3 and 13.0, respectively; p=0.0001) and reduced fatigue (BFI) (baseline, 4.7 and 4.9; final visit, 3.5 and 4.3; p=0.0183). Effects were seen at the first post-baseline visit (week 4) and were maintained throughout the study. Armodafinil significantly improved quality of episodic memory but not measures of attention or speed of memory. Armodafinil did not adversely affect nCPAP use or nighttime sleep compared with placebo. The most common adverse events (≥5%) associated with armodafinil were headache, diarrhea, nausea, dizziness, and anxiety.

Conclusion: Armodafinil improved patients’ ability to sustain wakefulness and overall clinical condition in patients with OSA/HS and residual excessive sleepiness. Armodafinil improved subjective wakefulness, quality of episodic memory, and reduced fatigue. Armodafinil was well tolerated.

This study was sponsored by Cephalon, Inc., West Chester, PA.

0532 International Multi-Center Long-Term Study Of Treatment Satisfaction And Compliance In OSA: CPAP With Expiratory Pressure Relief Versus Conventional CPAP Rosenthal L,1 Hensbrough J,1 Zachek M,1 Gfuefler F,1 Betz S,1 Nash M,1 Pla-Ferrer T,1 Strobel R (1) Sleep Medicine Associates of Texas, Dallas, TX, USA, (2) Lehigh Valley Hospital, Allentown, PA, USA, (3) Graves Gilbert Clinic, Bowling Green, KY, USA, (4) Klinik Donaustauf, U of Regensburg, Bowling Green, Germany

Introduction: Patient dissatisfaction represents a significant challenge to CPAP therapy. This study compared satisfaction and CPAP compliance among OSA patients receiving either conventional CPAP therapy (CPAP) or CPAP with expiratory pressure relief (FLEX).

Methods: 188 newly diagnosed patients (in-laboratory PSG and titration) with severe OSA and EDS were randomized to receive FLEX or CPAP in a single-blinded study at 4 centers. Only patients averaging ≥4 hrs/night use in the first week of therapy were followed. Treatment compliance was recorded. Satisfaction with therapy (TS), treatment comfort (TC), and interface comfort (IC) were evaluated using 0 - 100 mm visual analog scales (higher scores reflecting favorable ratings). Patient satisfaction and CPAP adherence were measured at one, three and six months. Data were analyzed using analyses of variance or t-tests. Data reported as means±SD.

Results: 41 patients failed to meet initial compliance criteria. 147 subjects completed the study. Groups were comparable for age, gender, BMI, DrxRLD, and ESS. All centers showed the same pattern of patient satisfaction. Higher Satisfaction for FLEX vs CPAP was documented for all measures (TS p<0.05; FLEX 81±18 v. CPAP 74±22), (TC p<0.05; FLEX 75±21 v. CPAP 68±23) and (IC p<0.01; FLEX 66±24 v. CPAP 57±26). Across both groups TC improved over time (p<0.01), with the largest difference between 1 and 3 months (p<0.005) (1mo 66±24 , 3mo 73±1±21, 6mo 74.5±22). While there was no significant time-by-group interaction, there was a definite trend for the FLEX group showing higher levels of satisfaction at the 6-month follow up. Aggregate compliance at 6 months was significantly greater for FLEX v. CPAP (5.84±1.5 v. 5.3±1.3hrs, p<0.05).

Conclusion: The results of this study showed that patients using FLEX (C-Flex®, Respironics, Murrysville, PA) during the initial six months of therapy reported higher levels of satisfaction and CPAP adherence when compared to regular CPAP.

Respironics, Inc.

0533 Sdb In Children: Preliminary Findings From A Population Sample Bixler EO,1 Vgontzas AN,2 Lin H,2 Calhoun SJ (1) Sleep Research & Treatment Center, Penn State University, Hershey, PA, USA, (2) Health Evaluation Sciences, Penn State University, Hershey, PA, USA

Introduction: The epidemiology of sleep disordered breathing (SDB) in adults has been extensively studied. However, the epidemiology of SDB in children, especially in the general population, has received much less attention.

Methods: The overall objective of this two-phase protocol was to establish the prevalence of various types of SDB in children in a random sample of the general population. The first phase obtained general information by questionnaire from the parent about every child in a selected elementary school (K through 5).

Results: This is a preliminary report from phase 1 of this ongoing study (year 3/5) based on 4,637 questionnaires sent to parents and 3,751 returned (80.9%). This sample included 50.0% females, an average age of 8.3 ± 1.8 years, and an average age- and gender-adjusted BMI z-score corresponding to the 66th percentile. The following were reported occurring often or very often: trouble falling asleep (14.0%); restless during sleep (16.6%); EDS [falls asleep during day (3.6%)]; SDB [snoring (15.2%); or struggling to breath at night (2.1%)]; 'school work problems' (16.6%); EDS [falls asleep during day (3.6%)]; SDB [snoring (15.2%); or struggling to breath at night (2.1%)]; 'school work problems' (16.6%); EDS [falls asleep during day (3.6%)]; SDB [snoring (15.2%); or struggling to breath at night (2.1%)]; 'school work problems' (16.6%); EDS [falls asleep during day (3.6%)]; SDB [snoring (15.2%); or struggling to breath at night (2.1%)]...
SDB and EDS. Finally, ‘behavior problems’ was associated with nocturnal sleep disturbance, boys and SDB, but not EDS.

**Conclusion:** Parents in this general population sample reported that sleep difficulties were common in children aged 5-12 years. Nocturnal sleep disturbance, enlarged tonsils, BMI as well as school problems appeared to be associated with SDB. Nocturnal sleep disturbance and SDB also appeared to be associated with both behavior problems as well as school work problems. It remains, however, to be seen how these parental reports are related with objective data obtained directly from the child.

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**0534**

**Effect Of Increased Lung Volume On Sleep Disordered Breathing In Sleep Apnea Patients**


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**Introduction:** Previous studies have demonstrated that lung volume influences upper airway size and resistance particularly in sleep apnea patients. Continuous positive airway pressure (CPAP) is known to increase lung volume, which may partially explain its effect on sleep apnea. We sought to determine the influence of a lung volume increase on sleep disordered breathing in sleep apnea subjects during non REM sleep.

**Methods:** Twelve subjects [Apnea Hypopnea Index 62.3±5.9(SEM)] were studied during stable non REM sleep in a rigid head-out shell equipped with a positive/negative pressure attachment for manipulation of extrathoracic pressure. First, the CPAP level required to prevent flow limitation was determined using an epiglottic pressure catheter plus a mask/pneumotachometer. The increase in lung volume due to CPAP was determined with four magnetometer coils placed on the chest wall and abdomen. Subjects were then studied for ~ 1 hour in three conditions (in random order): 1) without any treatment (Baseline) 2) at the “CPAP lung volume”, with the increased lung volume being reproduced by negative extrathoracic pressure alone, not CPAP (Lung Volume 1). 3) 500 ml above the “CPAP lung volume” (Lung Volume 2).

**Results:** Respectively for the baseline, Lung Volume 1 and Lung Volume 2, the AHI ± SEM was 62.3 ± 11.2, 37.2 ± 5.5, 31.2 ± 7.4 (general effect p=0.009); the arousal index was 63.8± 9.0, 43.5 ± 6.3, 38.2 ± 5.6 (general effect p=0.039); the 3% oxygen desaturation index was 43.0 ±10.14, 16.1 ± 5.4,12.3 ± 5.3(general effect p=0.002); the mean oxygen saturation was 95.36 ± 0.29, 96.04 ± 0.24, 96.25 ± 0.27 (general effect p=0.001); % time awake was 17.4, 10.1, 8.6 (general effect NS); % stage 1 sleep was 27.8, 13.5, 14.1 (general effect p=0.001) and % stage 2 was 54.8, 40, 40, 40, 40, 40 (general effect p=0.001); the AHI ± SEM was 62.3 ± 11.2, 37.2 ± 5.5, 31.2 ± 7.4 (general effect NS); % stage 1 sleep was 95.36 ± 0.29, 96.04 ± 0.24, 96.25 ± 0.27 (general effect p=0.001); % stage 2 was 54.8, 40, 40, 40, 40, 40 (general effect p=0.001); the 3% oxygen desaturation index was 43.0 ±10.14, 19.4 ± 7.8, 19.4 ± 7.8 (general effect p=0.002); and lower minimum oxygen saturation (81.6±10.7 vs. 87.4±7.8; p<.0001). To examine the independent association between MS and sleep apnea, we compared AHI between patients with and without MS after successive adjustments to the MS criteria (BMI, TG, glucose, and HDL), first individually, and then to pairs and triplets of the MS variables. Adjustment to BMI reduced the significance level of the differences in AHI and in minimum oxygen saturation between the groups, from p<.0001 to p<.06 and from p<.0001 to p<.07. Adjustment to BMI and any of the other variables reduced the difference in RDI to non significant levels, and greatly attenuated the difference in minimum oxygen saturation.

**Conclusion:** Our study demonstrated that the association between MS and sleep-apnea was mostly mediated by obesity with a secondary contribution of nocturnal hypoxia.

**0536**

A Bench Study To Compare The Response Of Auto-Adjust CPAP Devices To Sleep Disordered Breathing Patterns

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**Introduction:** Auto-Adjust CPAP devices are an innovative method for titrating patients for CPAP therapy. The unique feature of Auto-Adjust devices is their ability to respond to changes in patient breathing patterns. Home care providers often evaluate products based on manufacturer claims and marketing material. The assumption is that these products all perform the same so purchasing decisions are based on product reliability, warranty, features, and price. The objective of this evaluation is to determine the performance capabilities of several commercially available Auto-Adjust units when subjected to a series of different breathing patterns.

**Methods:** Five different Auto-Adjust devices were tested using a Hans-Rudolph Model 1101 breathing simulator with breathing patterns simulating a variety of sleep breathing disorders (Apnea, Hypopnea, and Flow Limitation) in addition to a normal breathing pattern. Each Auto device was set to vary between a minimum of 4 cmH2O and a maximum of 20 cmH2O. Each device was subjected to a 30 minute pre-conditioning using a normal breathing pattern, following pre-conditioning a disordered breathing pattern stored in the breathing simulator memory was run for 30 minutes followed by a 90 minute period of normal breathing. The pressure response of each of Auto-Adjust units was recorded throughout the pre-conditioning and the duration of the test. The delivered pressures for each of the devices was compared for each of the sleep disordered breathing patterns.

**Results:** All of the devices responded to simulated Apnea breathing patterns; however the response patterns of each device differed among...
devices. Four of the five devices responded to simulated Hypopnea and only three of five devices responded to Flow Limitation breathing patterns.

**Conclusion:** Each device responded markedly different to each disordered breathing pattern. A clinician or doctor prescribing Auto-Adjust CPAP devices to a patient should be aware of these differences and be familiar with the capabilities of each device.

**0537 Adiponectin And C-Reactive Protein (CRP) In Sleep Apnea Syndrome**

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**Introduction:** Adiponectin, which is secreted specifically by adipose tissue, has been shown to have an anti-atheroscerotic effect and to improve insulin resistance. The aim of this study was to investigate plasma adiponectin concentration in sleep apnea and to determine its correlation with CRP, an inflammatory marker implicated in predicting atherosclerosis.

**Methods:** 96 OSA patients, 66 mild (AHI between 10 and 30, age - 44.8±10.2; BMI - 26.7±3.44 Kg/m2) and 30 severe (AHI greater than 30, age - 46.4±10.8; BMI 29.9±3.46), and 49 non-apneic controls (AHI less than 10, age - 38.2±11.4, BMI - 25.9±3.01) participated. Sleep apnea patients were free of cardiovascular disease or any other major chronic disease.

**Results:** The concentrations of plasma adiponectin and CRP determined after an overnight fasting did not differ between the three groups (adiponectin: controls: 4.9±2.24; mild OSA 4.9±2.67; severe OSA 4.3±2.03 microg/ml; CRP: controls 2.8±3.45; mild OSA 3.5±5.04; severe OSA 4.1±9.7 mg/L). In the OSA groups CRP was significantly positively correlated with BMI (.27, p<.0001), and negatively with triglycerides (-.51, p<.0001), glucose (-.20, p<.08), and tended to be negatively correlated with HDL (.20, p<.07). Adiponectin was significantly positively correlated with age (.20, p<.05) and HDL (.46, p<.0001), and negatively with triglycerides (-.51, p<.0001), glucose (-.31, p<.002) and with CRP (-.23, p<.04). A separate analysis of a subgroup of sleep apnea patients having AHI greater than 20 and BMI less than 27 (N=23) and controls having BMI less than 27 (n=24) similarly did not reveal any significant differences in CRP nor in adiponectin.

**Conclusion:** Adiponectin in sleep apnea patients is unrelated to the severity of the syndrome but appears to play a role in lipid metabolism and atherogenesis.

**0538 Insomnia And Clinical Co-Morbidities Are Associated With Subjective Failure Of Obstructive Sleep Apnea Syndrome Treatment With Intraoral Mandibular Repositioning Appliances**

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**Introduction:** Intra oral mandibular repositioner appliances (IOMRAs) are designed to enlarge pharyngeal airway space advancing mandible and increasing genioglossus tonus during sleep. Obstructive sleep apnea syndrome (OSAS) treatment with IOMRAs is valuable, but there is a lack of studies in the literature defining the target population more inclined to answer to this treatment. Besides many patients reach normal breathing during sleep, some of them say they did not improve. This study aims to identify causes of patient’s perception of treatment failure with IOMRAs, besides apnea-hypopnea index (AHI) <5/hour.

**Methods:** We contacted by telephone 188 previously treated (AHI<5) patients with IOMRA, detecting 20 not improved patients (Study Group), based on their opinion about their health status before and after treatment with IOMRA. Twenty improved patients of the remaining 168 were randomly matched for gender, age, AHI as Control Group. Both groups answered questionnaires for diagnosis of clinical problems, sleep disorders, depression (Beck), anxiety (IDATE), and sleepiness (Epworth). We did a descriptive and inferential statistical analysis. The inferential analysis was divided into two steps: univariate analysis using Fischer exact test and a multiple inferential analysis using a stepwise regression model.

**Results:** Although the final model included only insomnia, we concluded that the presence of gastric, neurological and rheumatic diseases also tended to be associated with the lack of improvement. The association between the accumulation of gastric, neurological, and rheumatic diseases and insomnia and improvement demonstrated that an increase in one of these diseases correspond to a two-fold increase in the chance of non-improvement. Restless legs syndrome and narcolepsy were not found in our sample.

**Conclusion:** Insomnia was the most important factor compromising the success of OSAS treatment with IOMRAs, and the isolated presence of gastric, neurological and rheumatic diseases, but especially their combination, reduces the success rate of treatment with IOMRAs.

**0539 Flexible CPAP With Expiratory Pressure Relief: An In-Laboratory, Polysomnographic Comparison With Conventional CPAP**

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**Introduction:** Continuous Positive Airway Pressure (CPAP) with expiratory pressure relief (FLEX) has been shown to improve patient comfort and satisfaction compared to conventional CPAP therapy. However, the effect on objective polysomnographic (PSG) parameters has not been studied.

**Methods:** Fifteen patients with severe obstructive sleep apnea (OSA), AHI of 51.4±25.3hr-1, and mean CPAP pressure of 12.3±2.3cmH2O, were enrolled in this study. Patients were randomized by treatment, and received FLEX or CPAP at optimal pressure (AHI<5.0hr-1) one night, followed by alternative therapy the second night. Sleep stage, respiratory event, and arousal data were collected and analyzed according to standard laboratory criteria. Data was analyzed using paired t-tests and all values were expressed as mean ± SD.

**Results:** Our sample (n=15) was comprised of OSA patients (9females, 6males) with BMI=43.1±8.4 kg/m2 and age=45.7±12.3yrs. Sleep parameters did not differ between the two groups (p>0.05) in respect to time in bed (FLEX=496±39.3 vs. CPAP=498±35.3), total sleep time (424.38±53.3min vs. 430.1±42.4min), sleep efficiency (0.85±0.07 vs. 0.86±0.05), wake after sleep onset (58.3±35.6 vs. 55.7±27.0), sleep latency (7.8±7.4min vs. 8.0±7.6min), and REM latency (77.0±93.8min vs. 91.1±119.2min). There was no difference (p>0.05) in the percentage of sleep stages according to sleep period or time in bed by therapy, nor arousal index (FLEX=8.8 ±4.7hr-1 vs. CPAP=7.2±3.1hr-1). Residual apnea-hypopnea index (AHI) was reduced, but not significantly (p>0.05), among the FLEX group (1.7±2.3hr-1) vs. CPAP (1.8±1.7hr-1). Minimum oxygen saturation (FLEX=90.1±4.9% vs. CPAP=88.1±4.9%) and average event nadir (FLEX=92.2±2.3% vs. CPAP=91.3±2.3%) was similar for both therapies.

**Conclusion:** FLEX (C-Flex™, Respironics, Murrysville, PA), with expiratory pressure relief, has been shown to improve patient satisfaction with therapy. This study shows comparable therapeutic effect with respect to residual apnea/hypopnea index, sleep architecture and sleep stage proportion, and arousals, as compared to conventional CPAP therapy.
0540
Sleeping Position Is Important Clinically And Predictively
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Introduction: Avoiding sleeping supine lowers respiratory distress index (RDI) and can be used in treatment of obstructive sleep apnea hypopnea syndrome (OSA). The RDI has been used as the measure of severity of OSA in studies of the causal role of OSA in hypertension and cardiovascular disease. Sleeping position was not examined as a contributory variable to the RDI. We provide data to encourage prescribing sleeping position clinically and to incorporate it in future studies of OSA in hypertension and other vascular diseases.

Methods: Respiratory distress indices over the diagnostic period (RDIs) and for the supine sleeping position (RDIs) and non-supine positions (RDIns) were tabulated for 50 polysomnographic evaluations for OSA. First, the difference between each RDIs and RDIn was listed and the mean and median for the total was computed. Secondly, each patient's RDI was assigned to one of four groups: 1(0-4.9), 2(5-14.9), 3(15-29.9), 4(30 and above). Each patient’s RDIs and RDIn were similarly assigned group numbers. The differences from his RDI group number were determined.

Results: Means, medians and ranges for RDIs: 24.8, 16.0, 1.2-72.9; for RDIs: 46.8, 49.5, 0.3-114.4; for RDIs: 15.7, 8.1, 0-62.1; for RDIs: 14.1, 26.1, 0.2-95.1. There were 10 individuals in Group 1, 16 in Group 2, 6 in Group 3 and 18 in Group 4. RDIs was higher by two groups for 5 patients in RDIs-Group 2; higher by 1 group in 6 patients in Group 1, 6 in Group 2, 5 in Group 3; and RDIs and RDIns fell in the same group for 4 individuals in Group 1, 5 in Group 2, 1 in Group 3, and 18 in Group 4.

Conclusion: Accepting that RDIs is a risk factor/predictor of hypertension with quantifiable odds ratio, and since RDIs is significantly increased by sleeping in the supine position, the benefit of reducing the RDIs by avoiding sleeping supine, is here given added weight as both an important therapeutic measure for some patients with OSA and as a way to reduce the odds of developing hypertension. Incorporating sleep position data into large population studies using RDI can enhance their predictive value.

0541
Construct Validity For Health Utilities Indices In A Sleep Center
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Introduction: Health related quality of life (QOL) is an important outcome for sleep disorders. One important measure of QOL is the health utilities index (HUI). The HUI expresses QOL as a single number, between 0 (dead) and 1 (perfect health). HUI is an important measure for economic analysis since it allows for the calculations of quality adjusted life-years, and the economic impact of QALYs gained or lost by a disorder or treatment. There are few data on the use of the HUI in patients with sleep disorders.

Methods: A cross-sectional survey was done in 86 patients presenting to the sleep disorders center (67 sleep apnea - OSA, 19 other sleep disorders). HUI Mark 2 and HUI Mark 3 were compared with other indices of QOL: SF12, Epworth Sleepiness Scale (ESS), functional outcomes of sleep questionnaire (FOSQ). Results: Age: 50.7 +/- 14.2 y, RDI (for OSA): 32.6 +/- 29.1, BMI: 32.9 +/- 7.6, HUI2: 0.73 +/- 23, HUI3: 6 +/- .35 (p=.0066 for difference from HUI2), SF12 physical components (PC): 43.6 +/- 12.1, SF12 mental components (MC): 45.6 +/- 11.2, ESS: 10.5 +/- 5.2, FOSQ: 16.4 +/- 3.5. Significant univariate correlations were found between HUI2 and HUI3, as well as between both of these and age, SF12PC, ESS, and FOSQ. Backwards stepwise multivariate regression revealed significant independent correlations between HUI2 and age, SF12PC and FOSQ, and between HUI3 and age, SF12PC, ESS, and FOSQ. There were no differences in QOL between OSA and non-OSA patients.

Conclusion: 1) Both HUI2 and HUI3 reflect other indices of QOL in sleep patients, 2) HUI3 scores are lower than HUI2 scores, 3) HUI2/3 QOL scores should be considered for inclusion in QOL and economic impact studies in patients with sleep disorders.

0542
REM RDI And NREM RDI
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Introduction: Respiratory events in OSA increase in REM sleep. However, there is often a surprising difference between the REM RDI and the NREM RDI. This study looks at the discrepancies.

Methods: We studied 179 patients having a PSG. Patients were excluded, if they had less than five hours of total sleep or 30 minutes of REM sleep, leaving 116 patients: 60 women, mean age 43 (SD= 11.6, 24 to 67) and 56 men, mean age 44 (SD = 10.7, 23 to 71).

Results: Mean RDI: Women 11.0 (SD 2.9), Men 24.5 (SD 3.0), Significant difference p<.002 Mean REM RDI: Women 25.1 (SD 3.5), Men 28.6 (SD 3.6), No significant difference Mean NREM RDI: Women 8.1 (SD 2.9), Men 23.5 (SD 3.0), Significant difference p<.0004. Considering the correlations between REM RDI & NREM RDI: Women: r = .46, p < .0001 Men: r = .68, p < .0001 Considering the same correlations but only in those with NREM RDI less than or equal to 5: Women (N = 38) r squared = .05 p < .19 (NS) Men (N = 17) r squared = .40 p < .007

Conclusion: The differences between the REM RDI and NREM RDI increase as the NREM RDI decreases. Curiously, there seems to be a greater degree of variability in the REM RDI vs. the NREM RDI in women as compared to men. These findings may be of use in deciding how much the degree of REM OSA should be considered in making a diagnosis of significant OSA.

0543
Efficacy Of Oral Appliance In The Treatment Of Obstructive Sleep Apnea
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Introduction: Many studies have shown that mandibular advancement splint effectively decreases apnea index and improves sleep quality, especially in patients with mild-to-moderate obstructive sleep apnea syndrome (OSAS). Oral appliances constitute an attractive noninvasive alternative for patients with sleep apnea, providing efficacy, compliance, long-term tolerance and satisfaction. This study aims to verify the efficacy of an intra oral repositioner appliance (IOMRA).

Methods: From 2000 to 2003 we received 300 patients with polysomnographic diagnostic of OSAS (AHI>5/h) to be treated with IOMRA. Thirty patients were excluded for TMJ problems or teeth problems. The remaining 270 started a 4 months protocol with IOMRA. Eight interrupted few weeks later for particular reasons and 262 completed the protocol. Only 83 returned for a control polysomnography, and among them 20 had mild, 40 had moderate and 23 severe apnea. We considered treated patients that achieved AHI<5/h. The results were analyzed using t-Test to compare polysomnographic data before and after IOMRA protocol, P<0.05 were
Sleep-disordered breathing (SDB) is associated with cardiovascular co-morbidity, and this relationship is likely to be in part mediated by increased pro-inflammatory markers. We assessed the relation of IL-6 expression. Of interest, morning IL6-sR levels were relatively higher than evening levels in SDB, even after obesity adjustment. Since morning IL6 levels are associated with obesity, this suggests that SDB is an important contributor to the diurnal variability in IL-6 and IL-6-sR levels.

**Results:**

- **AHI pre-treatment was 26(17.7)h and post-treatment 4.8(5.3)h (p=0.00005). From 83 patients 52 (62.6%) were treated (AHI<75%), and the sample was as follow: 15 (75%) had mild, 26 (65%) had moderate apnea, and 11 (47%) had severe apnea. In the treated group pre-treatment and post-treatment AHI to the mild, moderate and severe apnea were 10.4(2.8)/h and 1.9(1.3)/h; 22.2(4.6)/h and 1.8(1.6)/h; and 39.3(8.5)/h and 1.5(1.2)/h respectively. In the non-treated group pre-treatment and post-treatment AHI to the mild, moderate and severe apnea were 12.5(2.0)/h and 7.0(3.0)/h; 21.6(4.1)/h and 9.1(3.7)/h; and 55.0(26.4)/h and 13.2(6.9)/h respectively.

**Conclusion:** This study showed the efficacy of IOMRA in the treatment of OSAS. We can also notice that IOMRA use in severe apnea can be very satisfactory when patients cannot tolerate CPAP and when they are not eligible for surgery.

**0545**

**Oral Appliance In The Treatment Of Obstructive Sleep Apnea: Compliance Evaluation**


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**Introduction:** Despite its effectiveness in the treatment of the obstructive sleep apnea syndrome (OSAS), nasal continuous positive airway pressure is not fully accepted by all patients, and about 50% of them discontinue its use within a short period of time. Mandibular advancement devices have been proposed as an alternative strategy. The present study aims to evaluate the compliance of the Intra Oral Mandibular Repositioner Appliance (IOMRA) to treat OSAS patients.

**Methods:** We treated with IOMRA 300 referred OSAS patients (AHI >5/h) from 2000 to 2003. Thirty were excluded for tempromandibular joint and/or teeth problems. The remaining 270 patients started a 4 months protocol with IOMRA. Eight interrupted few weeks later for particular reasons (not clinical) and 262 completed the protocol. Eighty-three patients performed a polysomnographic control and gave information about their compliance. IOMRA compliance was classified as follow: total if 30 nights/month, high if 30/1year in all patients. After polysomnographic control the patients were divided into two groups: treated (AHI>5) (53 patients) and non treated (AHI>5) (30 patients). P<0.05 were considered significant.

**Results:** Forty three (81%) patients in the treated group had high or total compliance since they received IOMRA; 1(1.8%) had poor compliance e 9(16%) discontinued IOMRA use. In the non-treated group 23 (76%) had high or total compliance since they started IOMRA treatment; 1 (3%) had poor compliance, and 6 (20%) discontinued IOMRA use. Adherence was not different between treated and non-treated groups (p=0.84)

**Conclusion:** This study showed that compliance to IOMRA is total or high even in a polysomnographic untreated group. Discontinuation or poor users of IOMRA also were similar in both groups, suggesting that the motive for giving up treatment is not related to some residual sleep-disordered breathing on polysomnography.

**0546**

**Sleep Cyclic Alternating Pattern In Adults With Upper Airway Resistance Syndrome**

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**Introduction:** Upper airway resistance syndrome (UARS) patients complain of tiredness, sleepiness and fatigue, but increase in respiratory effort often terminates without EEG arousal. We questioned if sequences of flow limitation without apnea or hypopnea were associated with change in sleep EEG.

**Methods:** 30 successively seen patients (15 men), 20 to 59 years of age, were diagnosed as UARS (AHI <5, SaO2> 92%) based on clinical complaints and polysomnography. Sleep EEG was scored according to standard international rules and investigation of cyclic alternating pattern (CAP) was performed.

**Results:** Complaints were unrefreshing sleep (n=21), sleep onset (n=9) and sleep maintenance (n=24) insomnia, tiredness (n=25) and fatigue (n=30). Their mean BMI was 22.8 Kg/m2. Patients had an A1= 0, a mean AHI= 2.6/h, a mean RDI= 9.1/h, a mean lowest SaO2= 93.1%. Mean CAP parameters were calculated: CAP rate was 57.1 (9.5%), CAP time was 172 (40.8) minutes, cycle number was 374.2 (101.1), cycle duration was 27.9(2.3) seconds, duration of phase-A was 8.0 (1.0) seconds, and phase B was 19.9 (1.8) seconds. These results were significantly different.
from normal subjects (p<0.01), except the duration of CAP cycle. Patients with sleepiness showed higher CAP rate (p=0.01) and increased CAP time in stage 2 NREM sleep (p=0.04). The indexes of A-phase of CAP were: A1 phase is 59.3 (12.8) %, A2 phase is 24.5 (9.0) % and A3 phase is 16.1 (7.4) %. There were gender differences with an increase in duration of A2-subtypes in women, and a longer B-phase duration in slow wave sleep in men (p<0.05).

**Conclusion:** CAP indicates presence of an important instability of NREM sleep in UARS patients and of a much more disturbed sleep than suggested by usual sleep scoring. It represents better the clinical complaints of UARS subjects.

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### 0547

**Post-Operative Complications In Recovery Room Without CPAP Use In The High Risk Sleep Apnea Patients**

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**Introduction:** Obstructive sleep apnea remains a complicating factor in general anesthesia and conscious sedation. Narcotic analgesics further cause apnea and respiratory complications. Given the high prevalence of undiagnosed sleep apnea, many patients develop post-operative complications. Altered mental status, muscle tone and reflexes, and impaired breathing confound the problem. However, many of these patients are neither identified preoperatively nor offered CPAP post-operatively to prevent complications like re-intubation and cardio-respiratory arrest.

**Methods:** We reviewed the post-operative records of 214 patients with obesity based on body mass index or known obstructive sleep apnea. Preoperative data for 18 months were reviewed from five hospitals. A total of 214 patients were identified as high risk. Of the sample, 169 patients were not treated compared to 45 treated with CPAP. The following complications were reviewed: Snoring, De-saturation, Re-intubation, Airway reevaluation and Cardiac arrest.

**Results:** Of the 49 patients with snoring, 46 patients did not and three received CPAP. De-saturation was noted in 80 patients without CPAP compared to 15 with CPAP. Twenty patients without CPAP were reintubated compared to seven with CPAP. 23 patients without and 20 with CPAP required reevaluation. Cardiac arrest was not noted in either group. A significant percentage of patients, 169/214 (78.97%), suffered with complications post-operatively when CPAP therapy was not instituted despite high-risk profile. Only 45/214 patients treated with CPAP, had reduced number of complications. Chi Square test for the monitored parameters was significant at 25.331. A p value of less than or equal to 0.001 noted.

**Conclusion:** Given the high prevalence of obesity and obstructive sleep apnea, pre operative evaluation by the anesthesiologist should include identification of high-risk patients based on sleep specific history, body mass index and pre-diagnosed obstructive sleep apnea. Patients should be monitored post-operatively for snoring and apnea episodes, and CPAP therapy instituted to prevent complications.

### 0548

**Induction Of Periodic Breathing, The Influence Of Gender**

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**Introduction:** Periodic breathing (PB) is more prevalent among men than women. The difference between the PetCO2 during eupnea and at hypopneas/apneic threshold (PetCO2) in sleeping humans has been suggested as a predictor for development of PB. We hypothesized that the PetCO2 required to induce PB is decreased in men compared to women.

**Methods:** Under normoxic conditions, we studied 15 non-snoring, healthy subjects; 6 men (age = 28.33 +/- 2.16 years; BMI = 23 +/- 2.29 kg/m2) and 9 women (age = 28.78 +/- 3.67 years and BMI = 23.71 +/- 4.3 kg/m2). After onset of stable NREM sleep, hypocapnia was achieved by mechanical hyperventilation in the PSV mode. While expiratory positive airway pressure (EPAP) was maintained at 2 cmH2O, the inspiratory positive airway pressure (IPAP) was increased in steps of 2 cmH2O. Each step was maintained for 3 min. Step increases in IPAP continued until PB developed. At least 5 min of non supported spontaneous breathing was maintained between trials. Pre-apnea/hypopnea respiratory parameters including tidal volume, breathing frequency, minute ventilation and PetCO2 were measured breath-by-breath and expressed as means +/- S.E.M and were compared with each subject’s baseline values using unpaired t-tests.

**Results:** There was no statistically significant difference between men and women in the wake PetCO2 (40.2 +/- 1.5 mmHg men v. 38.2 +/- 4.1 women), NREM PetCO2 (42.7 +/- 2.1 mmHg men v. 40.5 +/- 3.2 mmHg women) or the apneic/hypopneic thresholds (39.2 +/- 1.4 mmHg men v. 37.4 +/- 3.5 mmHg women). The difference in Δ PetCO2 between men and women was not statistically significant (3.5 +/- 1.33 mmHg men v. 3.1 +/- 1.38 mmHg women).

**Conclusion:** There is no gender difference in susceptibility to PB between men and women when inducing hypocapnia using a PSV model. Therefore, the reduction of PetCO2 alone by hyperventilation may not be sufficient to account for the higher prevalence of PB among men compared to women.

### 0549

**Isolated REM Apnea/Hypopnea Index As A Predictor For Developing Sleep-Disordered Breathing In Women**

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**Introduction:** Little is known concerning the natural history of sleep-disordered breathing (SDB) that occurs primarily during REM-stage sleep. Some studies indicate that isolated SDB in REM may be more prevalent in women and suggest this condition may be less severe than SDB pervading all sleep stages. We investigated the relationship of initial REM-isolated Apnea/Hypopnea Index (AHI) to SDB progression over a 3-year period in midlife women enrolled in the Women’s Sleep Study, a subset of the Wisconsin Sleep Cohort Study.

**Methods:** Among the women who had been followed for 3 or more years, 65 had a total AHI <5 based on total sleep time (REM and non-REM) for their 2 polysomnography studies during year 1. Using logistic regression, REM AHI for year 1 was investigated as a predictor of progression to a mean total AHI of ≥5 for the four studies during years 2 and 3.

**Results:** Among women with total AHI <5 during year 1, initial REM AHI was a strong predictor for total AHI to increase to ≥5, even when controlling for initial age and BMI. An increase in 1 event per hour of initial REM AHI resulted in an OR = 2.1 (95% C.I.= 1.4 - 3.2) for having a mean total AHI ≥5 for years 2 and 3. The average initial REM AHI for those women whose total AHI increased to ≥5 was 8.7, versus an initial REM AHI = 2.9 for the women with follow-up total AHI that remained <5. Of the 11 women who had a follow-up total AHI ≥5, ten had an initial REM AHI >5.

**Conclusion:** In women, SDB in REM in the absence of a total AHI >5 is a risk factor for developing SDB that pervades all sleep stages.

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SDB contributes to poor sleep independent of other factors is not certain. Although it is often presumed that these differences reflect the impact of with OSAS and normal participants have included shorter sleep latency, Parallel standard multiple regression analyses were performed Reported difference in sleep architecture between patients

Introduction: We recently showed, in 38 adults evaluated by polysomnography for sleep-disordered breathing, that the tendency for sigma (13-15 Hz) electroencephalographic (EEG) spectral power to vary with the non- apneic respiratory cycle predicted next-day sleepiness as measured by mean sleep latency (MSL) on the Multiple Sleep Latency Test (AJRCCM, in press). We have now extended the analysis to explore sleep stage-specific sigma RCREC and their associations with sleepiness.

Methods: Nocturnal polysomnograms from 20 male and 18 female patients aged 42±14 (s.d.) years were scored manually by standard criteria (Rechtshaffen and Kales, 1968). A computer algorithm divided non-apneic respiratory cycles within all recorded sleep epochs into 4 time segments, as defined by airflow maxima, minima, and their midpoints. The sigma EEG power for each segment was computed using digital filtering on data recorded at C3-A2. Power for each segment was normalized to the power for the whole respiratory cycle, and results were averaged over all cycles during the sleep stage or stages considered. The maximum difference between mean segment powers was defined as a subject’s RCREC.

Results: The tendency of EEG power to vary with non-apneic respiratory cycles (RCREC) reached significance (ANOVA p<0.01) in stage 1 sleep for 47% of the patients; in stage 2 for 71%; in stage 3/4 for 47%; in REM for 16%; and in any single stage for 89%. The MSL correlated with RCREC during non-REM sleep (Spearman rho=−0.43, p=0.0069) and specifically stage 2 sleep (rho=−0.33, p=0.046), but not during any other single stage (each p>0.10).

Conclusion: Stage 2 sleep shows the most prominent sigma RCREC, the magnitude of which may predict sleepiness better than RCREC in other stages. The difference between stages may reflect the prominence of sigma activity in stage 2, underlying mechanisms that produce sleepiness, variable detection of RCREC in different sleep stages, or the longer observation period offered by non-REM sleep.

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0551

The Effects Of Host Factors And Sleep-Disordered Breathing On Sleep Architecture In Patients With Obstructive Sleep Apnea Syndrome

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Introduction: Reported difference in sleep architecture between patients with OSAS and normal participants have included shorter sleep latency, increased REM latency, decreased REM sleep and decreased SWS. Although it is often presumed that these differences reflect the impact of sleep disordered breathing (SDB) on sleep continuity, the extent to which SDB contributes to poor sleep independent of other factors is not certain.

Methods: Parallel standard multiple regression analyses were performed on data from 1779 participants, aged 18-85 years, in a clinic based study. Participants had a clinical diagnosis of OSAS with diagnostic PSG study. Dependent measures included the arousal index (33.8±21.0), % REM sleep (15.7±8.9), sleep efficiency (69.6±37.0) and %TST with SaO2<90% (9.2±19.5). Independent measures were age, gender, BMI (33.3±9.8), comorbid hypertension, comorbid depression, the respiratory disturbance index (RDI, 28.3±25.5) and use of prescription medication (categorical).

Results: Each of the predictor variables uniquely accounted for a significant amount of the variance in the sleep architecture variables. The total proportion of variance explained by the seven predictors was within the range of 9-24% for all criterions, except for AI where 68% of the variance was explained (primarily by RDI). The effect of medication was significant for all criterions at a similar magnitude to other previously identified predictors of sleep architecture (7-12%).

Conclusion: Sleep architecture in OSAS patients varies with age, gender, BMI, comorbid hypertension, comorbid depression, and use of medication, as well as with the RDI. Individual assessment of the effect of SDB on sleep quality in OSAS needs to account for these host characteristics. BMI, hypertension and depression aremodifiable factors that impact on sleep quality in OSAS patients. Significantly, the large proportion of unexplained variance in sleep architecture suggest that other individual factors need to be identified.

0552

The Prevalence Of Sleep Disordered Breathing In Hospitalized Patients With Atrial Fibrillation: Preliminary Data

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Introduction: Atrial fibrillation (AF) occurs more frequently in patients with obstructive sleep apnea (OSA) than those without OSA. However, the prevalence of sleep disordered breathing (SDB), including OSA, in patients who have a diagnosis of AF is unknown. We hypothesized that patients admitted to monitored units with a diagnosis of AF would have a high prevalence of SDB.

Methods: Patients admitted to monitored beds at an urban academic center who have a diagnosis of AF were eligible for the study. Once clinically stable, subjects were monitored for one night prior to discharge by a limited-channel polysomnogram (LC-PSG). The LC-PSG is comprised of 4 channels: heart rate, continuous pulse oximetry, thoracic excursions (for effort) and nasal thermistor (for air flow). Obstructive and central apneas were defined per standard criteria. Hypopneas were defined as a 30% reduction in air flow for 10 seconds or greater associated with a > 3% oxygen desaturation. The Apnea-Hypopnea Index (AHI) was calculated by dividing the number of respiratory events by the total recording time. SDB was defined as an AHI > 5.

Results: Eighteen subjects have participated in the study to date. Demographics: 39% Female, 50% Caucasian / 33% African-American / 16% Hispanic, mean age 66 +/- 10 years old, mean BMI 30.7 +/- 6 kg/m2 (44% BMI > 30). Baseline co-morbid conditions: CHF 39%, CAD 67%, Valvular Disease 17%, HTN 72%, DM 44%, COPD/Asthma 17%. Adapting diagnosis: CHF exacerbation 28%, chest pain 22%, AF with rapid ventricular response 22%, miscellaneous 28%. Echo data: mean ejection fraction (EF) 48% and 50% had an EF < 45%. LC-PSG found 14 out of 18 patients (78%) with an AHI > 5 (mean 15.4, median 16.2, 1st quartile 5.5, 3rd quartile 22.5). Four of these (22% of total sample) had primarily central apnea, all of whom had an EF < 45%. The remaining 10 (56% of total sample) had primarily obstructive events. There was no difference between subjects with CHF vs. without CHF in SDB (81% vs. 67%, p=0.26) or OSA (44% vs. 67%, p=0.34). In subjects without CHF and a BMI < 30 kg/m2, 2 of 4 (mean BMI 25 kg/m2) had OSA.

Conclusion: Patients with a known diagnosis of AF who are admitted to a monitored setting appear to have a very high rate of sleep disorder breathing. This suggests that this patient population should be targeted for aggressive screening for SDB. A larger population sample and comparison to a control population are needed to confirm these findings.
0553
The Effects Of Medication On Sleep Architecture In Patients With Obstructive Sleep Apnea Syndrome
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Introduction: Patients with OSAS often have co-morbid disorders that are treated medically. The central action of many medications suggests direct and indirect effects on the pathophysiology of OSAS, and on control mechanisms for sleep. Seratonin, for example, has been cited as both a possible contributor to OSAS, and a potential therapy. This study aimed to assess the prevalence of medication use by patients with OSAS, and to assess the impact of the most frequently used medications on sleep architecture.

Methods: An initial clinical sample included 1779 participants, aged 18-85 years with a clinical diagnosis of OSAS with diagnostic PSG study. Matched samples of 50 participants were selected for each of 6 contrast groups: nil drugs, amitriptyline, paroxetine/fluoxetine, sertraline, beta-blockers and aspirin. Effects of drug type on sleep architecture (arousal index, % REM sleep, sleep efficiency (SE) and %TST with SaO2<90%) were assessed with parallel analyses of covariance. Groups were matched for RDI and BMI, with age and gender covariates.

Results: 77% of the total sample were using at least one prescription medication. 44% used antidepressant medication and 21% were using a prescription antihypertensive medication. Paroxetine/fluoxetine and Sertraline decreased REM sleep by 7% (p<0.01) and SE by 10% (p<0.01). Amitriptyline decreased REM sleep by 10% (p<0.01) and SE by 20% (p<0.01). Aspirin and beta-blockers had no significant effects on the sleep architecture measures, and none of the medications reliably changed the arousal index or SaO2 levels.

Conclusion: The selective serotonin reuptake inhibitors and tricyclic antidepressants examined in this study had significant effects of sleep architecture after controlling for age, gender, BMI and RDI (with medium effect sizes) compared to patients on no medication. The high rate of antidepressant use in this population suggests that medication may contribute to poor sleep in a large proportion of patients with OSAS.

0554
Upper Airway Muscle Response To Raising CO2 During NREM Sleep
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Introduction: It is well known carbon dioxide (CO2) can stimulate breathing, but it is unclear whether CO2 can increase the activity of the pharyngeal airway muscles during sleep. It is also unclear whether any increase in upper airway muscle activity with rising CO2 is due to the increased negative pressure in the airway or respiratory neuronal activation. We, therefore, assessed CO2 responsiveness on and off CPAP (to eliminate negative pressure) awake and asleep.

Methods: We have studied to date 2 male and 2 female normal subjects (age 18-32), monitoring genioglossal EMG, ventilation, epiglottic pressure, end-tidal PCO2 (PET CO2), and sleep-wake status. We determined the nasal CPAP level required to produce the lowest EMG awake (CPAP, 6.69 ± 0.11 cmH2O). During wakefulness, we assessed muscle activity on and off CPAP at three PET CO2 levels (the normal eupnic level and at levels 5 and 10 mm Hg above the eupnic level). Similar measurements were made during stable NREM sleep in the supine position.

Results: During wakefulness, genioglossal activity increased with CO2 stimulation, but the response was greater off than on CPAP, implying two different drives to the muscle, respiratory promoter neurons (RPNs) and the negative pressure reflex. During stable NREM sleep off CPAP, baseline genioglossal activity tended to be higher than awake. With CPAP application muscle activity decreased, indicating negative pressure responsiveness. CO2 administration during NREM sleep on CPAP still yielded increased genioglossal activity. This response (CPAP on) was reduced when comparing sleep to wakefulness.

Conclusion: This study suggests that both RPNs and negative pressure reflex inputs to upper airway dilator muscle are still active during stable NREM sleep. However, the response rate to CO2 stimulation is reduced during NREM sleep.

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0555
Respiratory Cycle-Related EEG Changes (RCREC) At Multiple EEG Leads
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Introduction: We recently used nocturnal polysomnograms and Multiple Sleep Latency Tests, from 38 adults studied for suspected sleep-disordered breathing, to show that sigma-band (13-15 Hz) RCREC recorded at the C3-A2 lead 1) exist during non-apneic sleep, 2) may reflect numerous subtle inspiratory microarousals, and 3) predict daytime sleepiness (AJRCCM, in press). We now extend this analysis to explore whether data recorded from other EEG leads may yield similar information.

Methods: Nocturnal polysomnograms of 20 male and 18 female patients (42±14 s.d. years old) were scored by Rechtschaffen and Kales criteria. A computer algorithm divided non-apneic respiratory cycles during the first three hours of sleep epochs into 4 segments: early inspiration, late inspiration, early expiration, and late expiration. Digital filtering of the EEG recorded at the C3-A2, C4-A1, O2-A1, and O1-A2 leads (alternatively) was used to compute the sigma EEG power for each segment, which was normalized to the power for the whole respiratory cycle and then averaged over all cycles (about 2500). The maximum difference between mean segment powers was defined as the RCREC magnitude for any given subject.

Results: Subjects who had statistically-significant RCREC (ANOVA p<0.01) at the C3-A2 lead usually showed statistically-significant RCREC at each of the other 3 leads also (70% of the subjects). Spearman correlations between RCREC at the 4 leads ranged from rho=0.71 to rho=0.91 (all p<0.0001). The RCREC at the C3-A2 derivation predicted next-day mean sleep latency (rho=-0.49, p=0.0017) to an extent similar to that observed at the other leads (C4-A1 rho=-0.45, p=0.0048; O1-A2 rho=-0.40, p=0.0128; O2-A3 rho=-0.39, p=0.0144).

Conclusion: These data show for the first time that sigma RCREC exist to a similar extent bilaterally and at both central and occipital EEG leads. The RCREC computed from any of these sites may provide insight into levels of sleepiness in sleep-disordered breathing.

NIH grants HD038461 and HL080941
**Methods:** The indication of nasal therapy in OSAS patients using nCPAP. Nasal resistance is a risk factor of nCPAP failure. In this study, we discuss the role of sleep breathing disorder and nasal resistance and it is known that high nasal resistance needs nasal therapy to increase the compliance of nCPAP. We compare the nasal resistance and other parameters between patients with nasal therapy and without nasal therapy. In order to explain a risk factor of nasal therapy necessity, we use multivariate logistic regression analysis.

**Results:** Of the 124 patients continued nCPAP, 24% could not use nCPAP because of the nose obstruction complaint. And after the nasal therapy, clinical and surgical treatment nCPAP adherence was successful. In this group, the nasal resistance measurement was higher than in the group without nasal therapy. Conclusion: The results showed that OSAS patients with high nasal resistance need nasal therapy to increase the compliance of nCPAP and rhinomanometry is useful to evaluate nasal resistance and indicate nasal therapy for OSAS patients using nCPAP.

**Introduction:** It is reported that there is an association between severity of sleep breathing disorder and nasal resistance and it is known that high nasal resistance is a risk factor of nCPAP failure. In this study, we discuss the role of sleep breathing disorder and nasal resistance and without nasal therapy. In order to explain a risk factor of nasal therapy necessity, we use multivariate logistic regression analysis.

**Results:** Of the 124 patients continued nCPAP, 24% could not use nCPAP because of the nose obstruction complaint. And after the nasal therapy, clinical and surgical treatment nCPAP adherence was successful. In this group, the nasal resistance measurement was higher than in the group without nasal therapy.

**Conclusion:** The results showed that OSAS patients with high nasal resistance need nasal therapy to increase the compliance of nCPAP and rhinomanometry is useful to evaluate nasal resistance and indicate nasal therapy for OSAS patients using nCPAP.

**Effect Of Chronic Obstructive Pulmonary Disease On Severity Of Obstructive Sleep Apnea And Required Continuous Positive Airway Pressure Level**

**Introduction:** Multiple factors have been found to influence the severity of obstructive sleep apnea and the level of required CPAP in patients with Obstructive Sleep Apnea Syndrome (OSAS). The effect of pulmonary function tests (spirometry, lung volumes, and diffusion capacity) as independent factors in determining the apnea-hypopnea index and the CPAP have not been studied. We investigated the influence of PFTs on AH1 index and the amount of required CPAP in patients with COPD and OSAS.

**Methods:** A retrospective chart review at the Harry S. Truman Veterans Hospital, Columbia, Missouri was conducted. A total of nineteen subjects who carried diagnosis of OSAS and COPD were enrolled. OSAS was diagnosed by polysomnography and COPD was diagnosed based on smoking history and airway obstruction on PFTs. The following data was collected for each patient: age, height, weight, gender, AHI, CPAP level, and spirometry. Lung volumes were available for 7 patients, and diffusion capacity was available for 5 patients. There were one female (5%) and 18 males (95%) subjects. Their ages ranged between 41 to 79 years. Multivariate analysis was conducted between the AHI and CPAP pressure and the PFT parameters. A statistical significance was determined if p<0.04.

**Results:** There was no correlation between AHI or required CPAP and FEV1, FVC and diffusion capacity. The total lung capacity showed slight correlation with the AHI and the CPAP level but without any statistical significance. Comparing patients with mild or moderate airway obstruction (FEV1 ranged between 50 to 80%) with patients with severe airway obstruction (FEV1<50%), there was no difference in the AHI or the required CPAP level.

**Conclusion:** PFT parameters (spirometry, lung volumes, or diffusion capacity) do not influence the AHI or the required CPAP level among COPD patients with OSAS. Patients with increased total lung capacity tend to have higher AHI and they also require higher CPAP. Severity of airway obstruction did not affect the severity of obstructive sleep apnea, and it also did not result in higher CPAP level requirement.

**Efficacy And Cost Savings Of Ambulatory Versus In-Laboratory Obstructive Sleep Apnea Diagnosis And Treatment**

**Introduction:** Interest in ambulatory assessment of obstructive sleep apnea (OSA) has become increasingly common in recent years and continues to grow, particularly with recent technological advances spurring further development. Peripheral Arterial Tonometry (PAT) is one such technology, which records episodic changes in peripheral arterial tone in response to bursts of sympathetic nervous system activation with arousals from respiratory events. Little research has been conducted to assess patient outcomes when using ambulatory testing. The current study compares clinical outcome and cost savings of a novel approach to detecting OSA using PAT and prescribing auto-titrating positive airway pressure (A-PAP) with traditional split night polysomnography and CPAP.

**Methods:** 100 patients (70% men) between 18 and 60 years with symptoms of OSA were recruited. Individuals meeting criteria were randomly assigned to ambulatory OSA assessment (PAT) or split night polysomnography. Individuals received test results on the following morning and either auto-PAP or CPAP respectively, prescribed for significant OSA. Follow-up was at 4 and 8 weeks. Auto-PAP exchanged for set pressure at 8-week follow-up. Total hours of PAP use and mean daily usage were assessed at 4 and 8-week follow-up. Quality of life measures (SF-36v2, Beck Depression Inventory, and Functional Outcomes of Sleep Questionnaire) were assessed at 8-week follow-up and at 6-month follow-up.

**Results:** Individuals diagnosed at home via PAT did not differ significantly from those having split night polysomnography on measures of PAP compliance (total and mean hours of use) and daily functioning. Individuals using PAT reported being as satisfied with ambulatory testing as individuals tested via split night polysomnography.

**Conclusion:** Ambulatory assessment of OSA and prescribing A-PAP can be highly effective when used in the proper context and managed by a sleep specialist. Patient satisfaction is high and similar levels of improvement have been observed. The cost savings of the above strategy are significant.

This study was funded by Metropolitan Sleep Disorders Center and no outside funding was obtained. Metropolitan Sleep Disorders Center does have an agreement with Itamar (PAT developer) to manage the use of PAT in the Minneapolis / St. Paul, Minnesota area.
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Introduction: Multiple system atrophy (MSA) is a neurodegenerative disease characterized by combinations of progressive Parkinsonism, dysautonomia, cerebellar dysfunction and pyramidal signs. Sleep disordered breathing (SDB) is said to be common in patients with MSA and is thought to be one possible cause of sudden death. We examined the association between the severity of sleep disordered breathing and the progression of multiple system atrophy.

Methods: 5 probable MSA patients (M/F 2/3, aged 55.8 ± 9.6 yrs, body mass index 21.7 ± 2.9 kg/m2, MSA-C/MSA-P 5/0, disease duration 4.4 ± 2.1 yrs; mean ± S.D.) defined by Gilman classification entered the study. Standard polysomnographies and laryngoscopies under propofol anesthesia to evaluate vocal cord abductor paralysis (VCAP) and upper airway obstruction were performed at the beginning of the study and at mean intervals of 1.6 (range 0.8 - 2.5) years. No therapies were applied for SDB.

Results: The initial apnea-hypopnea index (AHI) was 14.6 ± 15.6 /hour and 3 patients (60%) had SDB with AHI > 5 /hour, of whom one was the central type and the remainder were the obstructive type. 3 patients showed VCAP; one of these had SDB. At follow up, worsening of the symptoms (International cooperative ataxia rating scale 44.2 ± 19.0 initially vs. 57.4 ± 25.6 at follow-up) and/or VCAP was seen in all patients, but AHI was 5.3 ± 4.7 /hour and SDB improved in 3 patients, unchanged in 1, and worsened in 1.

Conclusion: Despite documented progression of MSA, the severity of SDB worsened in only 1 of 5 patients. Additional studies are required to evaluate the association between MSA and SDB.

0560

Predictors Of Effective Continuous Positive Airway Pressure In Obstructive Sleep Apnea Are Population Specific

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Introduction: Attended continuous positive airway pressure (CPAP) titration is costly, time-consuming, and potentially limits access to therapy. We developed and tested a CPAP prediction formula in a healthy OSA population. We hypothesized that the components of a CPAP prediction formula would be specific to the population being studied.

Methods: Seventy-six untreated OSA patients were randomized to one of three treatments (CPAP, placebo-CPAP, nocturnal O2 at 3 L/min) for 2-weeks. Sleep quality was assessed at baseline, and after one and 14 days of therapy. Repeated measures ANOVA was used to evaluate treatment and time effects, and their interaction.

Results: Sixty-four patients completed the protocol. When compared to placebo-CPAP and nocturnal O2, CPAP corrected apnea hypopnea index, total arousal index, and all measures of oxyhemoglobin saturation (p ≤ 0.001). CPAP also increased REM sleep and significantly reduced stage 1 sleep, number of stage shifts, and REM sleep latency (p ≤ 0.05). CPAP increased spontaneous arousal and periodic limb movement indices (p ≤ 0.008). Oxygen corrected only mean nocturnal saturation (p ≤ 0.009). CPAP had no significant effect on stage 2 sleep, slow wave sleep or daytime sleepiness.

Conclusion: CPAP was effective in correcting the respiratory and arousal abnormalities of OSA. CPAP consolidated sleep by decreasing the number of stage shifts and stage 1 sleep. However, its effect on sleep architecture was only partial. The effectiveness of supplemental oxygen was limited to desaturation parameters.

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0561

Effect Of Continuous Positive Airway Pressure And Supplemental Oxygen On Sleep Quality In Obstructive Sleep Apnea: A Placebo-CPAP Controlled Study

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Introduction: Continuous positive airway pressure (CPAP) is considered effective therapy for obstructive sleep apnea (OSA); however, its specific effectiveness on sleep has been questioned. Supplemental oxygen (O2) has been suggested as an alternative therapy for patients intolerant of CPAP. We investigated the effectiveness of CPAP and O2 against a placebo-CPAP control in patients with OSA. We hypothesized that CPAP would improve sleep quality.

Methods: Seventy-six untreated OSA patients were randomized to one of three treatments (CPAP, placebo-CPAP, nocturnal O2 at 3 L/min) for 2-weeks. Sleep quality was assessed at baseline, and after one and 14 days of therapy. Repeated measures ANOVA was used to evaluate treatment and time effects, and their interaction.

Results: Sixty-four patients completed the protocol. When compared to placebo-CPAP and nocturnal O2, CPAP corrected apnea hypopnea index, total arousal index, and all measures of oxyhemoglobin saturation (p ≤ 0.001). CPAP also increased REM sleep and significantly reduced stage 1 sleep, number of stage shifts, and REM sleep latency (p ≤ 0.05). CPAP increased spontaneous arousal and periodic limb movement indices (p ≤ 0.008). Oxygen corrected only mean nocturnal saturation (p ≤ 0.009). CPAP had no significant effect on stage 2 sleep, slow wave sleep or daytime sleepiness.

Conclusion: CPAP was effective in correcting the respiratory and arousal abnormalities of OSA. CPAP consolidated sleep by decreasing the number of stage shifts and stage 1 sleep. However, its effect on sleep architecture was only partial. The effectiveness of supplemental oxygen was limited to desaturation parameters.

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0562

The Psychological Factors Associated With Subjective Sleepiness In Patients With Obstructive Sleep Apnea-Hypopnea Syndrome

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Introduction: The Epworth Sleepiness Scale (ESS) has been widely used to estimate subjective sleepiness (SS) in patients with obstructive sleep apnea-hypopnea syndrome (OSAHS). But the SS may not frequently correspond to the respiratory disturbance index. Some previous studies suggested that the psychological factors associated with SS. So we intend to clarify the influence of psychological factors on SS in patients with
OSAHS by evaluating Minnesota Multiphasic Personality Inventory (MMPI) and Self-rating Depression Scale (SDS).

Methods: The subjects were consecutive 229 male OSAHS patients under 60 years old who fulfilled the ESS items and underwent polysomnography at the Ota Sleep Disorders Center from January 2002 through December 2003. We excluded patients who took tranquilizers at the examination and who has periodic limb movement more than 5 per hour. Multiple linear regressions was used to model the relation of the ESS to explanatory variables including age, body-mass index, usual sleep time for the last month, respiratory arousal index (RAI), SDS, T-score of MMPI scales. Considering that SS mainly depends on the frequency of respiratory event related arousals, we created estimated ESS calculated from linear regression line with RAI. Then, logistic regressions were used to model the relation between the overestimation or underestimation of SS to the above explanatory variables.

Results: 1. The ESS has significant association with age, RAI and Hs score on MMPI. 2. The overestimation of SS has significant association with Hs and Ma score on MMPI. The odds ratio of Hs score was 2.39 (95% CI 1.29, 4.44). The odds ratio of Ma score was 2.25 (95% CI 1.14, 4.44). The underestimation of SS has no significant association with any variables.

Conclusion: From the above results, psychological factors were thought to influence on SS in OSAHS patients. Especially, the overestimation of SS seemed to be associated with the character trait of the patients.

0564

The Prevalence Of Central Sleep Apnea Syndrome In Japanese Outpatients

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Introduction: Central sleep apnea-hypopnea syndrome was defined as 5 or more central apneas plus hypopneas per hour of sleep accompanied by symptoms of excessive daytime sleepiness (normocarbic) and/or frequent nocturnal arousals/awakenings (AASM taskforce 1999). Definitive differentiation of central sleep apnea from obstructive sleep apnea requires esophageal pressure (Pes) measurement. We chose to use less invasive techniques to estimate the prevalence of central sleep apnea syndrome (CSAS).

Methods: Polysomnograms were performed without Pes in 3659 subjects suspected of sleep apnea syndrome in our associated hospitals in Niigata prefecture of Japan, from August 1999 to March 2004. Central apnea was defined as >10-second airflow cessation without thoracoabdominal movements. CSAS was defined as both 5 or more central apneas per hour and these comprised more than half of all apnea events.

Results: 1% of all our sleep apnea patients (36 of 3659) had CSAS. Mean age was 60.0 ± 14.8 years, body mass index was 24.6 ± 2.7 kg/m2, and apnea hypopnea index was (AHI) 36.3 ± 20.1/hour. Of these patients, 21 had hypertension, 11 had cardiovascular disease, and 9 had brain disease. No co-morbidity were seen in 4 patients. 31 patients had AHI > 15/h.

Conclusion: Only one percent of our sleep apnea patients manifest CSAS. CSAS patients tended to be older and less obese. Most, but not all, patients had other diseases. Further study is needed to elucidate if these patients have true central sleep apnea-hypopnea syndrome evaluated by PSG with Pes measurement.

0565

Replacing Polysomnography With Watch_PAT100 For Sleep Apnea Diagnosis Resulted In Considerable Savings

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Introduction: The Watch-PAT100 is an ambulatory device based on the Peripheral Arterial Tonometry (PAT). It was validated against polysomnography and in a previous laboratory study we have evaluated the clinical guidelines for its clinical use. The aim of this study was to evaluate the savings in full PSG studies in evaluating patients with suspected sleep apnea patients by using the Watch-PAT100.

Methods: Watch-PAT100 recordings were performed in 260 consecutive patients (male:female ratio 1:2.6, mean age 51 years old, mean BMI=31, mean ESS=11) referred to our Sleep-Wake disorders center because of suspected sleep apnea syndrome during 2003-2004. The Watch-PAT100 includes pulse oximetry, PAT probe and actigraphy sensors. Data collected during the night were analysed automatically using the Watch-PAT dedicated software package that provided information on Respiratory Disturbance Index (RDI), oxygen desaturation index (ODI), arousal index (ARI) and sleep duration. Final diagnosis and treatment decision were made by a multi disciplinary team based on these results as well as clinical impression.
Results: 12 out of the 260 cases were discarded from the study, because of technical difficulties with the PAT probe sensors (N=11), and arrhythmia that interfere with the recordings (N=1). In 28/248 cases the Watch-PAT100 results were inconclusive and a full PSG was needed in order to reach a final diagnosis. In 220 cases, the Watch-PAT100 results were sufficient to establish the final diagnosis and to decide on the mode of the treatment. Given the facts that a full PSG requires 30-60 minutes of patients preparation before sleep 30 minutes detachment time in the morning and 60 minutes of data scoring and interpretation, using the Watch_PAT100 will results in a considerable saving of time and costs.

Conclusion: The Watch-PAT100 results in 84% reduction in full PSG studies which represents a considerable cost and time saving.

0566
The Subjective And Objective Cognitive Measures In Patients With Obstructive Sleep Apnea
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Introduction: Obstructive sleep apnea is characterized by repeated cessation of breathing, sleep fragmentation and oxygen desaturation during sleep. Previous studies measured neurocognitive functions by using a variety of neurocognitive tests, and found that patients’ neurocognitive functions were affected by OSA’s symptoms. However, no study has focused on the subjective awareness of cognitive impairments, and then assessed the relationship between the subjective and objective cognitive functions. This study used a subjective rating scale to evaluate OSA patients’ perception of their cognitive impairments, and explore the relationship between subjective and objective cognitive functions.

Methods: An experimental group of 20 OSA patients and a control group of 20 normal subjects were used. Their performance on the neurocognitive test battery (including the Continuous Performance Test, Paced Auditory Serial Addition Test, Wechsler Memory Scale, Wechsler Adult Intelligence Scale, Wisconsin Card Sorting Test, Trial Making Test and Stroop Test) and subjective rating scales (including subjective sleepiness, health-related quality of life and the subjective rating of cognitive functions) was compared. In addition, the study sought to assess the relationship between the subjective and objective cognitive functions.

Results: On subjective rating scales, the OSA patients reported more sleepiness, poor health-related quality of life and impairment of their neurocognitive functions. The OSA patients didn’t perform as well as the control group on the logical memory and verbal paired associates test of the WMS, the similarity and information test of the WAIS, WCST and PPT test. on neurocognitive tests related to executive function, the OSA patients showed diminished performance. The OSA patients displayed inconsistency between their objective neurocognitive function and their subjective rating.

Conclusion: The inconsistencies displayed between OSA patients’ objective executive function and their subjective rating. Thereof, suggest that in measuring sleep-related disorders of clinical tests, used in conjunction with neurocognitive tests could provide additional data on the impairment of executive function that is absent from patients’ subjective reports.

0567
Sleepiness Related To The Respiratory Event Index In Comparison To The Apnea Hypopnea Index
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Introduction: Apnea hypopnea index (AHI) is a measurement of sleep disordered breathing that accounts for all apneas and only those hypopneas accompanied by a 4% decrease in oxyhemoglobin saturation. The Respiratory Event Index (REI) accounts for all apneas and those hypopneas with 1% or more oxyhemoglobin desaturation associated with arousal. It has been ruled by Centers for Medicare and Medicaid Services (CMS) that sleep disordered breathing can qualify for treatment when quantified by 5 or more AHI events per hour. The initial purpose of this study was to determine if apneas and hypopneas which result in sleep disturbance can cause sleepiness regardless of whether the oxyhemoglobin saturation drops 4% or more.

Methods: The study was conducted retrospectively and included 82 subjects who underwent overnight polysomnography (PSG) between August and November 2004. Each subject had completed the Epworth Sleepiness Scale (ESS) and then underwent a PSG. Current medications used by subjects were noted.

Results: Among the 82 subjects, 57% were female and 43% were male, average age was 48.6 and average BMI was 39.8. REI had a significant positive correlation with AHI (Spearman’s (p) = .958; P = 0.01). However, AHI did not correlate well with ESS (Spearman’s (p) = -.014; P = .898). Additionally, REI did not correlate well with ESS (Spearman’s (p) = -.020; P = .858). Subjects who were taking medications that could potentially affect sleepiness were eliminated from the analysis (n=27), but again ESS correlated poorly with AHI and REI.

Conclusion: The ESS correlated poorly with AHI and REI in this study, suggesting that the ESS may not be an effective tool in evaluating sleep disordered breathing. Although REI correlated well with AHI, a more reliable sleepiness measurement is needed to determine if REI is more strongly associated with sleepiness than the AHI.

0568
Obstructive Sleep Apnea Is Common In Pregnant Women
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Introduction: Incident snoring and symptoms of sleep-disordered breathing (SDB) are common among pregnant women. However, little is known about whether women are likely to develop obstructive sleep apnea (OSA) during pregnancy. We examined whether incident OSA is common among pregnant women, and characteristics of pregnant women with OSA.

Methods: We recruited 60 healthy pregnant women from the obstetrics practices at the Hospital of the University of Pennsylvania. Each woman completed diagnostic overnight polysomnography (PSG) during the 1st trimester (prior to 14 weeks of gestation) and again during the 3rd trimester, between 31 and 39 weeks of gestation. Demographic information including age and ethnicity was obtained. Neck circumference, height and weight were measured prior to baseline polysomnography and
again at the follow-up PSG. Fisher’s exact test was used to compare the number of women with an Apnea-Hypopnea Index (AHI) >=5 events/hr in the 1st and 3rd trimesters. Data on subject characteristics were analyzed using unpaired t-tests.

**Results:** The mean age of these subjects was 27.1 (SD 6.6) years. 95.0% were African-American. At the 1st trimester PSG, 5 subjects (8.3%) had an AHI >=5 events/hr. By the 3rd trimester PSG, 15 subjects (25.0%) had an AHI >=5 events/hr (p<0.0001). We compared subjects with (AHI >=5) and without OSA (AHI <5) on the 3rd trimester PSG. Although the difference was not clinically significant, 1st trimester AHI was slightly higher among women with OSA, (3.9 (3.8) v. 1.3 (1.3), p=.02). Subjects with OSA were significantly older (30.6 (5.9) v. 25.4 (5.8) years old), had a higher mean 1st trimester BMI (33.3 (8.4) v. 26.7 (5.4) kg/m2, p<0.01), and a larger mean 1st trimester neck circumference (36.8 (2.9) v. 35.4 (2.7) cm, p=0.008) than women without OSA. Women with OSA gained less weight gain during pregnancy (18.4 (13.0) v. 23.6 (13.0) lbs), but this difference was not statistically significant. Mean change in neck circumference during pregnancy was not significantly different between groups. Among women with OSA, the mean 3rd trimester AHI was 10.7 (9.4) events/hr.

**Conclusion:** Mild incident obstructive sleep apnea is common among pregnant women. Our data suggest that potential risk factors for pregnancy-associated OSA include older age, higher baseline BMI and larger neck circumference. Pregnant women with these characteristics should be considered for screening for sleep apnea.

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**0569**

**The Possible Association Of The Oxidative Stress With Neuropsychological Deficits On Patients With Obstructive Sleep Apnea Hypopnea Syndrome**

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**Introduction:** Recently, there has been evidence that repetitive hypoxia and reoxygenation (such as in OSAS) increases production of reactive oxygen species and induces memory deficits on animal models. The aim of this study was to verify whether oxidative stress is associated with neuropsychological dysfunction in OSAS patients.

**Methods:** This is a cross sectional study of a population sample of 19 middle aged adult men, aged 39 ± 7y (Mean ± DP), with BMI 29±4Kgm2, 11 years schooling, with clinical complaints of OAHS and IAH above 10. We also analyzed 12 volunteers matched for sex, age, BMI and educational level with the same method. All patients underwent the same protocols that included: physical examination, full night polysomnographic, ECG, Beck inventory, Epworth Sleepiness Scale, a number of neuropsychological tests (Toulouse Piron; Wescheler Memory Scale; Word list; Wisconsin, and Rey Figure) and blood sample analyses (T Bars, glutathione, SOD, catalase, antioxidant vitamins, homocysteine, uric acid, T3, T4, TSH). Finally we focused on a possible correlation between the stress oxidative measures and the neuropsychological deficits.

**Results:** The mean value of AHI in the sample was 43±29 versus 1.79±1.48 in the control group (Mean± DP). Patients showed reduced levels of vitamin B11 (4.7±1.3ng versus 9.6±2.7ng, p≤0.0001), vitamin E (10.5±3.3 umoles/L versus 19.2±7umoles/L, p≤0.0001) and SOD (8.7±3.1umMg versus 14.6±2.3UmMg, p≤0.0001) when compared to controls. Regarding the neuropsychological features, we found out a poor performance in attention (p≤0.01) and memory tasks (p≤0.01) in OSAS patients in comparison to the same parameters of the control group (T test). Finally, there were positive correlations (Pearson) between Vitamin E and Short-Term Memory (r=0.75; p≤0.0001) and between SOD and Rey Figure retrieval (r=0.50; p≤0.01).

**Conclusion:** The present study supports the relevance of a disruption on homeostasis between antioxidants and pro oxidants in OSA patients. The neuropsychological deficits might be related with this homeostasis disruption.

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**0570**

**Combined Therapy To Improve Adherence To CPAP**

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**Introduction:** Efforts to enhance adherence to Positive Airway Pressure (PAP) in obstructive sleep apnea (OSA) have been minimally successful. We examined the relative efficacy of two brief behavioral interventions, with and without flexible PAP, for enhancing 6-month adherence to treatment in OSA.

**Methods:** One hundred thirty-seven medically and psychiatrically healthy OSA patients (52.7 ± 10.7 years, 47 women), were randomized to one of three groups (Education, ED; Motivational Enhancement Therapy, MET; or Standard Care, SC), controlling for age, education, apnea severity, and subjective sleepiness. Two intervention sessions, one week apart, were provided after 1 week of CPAP use in the ED (N=42) and MET (N=51) groups. The SC group received no special therapy. The MET intervention was based on psychological theories of behavior change; the ED intervention provided OSA and CPAP education only. About half of the participants (67) were set up with CPAP, while the rest were given C-Flex in a sequential, non-randomized manner. Nightly CPAP use was monitored covertly.

**Results:** Five experimental groups (SC/C-Flex, ED/CPAP, MET/CPAP, ED/C-Flex, and MET/C-Flex) were compared to a reference group (SC/CPAP) in the prediction of Kribbs minimal and optimal use criteria at 6-months, using two separate logistic regressions. Individuals in the MET/C-Flex group were 4.4 times (p<.02) more likely to be minimal users at 6-months compared to SC/CPAP (72% vs. 36%). No other group showed an advantage over SC/CPAP, though ED/C-Flex showed a trend (65%; p=.07). Individuals in the MET/C-Flex group were also 4 times (p<.05) more likely to be optimal users (39% vs. 14%) compared to SC/CPAP. No other groups showed an advantage over reference.

**Conclusion:** Combined therapies, including new technologies and theory-driven, behavioral interventions show promise for improving PAP adherence in OSA. Continued follow-up is being conducted and the sample size increased to determine efficacy for larger samples over longer periods.

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0571
CPAP Normalizes PM/AM Systolic Blood Pressure Variation After First Night Of Therapy
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Introduction: The PM/AM variation of blood pressure (BP) may be a marker for cardiovascular health, is often lost in patients with Obstructive Sleep Apnea (OSA), and is restorable after long-term CPAP therapy. It is not known whether the normalization of PM/AM BP dynamics is an immediate or chronic effect of therapy. The purpose of this study was to investigate the possibility of an immediate effect of CPAP therapy on the PM/AM BP variation, before and after diagnostic and/or therapeutic polysomnography (PSG) under well-controlled conditions.

Methods: BP (mmHg) was measured in 200 consecutive patients before and after polysomnography, for which they were referred to evaluate sleep disordered breathing. BP determinations between 10 and 11 PM (before bedtime) and between 5 and 6 AM (after awakening) were recorded and correlated with PSG and sleep questionnaire findings. PM/AM BP variations were compared using Pearson correlation and paired student T-test in the following three groups: diagnostic PSG with RDI < 6, diagnostic PSG with RDI > 20, and split night therapeutic PSG with successful CPAP titration.

Results: In the split-night PSG group (initial RDI mean 54 +/- 3.3 events/hr; final RDI mean 1.6 +/- 0.9 events/hr) difference between PM systolic BP (138.6+/-3.7) and AM systolic BP (130.83 +/- 3.83) was statistically significant (7.7+/- 3.3, p < 0.03). PM/AM systolic BP difference was also significant in the diagnostic PSG with RDI < 6 group (12.4 +/- 6.1, p<0.05), but not in the diagnostic PSG with RDI > 20 group (2.1 +/- 0.6). Diastolic BP did not change significantly overnight in any group

Conclusion: CPAP treatment restores PM/AM systolic BP variation after as little as 2 hours of sleep at optimal therapeutic pressure. The findings, which require correlation with longer term follow up, nevertheless, suggest that favorable BP response to CPAP begins immediately.

0572
Markers Of Oxidative Stress But Not Of Inflammation Are Significantly Associated With Obstructive Sleep Apnea
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Introduction: Obstructive sleep apnea (OSA) is associated with elevated plasma levels of oxidative stress and inflammatory biomarkers that may play a role in the pathogenesis of atherosclerosis. The present study investigated the association between oxidative stress and inflammatory markers with respect to the severity of sleep apnea and obesity.

Methods: Fasting levels of plasma thiobarbituric reactive substances (TBARS), peroxides (PD), and the anti-oxidant enzyme paraxonase-1 (PON1) - biomarkers of oxidative stress - and C-reactive protein (CRP), haptoglobin and ceruloplasmine - biomarkers of inflammation - were investigated in 141 participants: 66 patients with mild OSA (AHI between 10 and 30), 30 with severe OSA (AHI greater than 30), and 45 non-OSA controls (AHI less than 10). All participants were free from cardiovascular or any other major disease. Biomarkers concentrations were compared between groups by analysis of the covariance using age, BMI, and smoking as covariates. Spearman rank order correlation was used to determine the relationship between variables.

Results: Significant differences in TBARS, PD and PON1 were found between the three groups. TBARS and PD were significantly higher in patients with severe (22.3±7.1 mmol MDAD/ml, 948.6±140.0 nmol/ml) than in mild OSA (15.3±5.0, 871.1±69.3) and in controls (13.0±3.5, 820.0±138.6); patients with mild OSA had significantly higher TBARS than controls. PON1 was lower in severe (81.3±10.4 U/ml/min) than in mild OSA (89.8±17.3) and in controls (93.5±18.0). Oxidative stress markers were significantly correlated with AHI (TBARS: 0.58, pA.001; PD: 0.32, pA.01; PON1: -0.33, pA.008), but did not correlate with BMI. There were no significant differences between groups in the concentration of any of the inflammatory biomarkers, which also did not correlate with RDI. Two of the inflammatory markers significantly correlated with BMI (CRP: 0.27, pA.02 and ceruloplasmin: 0.33, pA.003). None of the correlations between oxidative stress and inflammation biomarkers was statistically significant while all 3 inflammatory and 3 oxidative stress biomarkers were highly intercorrelated.

Conclusion: The levels of circulating oxidative stress biomarkers are significantly associated with the severity of sleep apnea while inflammatory markers are associated with obesity, and are unrelated to the oxidative stress biomarkers.

0573
The Use Of Digital Photogrammretics In The Evaluation Of Patients With Obstructive Sleep Apnea
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Introduction: To use digital photography in the assessment of anatomical features of patients referred for evaluation of OSA. To determine which photogrammetric parameters correlate with the severity of OSA. To compare patients with OSA to controls.

Methods: Patients referred to the Sleep Disorders Center, Winnipeg, Manitoba, for evaluation of OSA were included in the study. Patients underwent polysomnography (PSG) and were digitally photographed in profile, from a distance of one and half meters. Anatomical landmarks were indicated and measured using computer software. Correlations were calculated by Mann-Whitney U test and logistic regression analysis. Study patients were compared to non-snorers controls.

Results: Eighty-nine (89) patients were photographed for analysis, 50 male and 39 female. The mean age of subjects was 47.6 years. The NGnH angle was found to correlate most significantly with the severity of OSA as measured by apnea/hypopnea index (AHI). When compared to controls, study patients had significantly greater NGnH angle (p<.005).

Conclusion: The NGnH(chin) angle correlates most significantly with the severity of OSA in the patients studied. Our study suggests that digital photogrammrets could be employed as an adjunct in the evaluation of patients with OSA.

0574
Variations In The Functional Outcomes Of Sleepiness Questionnaire (FOSQ) In Relation To Long-Term CPAP Use
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Introduction: Obstructive Sleep Apnea (OSA) is a serious medical condition with significant daytime consequences. The FOSQ is a self-report measure designed to assess functional consequences associated with sleepiness. CPAP treatment has been shown to change FOSQ scores at 3-months, but longer studies with moderate-severe OSA patients have not been reported. The purpose of this study was to examine whether adher-
First, CPAP over a 6-month period moderates changes in FOSQ scores. **Methods:** One hundred ten medically and psychiatrically healthy OSA patients (53±11 years, RDI = 42±24; 37 women), were administered the FOSQ at baseline (prior to initiation of CPAP) and at 3- and 6-months post-CPAP initiation. Dependent variables included total FOSQ score and the subscales of activity level, vigilance, sexual intimacy, general productivity, and social outcome. Participants were grouped into adherent and non-adherent users using an established cutoff of 6 hours a night. Repeated measures ANOVA was used to assess change in time (BL, 3-, and 6-months) by adherence.

**Results:** The adherence groups did not differ on any demographic or severity measure at baseline. Significant improvement was seen on the subset of activity level (F = 4.41, p<0.01). Changes were seen primarily between baseline and 3-months, with stabilization between 3- and 6-months. Other subsets seemed to change most between baseline and 3-months as well (trend for vigilance, p = .10), though the change was not significant in the ANOVA.

**Conclusion:** High levels of CPAP adherence result in greater changes to activity level over 6-months. Most of these changes occur within the first three months. Changes in this and other subscales may be even more pronounced in those individuals who are impaired at baseline.

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**0575**
**Morning-Evening Variation Of Endothelial Function In Obstructive Sleep Apnea**

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**Introduction:** Obstructive sleep apnea (OSA) is associated with endothelial dysfunction (ED) that is considered to be an antecedent of cardiovascular morbidity. Peripheral arterial tone response to reactive hyperemia (RH-PAT) is a novel technique to assess endothelial function, with substantial advantages over the commonly used brachial ultrasound technique. We utilized the RH-PAT method to investigate the evening-morning difference in endothelial function in OSA patients. Based on previous reports we predicted endothelial dysfunction only during the morning and that it would be correlated with the severity of OSA.

**Methods:** 38 subjects participated (26m/12f). Mean age and BMI were 46±8.7 yrs and 29.6±5.5 kg/m2, respectively. 13 subjects had severe OSA (AHI ≥ 30); 5 had HTN/cardiovascular co-morbidity (1.71±0.39 vs. 1.88±0.36, p=0.26). ÉPAT% also tended to correlate positively with AHI (r=.28, p<0.1).

**Results:** Early morning RH-PAT index was inversely correlated with AHI (r=-.46, p<0.005) and was non-significantly lower in patients with cardiovascular morbidity (1.71±0.39 vs. 1.88±0.36, p=.26). ÉePAT% also tended to correlate positively with AHI (r=.28, p<0.01).

**Conclusion:** Our results confirm the existence of diurnal variation in endothelial function in OSA and that the morning decrease in endothelial function is related to the severity of OSA. Endothelial dysfunction tended to be more severe in patients with cardiovascular co-morbidity. These findings may implicate an elevated susceptibility of OSA patients to the diurnal peak in cardiovascular events in early morning hours.

**0576**
**Circulatory Response In Sleep Apnea Patients During Sleep Before And After CPAP Treatment**

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**Introduction:** Obstructive sleep apnea (OSA) impairs breathing and leads to repetitive hypoxia and arousals. OSA is associated with hypertension, heart failure arrhythmia and death. Apneic episodes are presumed to cause hemodynamic alterations, however few studies have documented these changes before and after treatment for OSA. The aim is to assess the circulatory response to various sleep stages in patients with OSA (before and after treatment) and normal controls using impedance cardiography (ICG).

**Methods:** We studied 5 OSA patients (AHI = 60/hr), 5 patients after CPAP (AHI 10/hr) and 3 controls (AHI = 8/hr). Hemodynamic monitoring was done non-invasively during entire overnight polysomnography using impedance cardiography by BioZ. ICG Monitor (Cardio dynamics Inc, San Diego, CA)

**Results:** The cardiac output (CO) and cardiac index (CI) decreased during sleep in both OSA patients and controls. The cardiac output decreased by 22%, cardiac index by 24%, and systemic vascular resistance (SVR) increased by 15% in OSA patients. This is compared to a decrease of 14% in both CO and CI and a decrease of 4% in SVR in control patients. Post CPAP treatment the CO increased by 10%, CI increased by 9%, whereas SVR decreased by 18%.

**Conclusion:** Significant hemodynamic changes occurring during sleep are much more pronounced in OSA patients as compared to controls. These changes are improved with treatment with CPAP. Possible explanations which remain to be explored are increased intrathoracic pressure during apneic episodes limiting cardiac contractility and stroke volume and/or decreased pulmonary vascular capacitance.

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**0577**
**Effect Of Cerebral Blood Flow On The Difference Between Eupneic PCO2 And The Hypocapnic Apnea Threshold PCO2**

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**Introduction:** Our previous work showed a diminished cerebral blood flow (CBF) response to change of PaCO2, especially during hypocapnia, in patients with central sleep apnea compared to those without apnea. Since CBF serves to buffer changes in H+ and pCO2 at the site of the central chemoreceptors, it may play an important role in maintaining breathing stability. If cerebral vessels are unable to constrict proportionally to metabolic chemoreceptors, it may play an important role in maintaining breath stability. If cerebral vessels are unable to constrict proportionally to metabolic chemoreceptors, it may play an important role in maintaining breath stability.

**Methods:** We used indomethacin to reduce CBF response to CO2 in seven normal subjects during sleep as previously reported. We measured the ∆PETCO2, an index of breathing stability, with and without indomethacin (100mg P.O) in random order. The apnea threshold was
determined using a ventilator in pressure support mode to gradually reduce $P_{ET}CO_2$ until apnea took place (absence of respiratory flow/effort for at least 10 sec). The hypopnea threshold was defined as the $\Delta P_{ET}CO_2$ resulting in a reduction tidal volume of ≤50% for at least 10 sec. 

**Results:** Administration of indomethacin significantly reduced the $\Delta P_{ET}CO_2$ required to produce apnea from 6.5±0.5 to 4.3±0.8 mmHg (p<0.01). The $\Delta P_{ET}CO_2$ required to produce hypopnea was also reduced (2.5±0.9 vs 4.6±0.8 mmHg, p=0.06). The smaller $\Delta P_{ET}CO_2$ resulted from a relative lower eupneic $P_{ET}CO_2$(45.7±1.0 vs 46.5±0.9, p=0.45) and a relative higher apneic threshold $P_{ET}CO_2$(41.4±0.9 vs 40.0±0.9, p=0.11).

**Conclusion:** Our data indicate that alterations in cerebral hemodynamics may increase the susceptibility to apnea and breathing instability.

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**0578** Control Of Mixed Sleep Disordered Breathing With The Use Of Carbon Dioxide Rebreathing And Positive Airway Pressure

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**Introduction:** Reducions in PCO2 (PaCO2) below the apnea threshold play a key role in the pathogenesis of central sleep apnea. Previous studies have shown that administration of CO2 enriched gas mixture and addition of deadspace eliminates apneas and hypopneas. Difficulty in optimizing treatment of sleep disordered breathing may be attributed to unrecognizable contribution of a central component such as periodic breathing. We hypothesized that minimization in fluctuation in CO2 by use of a non-vented mask and deadspace tubing in addition to positive airway pressure (PAP) could achieve better control of mixed sleep disordered breathing.

**Methods:** We studied patients with mixed obstructive and central sleep disordered breathing. All patients underwent overnight polysomnography. Patients were titrated with CPAP and/or BIPAP. They were all noted to have central events or periodic breathing not eliminated by PAP alone. A non-vented mask and in some cases additional deadspace tubing (75-150 cc’s) were used for CO2 rebreathing. Apnea/hypopnea index (AHI) before treatment, after PAP and after CO2 rebreathing were compared.

**Results:** The 15 patients who were studied had a mean age of 55±12. Mean AHI at baseline before PAP titration was 70.6±54.09. After PAP, mean AHI was 33.1 ± 31.29. After CO2 rebreathing, with the use of non-vented mask and deadspace, mean AHI decreased to 5.6 ± 6.02.

**Conclusion:** The use of minimal amounts of CO2 rebreathing with a non-vented mask and deadspace in addition to positive airway pressure achieved excellent control of sleep disordered breathing. This method is a possible practical approach to such patients who are otherwise poorly treated.

This study was supported by Guidant Corp.-CRM

**0580** Prediction Of Simulated Driving Performance By CPAP Adherence In Obstructive Sleep Apnea

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**Introduction:** Several studies have shown improved simulated driving performance in obstructive sleep apnea (OSA) patients treated with continuous positive airway pressure (CPAP). No study, however, has assessed the relationship between CPAP adherence and simulated driving performance. We examined whether CPAP adherence predicts simulated driving performance in OSA patients tested at 6-months post-treatment.

**Methods:** Twenty-two medically and psychiatrically healthy moderate to severe OSA patients (7 women, mean age 46.1 ± 11.2 years, mean RDI 45.1 ± 26.9, mean baseline Epworth score 11.1 ± 5.0) performed a 30-minute simulated driving task at baseline and 6 months post-CPAP initiation. The driving task appeared as a two-lane highway with lane markings, signs, and occasionally, other simulated vehicles. Participants were instructed to stay centered in the right hand lane and to maintain the posted speed. Dependent variables were lane position variability, speed variability, off-road incidents, and an overall composite measure of simulated driving performance. Nightly CPAP use was monitored covertly using Respironics SmartCard™ technology and summarized as average 6-month use.
Results: Repeated measures ANOVA indicated a trend for reduced off-road incidents at the 6-month session (F(1,21)=3.63, p=.07). Pearson correlations were significant between average 6-month use and 6-month tracking variability (r=.58, p<.05) and overall driving performance (r=.47, p<.05). Stepwise multiple regression indicated that average use at 6 months accounted for 18.3% of the unique variance in overall driving performance beyond that accounted for by age and RDI (F(1,19) = 5.47, p<.05).

Conclusion: Average 6-month CPAP use predicted simulated driving performance at the 6-month session. There was also a trend for improved driving performance post-treatment. Consistent nightly long-term CPAP use may therefore be important for neurobehavioral task performance in OSA patients.

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0581 Sleep Disordered Breathing And Daytime Sleepiness In Older Women: A Prospective Study With Objective Measures Of Sleep
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Introduction: Previous studies have demonstrated an association between obstructive sleep apnea and daytime sleepiness among middle-aged adults; however, the evidence concerning these relationships in older adults is mixed. This study is the first to combine objective measures of sleep time and sleep-disordered breathing (SDB) to examine their relationship to daytime sleepiness in a large cohort of primarily non-institutionalized older women.

Methods: Subjects are participants from the multi-center Study of Osteoporotic Fractures that began in 1986-88. During the eighth study visit from 2002-3, a sample of 461 surviving older women underwent in-home overnight polysomnography and wrist actigraphy for a minimum of three 24-hour periods. Daytime Sleepiness was assessed using the Epworth Sleepiness Scale (ESS). We examined the relationship between severity of SDB and ESS scores using logistic regression analysis. All models were adjusted for age, body mass index, medical comorbidity index, and the use of sleep medications. We further explored whether these associations are mediated by sleep deprivation by adjusting models for total sleep time (TST).

Results: The mean age was 82.9 years, and mean body mass index was 27.9±5.1 kg/m². Mean respiratory disturbance index (RDI) was 15.7±15.1, and the mean percentage of sleep time with oxygen saturation below 90% was 4.0±9.7. Before adjustment for TST, RDI and the percentage of sleep time with oxygen saturation below 90% were associated with daytime sleepiness (ESS score ≥10). Compared to those with RDI in the lowest tertile (< 7.06), those in the highest tertile (≥ 17) were twice as likely to suffer from daytime sleepiness (relative hazard=2.1, 95% confidence interval 1.1, 3.9). This relationship was only modestly attenuated by adjustment for TST (RH=1.8, 95% CI 1.0, 3.5) and comorbidities.

Conclusion: Severity of SDB in community-dwelling older women is associated with daytime sleepiness. This relationship is not entirely explained by decreased sleep duration among those with severe SDB.

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0582 Sleep And Endothelium Activation In Patients With UARS And Severe OSAS, Preliminary Report
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Introduction: OSAS and hypoxia are reported to alter vascular endothelium. However, studies have considered moderate to severe OSAS. Objective-To evaluate sleep and vascular endothelium parameters in UARS and severe OSAS patients.

Methods: Patients were classified in 2 groups matched by age and gender, according to clinical and PSG diagnosis as (UARS, n=15, mean age 45.5 - 12.3) and (severe OSAS, n=45, mean age, 51.6 - 10.5), AHI>30. Anti-endothelin radioimmunoassay, ICAM, thrombomodulin, were isolated from serum and plasma, respectively. Presence of snoring, hypertension, arousals, and SaO2 parameters are reported.

Results: Arousal index and BMI were lower in UARS group (p<0.01, all), but awake baseline SaO2, min SaO2, SaO2 time spent bellow 90%, were lower in OSAS subjects (p<0.01, all). The only significant vascular parameter was endothelin 1, higher in OSAS group (p<0.05). Increased hypertension diagnostic was found in OSAS group (8.3 vs 40%/%, p<0.01). All patients with positive endothelin 1 activation had BMI>30. There was no association between BMI and ICAM and thrombomodulin positivity. Logistic Regression for endothelin 1 and variables: snoring, AHI, hypertension, SaO2 time spent bellow 90% showed that only hypertension, and snoring intensity were significant predictors for endothelin 1 activation (beta=.38, .46; respectively, p<0.05)

Conclusion: BMI was highly associated with endothelin activation, but not with thrombomodulin or ICAM. This data suggest that endothelin increase in OSAS patients is related to high BMI, in this case, > 30 kg/m². Presence of hypertension is predictor of endothelin activation, but again, this might be related to obesity or age. This is a preliminary report, and the authors suggest that higher number of subjects needs to be studied, including patients with low BMI. The role of increased respiratory effort, hypoxemia, and obesity still needs to be clarified.

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0583 Inter-Night Variability Of Sleep Disordered Breathing In An Atrial Overdrive Pacing Study
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Introduction: Sleep disordered breathing (SDB) adversely affects cardiovascular health. Recent studies have shown atrial overdrive pacing may reduce patients’ apnea-hypopnea index (AHI) or improve oxygen saturation. However, such positive effects were not consistent in previous
Studies. The purpose of this study was two-fold: to assess SDB variability as a means to understand overdrive pacing trial results and to evaluate the needs for long term SDB monitoring.

**Methods:** Pacemaker patients (Guidant PULSAR MAX I/II or INSIGNIA) underwent full polysomnography to screen for SDB with lower rate limit (LRL) set at 50 bpm. We studied eight male pacemaker patients, who screened positive (AHI≥15). Within four weeks, we repeated the sleep study at the same pacemaker LRL setting as the screening study. There was no change in medical treatment received on both nights. The differences in AHI and other SDB parameters were compared using t-test between screening (S) and control (P0) studies. Results are displayed as the mean±standard deviation.

**Results:** The time interval between the studies was 12.75±5.87 days. The average heart rate was 57.8±7.3 during S studies and 57.6 ± 9.0 during P0 studies (p = 0.95). AHI varied by 9.94±17.02 between S and P0 nights (p = 0.14). Oxygen desaturation varied by 0.9%± 3.1% (p=0.44). Other SDB measurements varied significantly between S and P0 nights for some patients. There was no correlation between changes in AHI and other SDB measurements.

**Conclusion:** Individual patient’s AHI values were observed to vary by clinically significant values between two sleep studies at the same minimal pacemaker LRL. Other aspects of SDB also varied. Night-to-night variability should be taken into consideration in designing and interpreting therapeutic intervention studies, including pacing, for SDB. Additionally, long-term trending apnea diagnostics rather than single-night studies are needed to assess change in SDB over time.

This study was supported by Guidant Corp.-CRM

**0584**  
A Bench Study On Performance Characteristics Of Direct Connect Nasal CPAP Interfaces  
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**Introduction:** Direct connection nasal interfaces are increasing in popularity as an alternative to traditional Nasal CPAP masks. Direct connect nasal interfaces offer the promise of being easier to fit to individual patients. However, home care providers and practitioners evaluate products based on marketing material. The main assumption is that all of the products are equivalent from a performance perspective, therefore purchasing decisions are based on features and price. The objective of this study is to determine the performance capabilities of several commercially available direct connect nasal interfaces.

**Methods:** Six different families of direct connect nasal interfaces were tested for Exhaust Flow, Pressure Drop, and Mean Pressure Deviation. Multiple sizes of each type of device were compared. The exhaust flow for each family was tested at CPAP pressures of 4 cmH2O and 20 cmH2O. Pressure Drop for each device was measured at inspiratory flow rates of 30 and 50 L/Min. Pressure deviation from the mean CPAP pressure was measured from the tachogram. CVHR was defined as 0.14). Oxygen desaturation varied by 0.9%± 3.1% (p=0.44). Other SDB measurements varied significantly between S and P0 nights for some patients. There was no correlation between changes in AHI and other SDB measurements.

**Conclusion:** Individual patient’s AHI values were observed to vary by clinically significant values between two sleep studies at the same minimal pacemaker LRL. Other aspects of SDB also varied. Night-to-night variability should be taken into consideration in designing and interpreting therapeutic intervention studies, including pacing, for SDB. Additionally, long-term trending apnea diagnostics rather than single-night studies are needed to assess change in SDB over time.

This study was supported by Guidant Corp.-CRM

**0585**  
Effects Of Supine Bent Knees Posture On Sleep Disordered Breathing  
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**Introduction:** Previously we reported a case that showed a reproducible, near total ablation of SDB when asleep in the supine knees up posture relative to a supine knees down posture (Sleep Breath 2004; 8: 43-7). In this study, we attempt to replicate this finding in a series of OSA patients.

**Methods:** Patients (n = 24) were recruited from an advertisement requesting patients with previously diagnosed OSA (X RDI = 35.8). Most routinely used CPAP at home. On Nt 1, patients slept without CPAP without restriction on posture. On Nt 2, patients slept supine without CPAP with a foam wedge placed underneath both knees, elevating approximately 60 degrees. Supine RDI was calculated from Nt 1 and for supine knees up on Nt 2.

**Results:** Only 19 pts slept 58 mins or more supine with the wedge, the remainder finding it too uncomfortable. For these 19 pts, X Nt 1 supine (knees down) RDI was 44.5 and X Nt 2 knees (knees up) RDI was 39.3. This comparison approached significance (Wilcoxon matched pairs signed rank test, p = .12). Case analyses indicated that 8 individuals decreased RDI on Nt 2 of at least 10 events/hr whereas 3 individuals increased RDI on Nt 2 of at least 10 events/hr. Analyses of Nt 2 data only on 10 patients showing at least 58 mins of supine sleep in the Knees up and knees down position showed no trend towards significant difference (p = .49).

**Conclusion:** Our exceptional case notwithstanding, these results do not suggest that sleep in the supine, knees up position will be a robust treatment for OSA. Trends in selected results leave open the possibility that alternative mechanisms (e.g., increased lung volumes resulting from unloading diaphragm, altered venous return affecting upper airway caliber) may contribute partially to maintaining airway patency in sleep.

**0586**  
Cyclic Variation Of Heart Rate In Pacemaker Patients During Atrial Overdrive Pacing  
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**Introduction:** Cyclic variation of heart rate (CVHR), a pattern of brady-tachycardia, is associated with sleep apnea (SA) in patients with normal sinus function. CVHR reflects increased cardiac vagal tone during apnea followed by rebound tachycardia. Atrial overdrive pacing (AOP) was proposed to reduce SA by preventing SA onset bradycardia. We studied the presence of CVHR in pacemaker (PM) patients with sick sinus syndrome (SSS) and the effect of AOP on CVHR and SA.

**Methods:** PM patients (Guidant PULSAR Max I/II or INSIGNIA) were screened for SA by sleep study. Patients with apnea/hypopnea index (AHI) ≥ 15 and baseline heart rate (BHR) ≤ 70 bpm were randomized to 3 nocturnal pacing modes: backup pacing at 50bpm (P0), AOP at BHR+10bpm (P10), and BHR+20bpm (P20). CVHR was visually analyzed from the tachogram. CVHR was defined as ≥ 5 consecutive brady-tachycardia cycles (>5bpm) during concurrent SA. CVHR amplitude was...
defined as the peak to trough difference of the brady-tachycardia cycle.

**Results:** During screening, 9 of 13 patients (69%) demonstrated CVHR. CVHR amplitude correlated with AHI (r=0.72). Seven of the 13 patients had SA(AHI≥15) and were randomized to AOP. Six (89%) of these patients demonstrated CVHR with an amplitude of 12.2±2.2 bpm during P0, 2.7±4.3 bpm during P10 and 0.0±0.0 bpm during P20. At P20, AOP completely suppressed CVHR in all patients, yet SA patterns remained. Compared to P0, CVHR was significantly reduced both during P10 (p<0.01) and P20 (p<0.001), while AHI was unchanged (p=0.84, p=0.97, respectively).

**Conclusion:** CVHR was seen in PM patients with SSS and its amplitude correlated with SA severity. CVHR amplitude was reduced when the AOP rate was above the minimum CVHR rate, and completely suppressed when the AOP rate was above the maximum CVHR rate. Suppression or elimination of CVHR, however, is not a plausible explanation for previously reported beneficial effects of AOP on SA.

This study was supported by Guidant Corp.-CRM

**0587**

Nervous Lesions In The Upper Airway Of Patients With Obstructive Sleep Apnea And Snoring


**Introduction:** We aimed at evaluating the presence of sensory nerve lesions in the oropharynx of patients with obstructive sleep apnea using quantitative sensory testing. We also studied possible motor nervous lesions by means of concentric needle EMG.

**Methods:** For sensory studies, 17 OSAS-patients were investigated, 8 with AHI >20 and 9 with AHI 10-19. Comparison was made to 9 normal, non-snoring subjects. Vibration and cold detection thresholds were examined at the tonsillar pillars, lip and thenar. EMG was performed in the palatopharyngeus muscles in OSAS-patients, habitual snorers and normal controls.

**Results:** Mean vibration thresholds at the palatal level were 30.8 for grave OSAS, 22.1 for mild OSAS and 8.6 for normals. Significant difference (p<0.0001) between both groups of OSAS-patients and normals, but not between grave and milder OSAS-cases. There were no significant differences between any of the groups for the lip or hand. Mean thresholds for palate cold detection were 4.9°C for grave OSAS, 2.5 for mild OSAS and 1.9 for normals. The difference was significant (p≤0.0001) between grave OSAS and normals, and also between grave and milder OSAS-cases (p=0.002), but not between mild OSAS and normals. EMG-findings: 10/12 OSA patients had signs of nervous lesions. Five/5 normal subjects and 12/15 snorers had normal EMG. Three of 15 snorers showed signs of a slight to moderate nervous lesion (reduced interference pattern, polyphasic motor unit potentials).

**Conclusion:** Our findings support the hypothesis of a local nervous lesion in the oropharynx in OSA patients, since both signs of motor and sensory pathology was found. No patient had signs of polynuropathy. A local peripheral nerve lesion in the oropharynx, probably due to snoring-induced vibration, could be a contributing factor in progressive OSA. These methods could be used in clinical routine to evaluate the presence of nervous lesions in OSA-patients and snorers.

**0588**

Detection Of Sleep Apnoea Syndrome By Using The Watch-Pat Device

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**Introduction:** Sleep apnoea syndrome known as common sleep disorder for many years. It is a major public health problem, which affects between 2%-4% of the adult population. The Polysomnographic (PSG) studies are considered the gold standard for the diagnosis of sleep apnoea syndrome. The full PSG is a time consuming and an extensive practice. Due to a high prevalence of the syndrome there is an increasing need to simplify the diagnosing procedure. The watch-PAT is a portable device based on the Peripheral Arterial Tonometry (PAT). The objective of the present study was to evaluate the Watch-PAT device for the diagnosis of sleep apnoea syndrome.

**Methods:** 41 patients (mean age 49 yrs-old, mean BMI=26, mean ESS=10) were diagnosed with sleep apnoea syndrome by the Watch-PAT device in the sleep laboratory at our centre. 22 Patients underwent full PSG in the same night as the Watch-PAT measurement and 19 patients during another night. The Watch-PAT device includes pulse-oximetry, PAT probe and actigraphy sensors. Automated analysis of the Watch-PAT sensors calculated a PAT-respiratory disturbance index (RDI) and sleep/wake cycle. Oxygen desaturation index (ODI) was measured with the oxymeter inside the Watch-PAT. The PSGs were scored manually using the American Academy of Sleep Medicine (AASM) criteria. The scorer was blinded to the results of the Watch-PAT device. The RDI and ODI (<4%) determined by PSG were compared with the RDI and ODI determined from the Watch-PAT device.

**Results:** The PAT-RDI/ODI levels were highly correlated to the PSG-RDI/ODI. Mean RDI and ODI determined by PSG were 25.02 and 12.52 compared with mean RDI of 24.34 mean ODI of 11.67 determined by the Watch-PAT device. The overall correlation between RDI-PAT:PSG is 0.97 and ODI-PAT:PSG is 0.93.

**Conclusion:** The Watch-PAT device is a powerful tool for simple and fast diagnosing patients with suspected sleep apnoea syndrome.

**0589**

Changes In Ultradian Heart Rate Variability Rhythm In Sleep-Disordered Breathing

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**Introduction:** Sleep-disordered breathing (SDB) can lead to impairment of autonomic function which, in turn, could lead to increased risk of cardiovascular disease. The main purpose of this study was to determine whether a “dose-response” relationship exists between severity of SDB and various markers of cardiac autonomic function, including their ultradian characteristics, during sleep.

**Methods:** RR-intervals (RRI), respiration and sleep stage sequences were extracted from twenty-four polysomnograms selected from the multi-center Sleep Heart Health Study (SHHS). All participants were nonsmoking males (age: 64.9 ± 2.8 years, BMI: 27.9 ± 2.3 kg.m-2), with no prior history of cardiovascular disease, and with respiratory disturbance index (RDI) ranging from 0.9 to 43. For each subject, 6 spectral indices of heart rate variability (HRV) and mean RRI (MnRRI) were computed from each successive 5-minute segment of data. Each sleep-stage epoch was classified into one of 4 numeric levels representing wake, REM, light sleep and deep sleep, and the spectrum of the resulting sequence was calculated. We identified the oscil-
lation (between 0 and 0.8 cycles/hour) in each HRV index that was closest to the dominant ultradian sleep-stage oscillation. Correlation coefficients were computed between RDI and each HRV parameter.

**Results:** RDI was positively correlated with the frequency of the dominant LHR (ratio of low to high frequency power of RRI) oscillation (r=0.52, p<0.01) and negatively correlated with LHR oscillation magnitude (r=-0.44, p=0.03). RDI was also correlated (r=0.60, p<0.01) with frequency of the dominant oscillation in MnRRI.

**Conclusion:** Our findings indicate that higher RDI is associated with more frequent cycling of ultradian changes in sympathetic and parasympathetic activity. On the other hand, in subjects with more severe SDB, these ultradian fluctuations become smaller in amplitude. We conclude that severity of SDB leads to graded changes in the characteristics of ultradian oscillations in cardiac autonomic activity during sleep.

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**0590**

**Nocturnal Oxygen Titration In The Sleep Clinic**

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**Introduction:** Subjects were randomized to PSG in order to titrate oxygen associated or not with positive airway pressure. Objective: To evaluate the sleep and clinical characteristics of patients that underwent polysomnography with oxygen titration during sleep.

**Methods:** Data of patients referred to PSG with oxygen titration were obtained from a database from January 2003 to October 2004, comprising 13,106 adult patients.

**Results:** The following results refer to the data of 51 patients obtained from the database. Patients age (mean SD) was 57.5 - 13.4; mean BMI, 31.4 - 10.2; EPW scoring, 10.8 - 6.8; awake baseline SaO2 91.0 - 5.8; min SaO2 74.2 - 17.0. 63% of patients smoked; other 63%, were diagnosed as having pulmonary disease; 47% were referred to PAP titration; 55% were diagnosed asOverlap condition; and 84% had any Sleep-Disordered Breathing (SDB). Characteristics according to PAP indication: youngest subjects (52.6 - 12.8 vs 61.9 - 12.6); higher BMI (36.3 - 7.6 vs 27.0 - 10.6); lower awake baseline SaO2 (88.7 - 4.2 vs 93.0 - 6.6) p≤0.01, all. Awake baseline SaO2, and minimum SaO2 (89.1 - 6.7 vs. 93.3 - 3.5; 67.6 - 18.4 vs. 82.3 - 10.8, respectively) were lower in patients with overlap condition, p≤0.01. Logistic Regression for PAP considering the independent variables, gender, age, BMI, smoking, EPW showed that only BMI was a significant predictor for PAP indication (odds ratio 1.14, CI 95%= 1.04; 1.25).

**Conclusion:** Patients referred to the Sleep Clinic for Oxygen titration are predominantly overweight, had any SDB including hypoventilation and severe OSAS. The presence of SDB and PAP indication were associated with lower awake SaO2, and min SaO2 during sleep. Higher BMI was the only predictor for PAP use and indication in this group.

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**0591**

**A Single Question Rating Sleepiness Correlates Positively With The Epworth Sleepiness Scale Score**

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**Introduction:** The Epworth Sleepiness Scale (ESS) asks likelihood of dozing in certain situations. The question “Please measure your sleepiness on a typical day: (0-10)” yields a new measure of subjective sleepiness (SS). This study examined the correlations between ESS and SS, and whether those correlations were affected by sex or diagnosis of sleep apnea.

**Methods:** This retrospective chart review identified 559 consecutive adults who had undergone polysomnography and multiple sleep latency testing (MSLT). Subjects (n=312 [37% men]) completed the ESS and SS within 2 months of testing. Means, standard deviations, and correlations between the ESS, and SS were determined using GraphPad Prism software. Pearson r correlation coefficients were calculated for each comparison. Significance was determined by calculating P values.

**Results:** ESS and SS scores correlated positively and significantly in all subjects (r = 0.50, P < 0.0001), men (r = 0.46, P < 0.0001), women (r = 0.50, P < 0.0001), sleep apneics (r = 0.46, P < 0.0001), non-sleep apneics (r = 0.50, P < 0.0001), male sleep apneics (r = 0.44, P = 0.0001), female sleep apneics (r = 0.48, P < 0.0001), male non-sleep apneics (r = 0.5432, P = 0.0002), and female non-sleep apneics (r = 0.45, P < 0.0001).

**Conclusion:** The correlation between SS and ESS in all groups studied shows that the single question used in the present study may be a valuable alternative to the Epworth Sleepiness Scale to measure subjective sleepiness. While the ESS is easy and inexpensive to administer, few non-sleep specialist physicians use it. The SS provides a simple, clinically useful alternative that correlates with the ESS regardless of sex or sleep apnea diagnosis and may help physicians screen for sleep disorders. Further investigation is needed to determine if the SS correlates with the mean sleep latency on MSLT.

**0592**

**The Effects Of Tonsillectomy And Nasal Surgery Respectively On Same OSAHS Patients**

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**Introduction:** There has been no study that tried to evaluate the efficacy of tonsillectomy and nasal surgery respectively on same obstructive sleep apnea hypopnea syndrome(OSAHS) patients. Thus, we studied 9 OSAHS patients with tonsillar hypertrophy and nasal obstruction to assess the efficacy of tonsillectomy and nasal surgery respectively on same obstructive sleep apnea.

**Methods:** All underwent nocturnal polysomnography 3 times (before the surgeries, after tonsillectomy and after the nasal surgeries). All underwent tonsillectomy at first. 3 months later, all underwent the nasal surgeries. Subjects were 7 male and 2 female patients (ages 29.6 ± 6.1 years).

**Results:** Average body mass indexes were not changed significantly between and after the surgeries (before 27.5 ± 4.1, after 27.3 ± 3.9 kg/m2). Sleep parameters (apnea index(AI, h/r), apnea hypopnea index(AHI, h/r), the lowest SpO2 (%), arousal index(Ar-I, h/r), oxygen desaturation time (ODI, min.<90%) ) were changed significantly after tonsillectomy comparing before surgeries, though not significantly after the nasal surgeries comparing after tonsillectomy. With sleep stage, %stage 1 were reduced significantly after tonsillectomy comparing before surgeries, %stage 2 were increased significantly both after tonsillectomy comparing before surgeries and after the nasal surgeries comparing after tonsillectomy. %stage REM and %stage 3÷4 were changed significantly after tonsillectomy and nasal surgeries. ESS were changed significantly after tonsillectomy comparing before surgeries and after the nasal surgeries comparing after tonsillectomy (11.3 ± 3.7– 6.0 ± 4.0–3.0 ± 3.7).

**Conclusion:** Therefore tonsillectomy can improve objective sleep param-
eter more than the nasal surgeries. The nasal surgeries may have potential power which can change subjective value of sleepiness (ESS).

none

0593

Male And Female Predictors For Obstructive Sleep Apnea (OSA) In Morbidly Obese Patients Referred For Bariatric Surgery
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Introduction: Although obesity be consider a risk factor for OSA, its prevalence in morbidly obese patients referred for bariatric surgery is not well known. Good predictors for OSA are: stop breathing related for bed partner, loud snoring, BMI, Neck circumference and visceral adiposity. However is not well documented the value of these parameters in this morbid obesity patients as well how the gender affects them. AIM: To determine the OSA prevalence as well as its predictors in both gender of morbid obesity patients.


Results: OSA prevalence was in 67% of man and 48% of women. Male versus Female Characteristics (X ±SD): Age: 38.7 ±41.2 vs 43.6 ±11.7 years; BMI: 49.1 ±8.1 vs 48.4 ±7.6 kg/m2; neck circumference: 48.4 ±4.3 vs 40.4 ±3.2 cm *; Epworth scale: 11.5 ±6.8* vs 9.6 ±5.8; AH1: 53.7 ±50 vs 15.8 ±21.1* (*) p ≤ 0.01). Correlations Male: BMI vs AH1 (r = 0.40, ns); neck circumference vs AH1 (r = 0.38; ns) neck circumference vs nadir SatO2 (r = 0.83; p ≤ 0.01); Epworth vs AH1 (r = 0.43, ns) -Female: BMI vs AH1 (r = 0.50, p≤ 0.01); neck circumference vs AH1 (r = 0.20; ns) neck circumference vs nadir SatO2 (r = 0.47; p≤ 0.01); Epworth vs AH1 (r = 0.3, ns).

Conclusion: OSA is prevalent in morbidly obese patients. Neck circumference was the best predictor for OSA in both gender and stronger in male, however BMI was a weak one and better in female.

AFIP and FAPESP/CEPID, Brazil

0594

Comparison Of Standard And Respiratory Event Monitoring Continuous Positive Pressure (CPAP) Units At One-Month Following CPAP Initiation
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Introduction: Patient compliance limits the effectiveness of continuous positive airway pressure (CPAP) for obstructive sleep apnea syndrome (OSAS). We tested a CPAP unit that monitored home respiratory events and mask leak. We expected a monitoring unit would facilitate pressure and mask adjustments of patients on CPAP. We hypothesized that these adjustments would improve both clinical outcomes and patient compliance.

Methods: After informed consent, adult sleep disorder center patients with primary complaints of excessive daytime sleepiness or sleep-related disordered breathing were asked to participate in a one-year study of CPAP compliance. Those diagnosed with OSAS via polysomnography were randomly prescribed a CPAP device that either monitored respiratory events and air leak (MT) or one that provided only compliance data (ST). Follow-up visits were scheduled for 4-6 weeks (1-month), 6 months, and 1 year.

Results: Of 427 patients completing polysomnography, 219 were placed on CPAP using either the ST or MT unit. Fifty-three percent (116) returned for their 1-month follow-up visit to see one of five clinicians (4 MDs and 1 nurse practitioner). Data downloaded during their visit indicated that the ST group used CPAP for a mean of 257 (+129) minutes and MT participants used CPAP for a mean of 281 (+123) minutes, p=ns. No participant had adjustments made based on respiratory event information from the MT unit. However, because of clinical complaints, four patients had CPAP pressures increased (1 MT and 3 ST) and 2 had the pressure decreased (1 MT and 1 ST).

Conclusion: An MT CPAP unit did not affect compliance at the one-month follow-up visit. However, changes in weight, medication, and health status are more likely to occur at the 6-month and 12-month follow-up visits that will require pressure adjustments. These subsequent follow-ups may provide a better test of any benefit from respiratory event monitoring CPAP units.

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0595

Gender Differences In Normals And Apneics In The Volume Of The Upper Airway And Surrounding Soft Tissue Structures
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Introduction: Gender is thought to play an important role in the size of upper airway and surrounding soft tissue structures. In order to examine gender differences in the upper airway, we performed a case control study of men and women (normals and apneics) with volumetric MRI.

Methods: 55 controls (AH1≤5events/hour; 27 men/28 women) and 55 apneics (AH1>15events/hour; 27 men/28 women) underwent overnight polysomnography and MRI. Awake axial T-1 images were obtained using a 1.5T magnetic resonance scanner. Volumes of the soft tissues in the upper airway were objectively quantified using validated computerized software (Volumetric Image Display Analysis). We quantified tissues from the level of the hard palate to the base of the epiglottis.

Results: Normal men (age 36.6±8.0years, BMI 25.7±3.9kg/m2, AH1 2.4±1.9events/hour), normal women (age 45.3±10.4years, BMI 26.1±5.2kg/m2, AH1 1.8±1.5events/hour), apneic men (age 41.1±10.0years, BMI 31.2±5.6kg/m2, AH1 42.6±27.9events/hour) and apneic women (age 47.9±8.3years, BMI 39.6±8.8kg/m2, AH1 3.4±25.3events/hour) were studied. In normals, after adjusting for age, ethnicity, head size and upper airway adipose tissue, volumes of the total airway (p=0.001), tongue (p<0.001), lateral pharyngeal wall (p<0.001), soft palate (p<0.001) and total soft tissue (p<0.001) were significantly greater in men than women. Parapharyngeal fat pad volume was not significantly different (p=0.21) between men and women. In apneics, adjusting for the same covariates, volumes of the tongue (p<0.001), lateral pharyngeal wall (p=0.009), soft palate (p=0.001) and total soft tissue (p<0.001) were significantly greater in men than women. Total airway volume (p=0.084) and parapharyngeal fat pad volume (p=0.12) were not significantly different between apnic men and women.

Conclusion: Airway volume and the size of the upper airway soft tissue...
structures were larger in men than women. The increased size of the upper airway soft tissue structures in men compared to women may explain the increased prevalence of sleep apnea in men compared to women.

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0596
Fatigue Improves Independently Of Sleepiness In Treatment Of Sleep Apnea
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Introduction: Obstructive sleep apnea (OSA) can be associated with fatigue, with or without daytime sleepiness, but the extent to which fatigue improves with OSA treatment is not clear.

Methods: Consecutive referred adults with OSA were included if they 1) had polysomnography (10/2002-08/2004) at a single accredited sleep laboratory (Saint Francis); 2) subsequently used positive airway pressure Â–U 4 weeks, ÂU 50% of nights, and ÂU 5 hours/night; and 3) completed pre-treatment Epworth Sleepiness Scales and Fatigue Severity Scales, repeated 5 Â± 4 (s.d.) months later. Indices (ESSi, FSSi) were a percent of total possible points. Mild OSA was defined as apnea/hypopnea index < 15 events/hour of sleep.

Results: Subjects (n = 164) had a mean age of 51 Â± 12 (s.d.) years and 68% were male. Mean pre-treatment FSSi was higher than ESSi (60 vs. 44, paired t test p < 0.0001). Each improved after treatment (FSSi to 51, p < 0.0001; ESSi to 31, p < 0.0001), and these changes were correlated (rho = 0.39, p < 0.0001). However, 89 subjects who initially were not sleepy (ESS < 10) still showed a decline in FSSi from 54 to 30 (p < 0.04). The FSSi and ESSi improved about as much among the 24 subjects with mild OSA as among remaining subjects: the FSSi by 7 (p = 0.17) and the ESSi by 18 (p = 0.0005) in the mild group, vs. 10 (p < 0.0001) and 12 (p < 0.0001) in remaining subjects (p > 0.10 for differences in improvement between mild and other subjects).

Conclusion: Treatment of OSA is associated with substantial reduction in subjective fatigue, in addition to sleepiness, even in some patients who complain of little sleepiness and others who have only mild OSA.

0597
An Audit Of The Diagnosis And Treatment Of Obstructive Sleep Apnoea At Two Different National Health Service Clinics In Central London Uk
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Introduction: The aim was to show differences in management of Obstructive Sleep Apnoea (OSA) in two sleep centres and compare these with the Scottish Intercolligate Guidelines (SIGN) for the diagnosis and management of OSASH.

Methods: A surgically run (RNTNE) and a physician run (STH) sleep centre were selected for this audit. A retrospective analysis of clinical information from patients’ hospital notes was made. The notes analysed were those of all patients referred with suspected OSA who had first attended clinics at either hospital between February 1st 2003 and April 30th 2003.

Results: 89 notes were analysed at STH and 34 at the RNTNE. The population demographics of sex, age and BMI were similar for both groups. AHI was higher in the STH group. Most RNTNE patients were referred from General Practitioners (GP) whereas at STH most were referred from ENT surgeons. Waiting time was doubled at both sites if the GP referred to a non sleep specialist first who then referred on to the sleep clinic. More home cardiorespiratory studies and full polysomnography were done at the RNTNE and more home simple oximetry at STH. 24% of patients attending the RNTNE had surgery as treatment compared to 4% at STH. 47% of RNTNE patients underwent Sleep Nasendoscopy (SNE) compared to less than 2% of STH patients. 21% of patients were prescribed CPAP at the RNTNE as compared to 42% at STH. This showed that anaesthetic and surgical intervention was higher in patients referred to the surgically run service and CPAP was more common in the medically run service.

Conclusion: Neither centre followed SIGN guidelines. Despite the small numbers of patients to infer from it is likely that an individual’s treatment was affected by where they were referred to. Further work should be done towards creating UK national guidelines for the diagnosis and management of OSA.

0598
Autonomic Dysfunction In Obstructive Sleep Apnea Is Associated With Impaired Glucose Regulation
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Introduction: Obstructive sleep apnea (OSA) and impaired glucose regulation (IGR) manifested by diabetes, impaired glucose tolerance, and impaired fasting glucose are associated with abnormalities of autonomic function and cardiovascular disease. However, it is unclear if autonomic dysfunction in sleep apnea is due to OSA by itself, or to co-existent IGR. Previous studies of autonomic function in OSA only utilized either a fasting glucose or patient report to screen for diabetic conditions.

Methods: Twenty subjects aged 23 to 76, including 6 women, with symptoms of sleep apnea received cardiac and peripheral autonomic testing consisting of a) heart rate response to deep breathing; b) valsalva maneuver and beat to beat blood pressure variation (BPV); c) tilt table testing with BPV; d) quantitative sudomotor axon reflex test (QSART). A ten point composite autonomic score (CASS) was calculated for each subject. Subjects underwent polysomnography (PSG) followed by an oral glucose tolerance test (oGTT).

Results: Fourteen patients (70 %) had an apnea hypopnea index (AHI) greater than 5 events/hr (range 6.0-86.8) consistent with OSA. Eleven of those fourteen OSA subjects (79 %) were newly diagnosed with IGR, including four with diabetes. Of six subjects without OSA, two had an abnormal OGTT. CASS scores ranged from 0 to 5. Subjects with OSA had slightly higher scores (1.79 vs. 0.83). Subjects with IGR had higher scores than normoglycemic subjects (2.07 vs. 0.43). Logistic regression demonstrated that glucose significantly predicted an abnormal CASS alone (p value=0.02), but not after adjusting for age (p value=0.23). AHI by itself did not predict autonomic dysfunction (p value=0.36).

Conclusion: Our data confirm that IGR is common in OSA, and oGTT evaluation should be included in studies of subjects with autonomic dysfunction. Further studies are needed to be able to separate the individual contributions of OSA and IGR on autonomic dysfunction.

This study was supported by the University of Michigan General Clinical Research Center and the Ann Arbor Veterans Administration Medical Center.
Methods: We therefore assessed the portion of subjects seem to respond quite well. We believe this variable in magnitude than the perturbation (loop gain to perturbation (e.g., apnea) ratio. When the response is equal or greater in AHI (from 64 ± 59 off oxygen to 39 ± 38 on oxygen) in the high loop gain group versus only a 10% reduction (from 46 ± 41 off oxygen to 40 ± 34 on oxygen) in the low loop gain group. Conclusion: These data suggest that ventilatory instability plays a greater physiologic role in some OSA patients than others, which may help explain the discrepant results of previous studies. In the future, tailoring oxygen therapy to patients with increased ventilatory instability may be beneficial, although more subjects are needed to definitively test this hypothesis.

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0601
Experimental Sleep Apnea Decreases Myocardial Infarction Size
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Introduction: Obstructive sleep apnea (OSA) is characterized by intermittent hypoxemia and has been linked to the development and progression of cardiovascular disease. OSA worsens ischemic heart disease and could subsequently lead to poorer outcomes after myocardial infarction (MI). However, the survival rate in patients with OSA following myocardial infarction is similar to the survival rate in patients without OSA, suggesting OSA may provide a cardioprotective effect. We hypothesized that intermittent hypoxia that mimics sleep apnea would decrease MI size similar to myocardial preconditioning.

Methods: We randomized adult male Sprague-Dawley rats to either two weeks of intermittent hypoxia (n=10) that mimics sleep apnea (alternating 21% and 10% oxygen every two minutes for twelve hours per day) or control treatment (no hypoxia) (n=8). Two additional groups were assigned to hypoxia (n=8) or control (n=8) and received ischemic preconditioning (five minutes of left coronary artery (LCA) occlusion followed by five minutes reperfusion for three cycles) prior to induced MI. In all groups, MIs were induced by occlusion of the LCA for 30 minutes followed by 60 minutes of reperfusion. Hearts were stained and excised for infarct size analysis. Infarct size was calculated as a ratio of the infarcted area to area at risk determined by computer morphometry of Evans blue/tetrazolium stained sections.

Results: Control rats had a mean infarct size of 39±4% of the area at risk (AAR). Rats exposed to intermittent hypoxia had a reduced mean infarct size of 29±3% of AAR (p=0.04 vs control). Infarct size in hypoxia rats was similar to rats that received ischemic preconditioning (26±3% for both preconditioning groups) (p=NS).

Conclusion: Exposure to intermittent hypoxia prior to MI reduces infarct size similar to myocardial preconditioning through an unexplored mechanism. Therefore, myocardial protection from intermittent hypoxia may offset some of the detrimental myocardial effects of OSA.

0602
Regular Exercise Is Associated With Significant Reduction Of Sleepiness In Men With Sleep Apnea
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Introduction: Metabolic abnormalities such as obesity and diabetes/insulin resistance are independent predictors of excessive day-
time sleepiness in patients with sleep apnea and in the general population. It is known that exercise improves insulin resistance and visceral adiposity independently of weight. In this study we evaluated the role of exercise on daytime sleepiness in patients with sleep apnea.

**Methods:** Participants included 707 consecutive patients (471 men and 236 women) who were referred to sleep disorders clinic for symptoms consistent with sleep apnea and demonstrated an apnea/hypopnea index of ≥ 5. Daytime sleepiness was assessed with the Epworth Sleepiness Scale (ESS) and activity was evaluated with a quantifiable Physical Activity Questionnaire (Wolf et al., 1994). In the logistic regression analysis, the independent variable was sleepiness and dependent variables were age, BMI, logAHI, physical activity, depression, hypertension, cardiovascular problems, and diabetes.

**Results:** Men compared to women had higher AHI (39.5±1.4 vs. 28.6±2.1), lower BMI (35.4±0.3 vs. 39.8±0.6), and higher physical activity (22.0±1.2 vs. 16.1±1.8) (all P<0.05). Men and women were of similar age (51.1±0.6 vs. 51.6±0.8) and Epworth score (11.1±0.2 vs. 11.4±0.4). In men the strongest predictor of sleepiness was exercise (effect size -0.41, P ≤ 0.04) followed by depression (effect size +0.47, P ≤ 0.08). In women, the strongest predictor of sleepiness was age (effect size -0.04, P ≤ 0.01) followed by logAHI (effect size +0.34, P ≤ 0.05).

**Conclusion:** In obese apneic men regular exercise was associated with a significant reduction of sleepiness after controlling for weight, apnea, age, and other covariates. The lack of association of exercise in women with apnea may be related to reduced exercise in women compared to men. These results suggest that insulin resistance/visceral adiposity are strong determinants of sleep apnea/sleepiness and that regular exercise should be routinely recommended in men with symptomatic sleep apnea.

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**0603**

**Does REM Related Sleep Disordered Breathing Get Worse With Age? The Relationship Between REM Apnea-Hypopnea Index And Age Goldstein D,1 Tirunahari V, Walters A, Siddiqui F, Lahey M1 (1) Sleep Disorders Center of NJ, Scotch Plains, NJ, USA, (2) NJ Neuroscience Institute, JFK Medical Center, Edison, NJ, USA**

**Introduction:** It has been well-established that sleep disordered breathing can increase with age and also during REM sleep in patients with obstructive sleep apnea, probably due to decreases in muscle tone during REM sleep. It is hypothesized that as one gets older, the ability to maintain the same amount of muscle tone during REM sleep diminishes, thus causing the AHI to rise higher in REM sleep for older subjects. The purpose of this study was to determine if older patients have greater amounts of sleep disordered breathing in REM sleep as compared with younger patients.

**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. All patients scheduled for polysomnographic evaluation for the purposes of ruling out OSA had patient demographics and patient questionnaires completed. 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 age brackets of Less than 40 years old, 40 to 60 years old, Greater than 60 years old. The average AHI, REM AHI, NREM AHI, and ΔAHI (REM AHI - NREM AHI) were calculated for each group.

**Results:** Of 226 patients with documented OSA, 55 were less than 40 years old, 132 were between 40 and 60 years old and 39 were older than 60 years. There was a trend for patients to have a higher REM AHI than NREM AHI except for the oldest age bracket. In the oldest age bracket, there is no statistical significance between NREM and REM AHI.

**Conclusion:** This data supports well established evidence that AHI worsens with age and that REM AHI tends to be higher than NREM AHI. However, the hypothesis that as age increases so does ΔAHI appears to be incorrect. Further investigation into other factors besides age appears to be needed, for example whether or not there is a higher morbidity or mortality in patients with more severe REM related OSA so that only the milder older OSA patients come to medical attention.

For < 40 Yrs - AHI=42.7 REMAHI=49.0 NREM AHI=41.5 ΔAHI=7.5
For 40-60 Yrs - AHI=42.9 REMAHI=51.4 NREM AHI=41.6 ΔAHI=9.8 For > 60 Yrs - AHI=49.8 REMAHI=49.8 NREM AHI=49.9 ΔAHI=0.1

**0604**

**Treatment Of Moderate Obstructive Sleep Apnea Syndrome With Acupuncture: A Randomized, Single-Blind, Placebo-Controlled Trial Freire AO,1 Sugai GC,2 Chrispin FS,1 Togeiro SM,1 Yamamura Y,1 Mello LE,1 Tajik S1 (1) Psychobiology, Univ Fed Sao Paulo, Sao Paulo, SP, Brazil, (2) Physiositol, Univ Fed Sao Paulo, Sao Paulo, SP, Brazil, (3) Orthopedics and Traumatology, Univ Fed Sao Paulo, Sao Paulo, SP, Brazil**

**Introduction:** Obstructive sleep apnea syndrome (OSA) is a serious medical condition characterized by repetitive cessation of breathing during sleep, which may occur despite a normal central respiratory drive. These events provoke tremendous fluctuation in the autonomic nervous system activity, heart rate, and pulmonary and systemic vascular resistance. There is considerable evidence for the involvement of sympathetic nervous mechanisms in acupuncture effects as well as the endogenous opioids systems.

**Methods:** A randomized, placebo-controlled, single blind study was carried out on the Department of Psychobiology, Regional University of Sao Paulo, Brazil, where 36 patients with an apnea-hypopnea index of 15 to 30 per hour were randomly assigned to 3 groups: acupuncture group; sham group (submitted to treatment with needle insertion in non acupoints); and the control group. Twenty-six patients completed the study. Acupuncture was applied in true acupoints accompanied by needle manipulations in the acupuncture group; and for the sham group the needles were inserted outside of acupoints and no manipulations were made. Inserted needles were left in situ for 30 minutes in all patients.

**Results:** Treatment efficacy was examined by polysomnography, questionnaires of functional quality of life (SF 36) and excessive daytime sleepiness (Epworth). The AHI (before 19.9; after 10.1. P = 0.005) and the number of respiratory events (before 116.1; after 66.5. P = 0.005) decreased significantly in the acupuncture group, but not in the placebo group (sham). In the other hand, the control group had a significant deterioration in some of the polysomnographic parameters as well as in life quality. In addition the acupuncture group significantly improved in several dimensions of the SF 36 and Epworth questionnaires.

**Conclusion:** Acupuncture is an effective treatment for OSA and the treatment of this condition should be initiated as soon a diagnosis is made.

FAPESP/CEPID; AOF is a FAPESP (01/08063) and GCMS a CNPq fellow.
Correlation Of Subjective Sleepiness With Mean Sleep Latency In Men, Women, Apneics, And Non-Apneics

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Introduction: Subjective sleepiness may differ from objective sleepiness. The Epworth Sleepiness Scale (ESS) and the question “Please measure your sleepiness on a typical day: (0-10)”, which yields the Subjective Sleepiness score (SS), assess subjective sleepiness. The Multiple Sleep Latency Test (MSLT) yields the standard objective measure of sleepiness (mean sleep latency, MSL). This study examined correlations between MSL and ESS or SS, and whether sex or diagnosis of sleep apnea affected these correlations.

Methods: This retrospective chart review identified 559 consecutive adults who had undergone polysomnography and MSLT. Subjects (385) completed the ESS and SS within 2 months of testing. MSL was the mean latency to sleep onset of all (4 or 5) naps. Means, standard deviations, and correlations were determined by statistical analysis using GraphPad Prism® software. Pearson r correlation coefficients were calculated for each comparison. Significance was determined by calculating P values.

Results: ESS and MSL correlated negatively and significantly in all subjects (r = 0.2911, P < 0.0001), men (r = 0.3291, P < 0.0001), women (r = 0.3132, P < 0.0001), non-sleep apneics (r = 0.3256, P < 0.0001), and female non-sleep apneics (r = -0.2992, P < 0.0001). ESS and SS did not correlate in sleep apneics (r = 0.0934, P = 0.2257) or male non-sleep apneics (r = 0.2253, P = 0.1503). SS and MSL correlated negatively and significantly in men (r = -0.1186, P=0.0353) and non-sleep apneics (r = 0.1630, P = 0.0485). SS did not correlate with MSL in all subjects (r = -0.08327, P = 0.1447), men (r = -0.02731, P = 0.7691), or sleep apneics (r = 0.03973, P = 0.6070).

Conclusion: These results suggest that subjective and objective sleepiness are different, and while ESS and SS may reflect MSL in some groups, they do not substitute for MSLT.

Sleep Apnea In Obese Adults With Type 2 Diabetes: Baseline Results From The Sleep Ahead Study

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Introduction: Sleep AHEAD (Action for Health in Diabetes) is a 4-site ancillary study of the Look AHEAD Study, a multicenter, randomized controlled trial of a weight loss intervention in obese adults with type 2 diabetes. The primary aim of Sleep AHEAD is to determine the effect of weight loss on sleep disordered breathing in a subset of Look AHEAD participants. We herein report cross-sectional data from baseline evaluations performed on Sleep AHEAD participants recruited between March 2002 and June 2004.

Methods: Of the 1143 Look AHEAD participants contacted, 301 with no previous diagnosis of sleep apnea consented to participate in Sleep AHEAD and performed a home, unattended polysomnogram (PSG) using a portable monitor (PS2, Compumedics). All PSGs were scored manually with the aid of computer software at a centralized reading laboratory by a certified technologist. The PSG failure rate was 8% and the interclass correlation coefficient for apnea-hypopnea index (AHI) on intrascorer reliability testing was 0.89.

Results: The mean age of the participants was 62.2 ± 6.7 (SD) yr, mean BMI 36.5 ± 6.1 kg/m2, mean neck circumference 41.2 ± 4.1 cm, and mean Epworth Sleepiness Scale score 7.9 ± 4.6. 180 individuals (59.8%) were women and 72 (24%) were non-Caucasian. AHI was > 5 events/hr in 97% of participants and all of these subjects had obstructive sleep apnea-hypopnea (OSAH). Only 8 (~3%) individuals had an AHI < 5. The mean AHI was 30.1 ± 19.6 events/hr. 22% of participants had mild OSAH (5 ≤ AHI < 15), 34% moderate OSAH (15 ≤ AHI < 30), and 42% severe OSAH (AHI ≥ 30).

Conclusion: The results reveal an exceedingly high prevalence of undiagnosed OSAH in obese patients with type 2 diabetes with over 75% of individuals having moderate or severe OSAH.

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Are The Same Cut-Off Values For Large Neck Applicable For Black Patients As A Risk Factor For Obstructive Sleep Apnea?

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Introduction: A large neck circumference is one of the best predictor for obstructive sleep apnea. However, all previous studies showing the cut-off value for a large neck circumference examined Caucasian population. On the other hand, black people are known to have different morphology of the head and face (i.e. brachycephaly). Thus, we conducted this study to determine whether the same cut-off value is applicable for black patients.

Methods: Self-described black patients who had supervised nocturnal polysomnography at Kings County Hospital were enrolled in the study. The neck circumference was measured in sitting position at the cricoid cartilage level perpendicular to the long axis of the neck. Their baseline characteristics and the results of the polysomnography were recorded. ROC curves were used to determine the best combinations of sensitivity and specificity to detect obstructive sleep apnea with apnea-hypopnea index (AHI) >15. C-statistics were used to calculate the area under the curve.

Results: 134 patients were included in the study (63 male, 71 female). Their baseline characteristics were the following (mean ±SD): mean age 47.4 ± 13.4 year-old, weight; 258.7 ±72.02 lbs, height; 66.4 ±5.96 inches, BMI; 41.6 ±12.4, neck circumference; 17.3 ±1.9 inches. Their mean apnea-hypopnea index was 32.2 ±33.4 in the polysomnography. There is a statistically significant correlation between the neck circumference and AHI [Pearson correlation +0.37, p<0.001]. The neck circumference cut-off values of 17 inch for male (sensitivity 66%, specificity 47%, area under the curve 0.616) and 16 inch for female (sensitivity 64%, specificity 71%, area under the curve 0.717) yielded best combinations of sensitivity and specificity.

Conclusion: The same cut-off values of 17 inch for males and 16 inch for females can be used for black populations to determine large neck circumference as a risk factor for obstructive sleep apnea.

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Conclusion: The same cut-off values of 17 inch for male and 16 inch for female can be used for black population to determine large neck circumference as a risk factor for obstructive sleep apnea.

0608

Subjective Complaints In Relation To Objective Sleepiness In Sleep Apnea And Narcolepsy

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Introduction: Sleep disorders can cause complaints of sleepiness or fatigue, but the comparative frequency of each in specific disorders of hypersomnia has received little study.

Methods: This retrospective chart review identified adults with narcolepsy (n=29) or obstructive sleep apnea (n=359) who had been assessed for objective sleepiness (mean sleep latency, MSL, on a Multiple Sleep Latency Test), subjective sleepiness (Epworth Sleepiness Scale, ESS), and subjective fatigue (Fatigue Severity Scale, FSS). In addition, self-rated sleepiness (SS) and fatigue (SF) were obtained by asking patients to “Please measure your [fatigue or sleepiness] on a typical day: (0-10).”

Results: The MSL and ESS showed a significant association in narcoleptics (r = -0.51, P = 0.005) but not apneics (r = 0.42, P = 0.17). The MSL and FSS did not show a significant correlation in either group (narcoleptics P=0.88, apneics P =0.33). Among apneics, women in comparison to men had higher FSS scores (38.33 ± 0.86 vs. 35.35 ± 1.1, P = 0.02); ESS did not differ (P=0.59). Similar results were obtained with SF (6.1 ±2.177 vs. 5.3 ± 2.232, P= 0.0001) and SS (P=0.51).

Conclusion: Subjective sleepiness reflects objective sleepiness in narcolepsy to a greater extent than sleep apnea. The Multiple Sleep Latency Test may not perform optimally in a condition (sleep apnea) that can impair sleep. The complaint of fatigue shows little association with objective sleepiness in either narcolepsy or sleep apnea, and may depend to a extent greater than subjective sleepiness on gender or other factors.

0609 Obstructive Sleep Apnea In Morbid Obesity: Lessons Learned Regarding Gender Differences

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Introduction: Twenty three million American have a BMI ≥ 35 kg/m2 and 8 million have a BMI ≥ 40 kg/m2. The prevalence of obstructive sleep apnea (OSA) in bariatric surgery patients, most of whom are women, is estimated at 75%. Women are 8-13 times less likely to be referred for polysomnography (PSG), despite similar symptoms as their male counterparts.

Methods: This prospective study included 177 patients (42 men) evaluated for bariatric surgery (BMI= 51.2 ± 11 kg/m2). Patients completed the Berlin Questionnaire (BQ), a standardized instrument to identify patients at risk for OSA, the Epworth Sleepiness Scale (ESS), and a 13-item self-report inventory of OSA symptoms rated 0 (never) to 4 (nightly). Laboratory PSG was performed in 164 patients.

Results: The mean age for the total sample was 43 ± 11 years. Men had a higher BMI (54.3 vs. 51.0; p=0.03), a higher ESS score (9.8 vs. 6.8; p=0.001), and reported more frequent snoring (3.3 vs. 2.5; P=0.001). Sixty percent of women and 98% of men had an AHI ≥ 5. Among the patients with OSA, men had a higher ESS score (10.1 vs. 7.7; p=0.02). In the 75% of men and 21% of women with severe OSA (AHI ≥ 30), there were no gender differences in age, BMI, ESS, snoring frequency or other self-reported symptoms of OSA. In men, the sensitivity of the BQ was 0.87 and the positive predictive value (PPV) was 0.97. The PPV of the BQ for women was 0.71 for an AHI ≥ 5, 0.47 for an AHI ≥ 30, and the likelihood ratio for a positive BQ across all AHI levels was 1.5.

Conclusion: Obstructive sleep apnea afflicts almost all morbidly obese men and nearly two thirds of women. The BQ is not an adequate screening tool in the primary care setting for morbidly obese women. Polysomnography should be performed in all morbidly obese men and should be considered more in morbidly obese women.

0610 Use Of The Terms Fatigue Vs. Sleepiness Does Not Reliably Predict Diagnosis, Apnea Severity, Or Primary Symptoms

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Introduction: Fatigue and sleepiness are considered to be different symptoms by many sleep specialists, but the diagnostic implications of these terms as used by referring physicians and their patients have not been well studied.

Methods: This retrospective chart review investigated adults referred by physicians to the OSF Saint Francis Sleep Disorders Center. Patients referred for “Fatigue” or “Sleepiness,” but not both, were compared on the basis of two well-validated scores: the Fatigue Severity Scale (FSS) and the Epworth Sleepiness Scale (ESS). In addition, patients had been asked two separate questions, “Please measure your [fatigue or sleepiness] on a typical day: (0-10)” to generate subjective fatigue and subjective sleepiness ratings. The primary symptom was considered to be that which was rated as more severe.

Results: Referral groups (“Fatigue” n=263, 73%, “Sleepiness” n=99) did not differ significantly in age (50.51, 50.16 respectively; unpaired two-tailed t-test P =0.98), gender (M:F=0.98, chi-square test P=0.65), mean RDI (29.86, 27.10, P=0.46), FSS (58.14, 55.95, P=0.93), or subjective fatigue ratings (5.62, 5.67, P=0.72). Nor did they differ in final diagnosis of “sleep apnea” or “sleep disorder other than sleep apnea” (P=0.10). ESS and subjective sleepiness ratings were only mildly higher among patients referred for sleepiness than among those referred for fatigue (ESS: 48.96, 40.22, P=0.002; SS: 5.69, 5.03, P=0.006). In 35% of subjects, reason for referral differed from primary symptom (P=0.01).

Conclusion: Referral for fatigue or sleepiness does not reliably predict diagnosis (apnea vs. other sleep disorder) or apnea severity, and only correlates with primary symptom to a limited degree. Referring physicians or their patients may not distinguish between these terms in a manner that will be meaningful at the time of evaluation at a sleep disorders center.

0611 Chemical Control Stability In The Elderly

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Introduction: Elderly individuals are more likely to exhibit periodic fluctuations in ventilation during sleep than young individuals. They are also more likely to have sleep apnea. We hypothesized that an age-related increase in chemical control instability might explain the higher prevalence of sleep apnea in this group.

Methods: To test this hypothesis, we measured loop gain during sleep using the proportional assist ventilation technique in 7 healthy elderly subjects (age 69 ± 6). Loop gain is an engineering term that describes the stability of feedback-controlled systems, such as the chemical feedback regulation of breathing. Mathematically, it is defined as the ventilatory response (e.g., hyperpnea) to ventilatory perturbation (e.g., apnea) ratio. When the response is equal to or greater than the perturbation (loop gain ≥ 1), unstable periodic breathing can develop. A loop gain close to zero, on the other hand, indicates a very stable chemical control system.

Results: Loop gain in this elderly cohort was compared to historical controls from our lab (n=8) (age 30 ± 5). Loop gain values in the elderly subjects were 0.10, <0.28, <0.17, 0.26, <0.29, 0.23, and <0.26. The < symbol indicates loop gain is less than the stated value. Loop gain in the con-
0612

Brain Spect Changes In Patients With Severe Obstructive Sleep Apnea/Hypopnea Syndrome (OSAHS) Before And After Continuous Positive Airway Pressure Treatment: Preliminary Results

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Introduction: Despite the well known effect of sleep disordered-breathing on cerebral hemodynamics, relative few studies have investigated changes in regional cerebral blood flow (rCBF) in awake OSAHS patients. Previous available data with SPECT did not agree about the presence of rCBF deficits. These discrepancies could be related to different methodology or population heterogeneity. We decided to study with SPECT more severe OSAHS patients, in order to find disturbances of rCBF, and the potential changes before and after CPAP treatment.

Methods: 13 OSAHS patients (10 males) were selected, diagnosed by PSG and with the following criteria: AH1>70, age>40, sat O2 <90%=>10% of TST, Epworth sleepiness scale > 14 and complaints of cognitive impairment. Patients underwent 2 SPECT studies: pre and post three months of CPAP treatment. A semi-quantification of rCBF was performed obtaining an uptake index from the average counts per pixel of regions of interest (ROIs) drawn in each hemisphere, and a reference area (cerebellum), by the formula: (ROI-reference)/reference, in order to observe regional differences pre and post CPAP.

Results: Mean age was 51.9±5.7, ESS score was 16.1±2.6. PSG findings were: AH1=86.3±11.5, % of sat O2 <90%<=33.3±11.5, BMI=34.6±3.5. Visual assessment of SPECT pre-treatment showed: 69.2% of patients had decreased frontal perfusion, 54% temporal, 38% parietal and 16% occipital. Data after CPAP treatment were compared for 8 patients, 4 were refused due to low CPAP compliance (less than 4.5 hours per day) and 1 for technical problems. We found significant changes in rCBF (Wilcoxon, p<0.05), with an increased perfusion in left temporal (-0.16±0.05 vs. -0.09±0.07), left parietal (-0.17±0.07 vs. -0.10±0.04) and right parietal (-0.15±0.07 vs. -0.09±0.06) lobes.

Conclusion: Regional deficits of cerebral perfusion in brain SPECT were found in OSAHS patients with a predominance of frontal region. After three months of CPAP treatment significant changes were observed only in left temporal and parietal regions.

0613

Rating Subjective Fatigue Greater Than Sleepiness Predicts Sleep Apnea Over Narcolepsy; Greater Sleepiness Is Not Predictive

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Introduction: Obstructive sleep apnea (OSA) and narcolepsy each can be associated with fatigue, with or without daytime sleepiness. This study sought to determine what proportion of patients with more fatigue than sleepiness have OSA rather than narcolepsy, and whether high single-item self-rated fatigue and sleepiness reflect commonly-used measures of subjective fatigue and sleepiness.

Methods: This retrospective chart review identified 462 adults with narcolepsy or sleep apnea (121 had narcolepsy) and compared those with high self-rated sleepiness (SS; n = 226 (48.92%)) to those with high self-rated fatigue (SF; n = 236 (51.08%)) based on final diagnosis, Epworth Sleepiness Scale index (ESSi), Fatigue Severity Scale index (FSSi), and ESS index/FSS index ratio (EFir). Index = (actual score/highest possible score)x100. SS and SF were responses to “Please measure your sleepiness [fatigue] on a typical day (0-10)”. Subjects with SS/SF >1 were called “sleepy” and with SS/SF <1 were called “fatigued.” ESSi, FSSi, and EFir were compared between subjects with EDS and fatigue.

Results: The proportion of “fatigued” subjects with OSA rather than narcolepsy (0.97) was significantly higher than the proportion of “sleepy” subjects with OSA (0.50; P < 0.0001), ESSi was higher in “sleepy” subjects (49.83 ± 23.37) than in “fatigued” subjects (37.06 ± 19.96; P < 0.0001), but FSSi did not differ. EFir was higher in “sleepy” subjects (0.94 ± 0.76) than in “fatigued” subjects (0.67 ± 0.45; P = 0.0027).

Conclusion: Patients with more single-item rated subjective fatigue than sleepiness are much more likely to have OSA than narcolepsy, whereas those who rate sleepiness higher have an increased risk of narcolepsy in comparison to other referred patients. Patients appear to use the word “sleepiness,” but not “fatigue,” in a manner consistent with validated scales for each construct.

0614

Nasal CPAP Therapy And Aerobic Exercise Training: Effects On The Heart Rate Response To Graded Exercise In Obstructive Sleep Apnea Patients

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Introduction: Obstructive sleep apnea (OSA) is associated with repetitive surges in blood pressure during sleep and increased sympathetic activity during wakefulness. Sustained increase in sympathetic activity has been suggested to desensitize stimulatory responses to β-adrenergic receptors. One consequence may be an inability to elevate heart rate (HR) sufficient to meet the metabolic demands imposed by graded exercise. This abstract presents findings from an ongoing clinical study evaluating cardiovascular responses to graded exercise before and after treatment in OSA patients compared to similar controls, without OSA.

Methods: 16 normotensive adults [BMI = 34.8 ± 7.5 kg/m²; age = 46.2 ± 11.4 yr; Apnea Hypopnea Index (AHI) = 29.1 ± 13.7 events/hr] and 10 controls [BMI = 28.8 ± 9.8 kg/m²; age = 41.4 ± 9.8 yr] completed maximal cycle ergometer exercise testing at baseline, 6-wk, and 12-wk. All OSA patients were fitted with an auto-titrating nCPAP device, and 9 patients were randomized to a moderate-intensity (50-60% of VO2pk) aerobic exercise training program 3 days/wk.

Results: Submaximal HR responses at baseline and 12-wk were significantly lower in the OSA group compared to controls (P = 0.007). Peak HR were significantly lower (pre-treatment) in the OSA group (P =
0.004), but were not different from control group peak HR at 12-wk (P = 0.08). These findings show a blunted peak HR response to graded exercise in OSA patients that was partially reversed after nCPAP treatment. This may be attributed to improved sympathovagal balance and β-adrenergic receptor upregulation resulting from reductions in nocturnal apneic/hypoxemic events and surges in sympathetic activity.

Conclusion: Exercise testing may provide unique and clinically relevant information to aid in identifying candidates for diagnostic polysomnography testing. Future studies should investigate the potential for exercise testing to assess OSA severity, and effects of primary and secondary clinical treatments, including aerobic exercise training.

ResMed Corporation, Poway, CA

0615
An Investigation Of Bispectral Index For Detection Of Sleep-Disordered Breathing
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Introduction: Bispectral Index (BIS) is a device that has been developed by Aspect Medical Systems (Natick, MA) to measure the level of induced hypnosis during surgery by measuring EEG. In this study, BIS was investigated as a means to detect sleep disturbances resulting from sleep disordered breathing (SDB).

Methods: Eleven SDB and 14 normal volunteer subjects underwent standard nocturnal polysomnography, while continuous low pressure (< 5 cm H2O) airflow was applied to their airways. BIS signal was recorded throughout the night. Statistical comparison of the mean and standard deviation of the BIS for both subject groups was conducted. Similar calculations were performed using the BIS values for individual hours of sleep. Additionally, the energy of the BIS signal (in 0-0.1 Hz range) for the entire night was evaluated as another discriminator between the normal and SDB subjects.

Results: The mean and standard deviation of the BIS value for the entire night were significantly different (p=0.00005 and p=0.0002, respectively). The comparison of the hourly mean BIS values for normal and SDB subjects were also significantly different for all (0.00009<p<0.0022) except the fifth hour (p=0.103), with the third hour of sleep being the most significantly different. Hence, the 15-minute and 30-minute subintervals for the third hour were examined. The mean BIS value during the second hour of sleep had 86% sensitivity and 89% specificity in distinguishing subjects; same results were obtained for the subinterval of 45-60 minutes of the third hour. The tests of the energy of BIS signal (0-0.1 Hz) for the entire night showed a sensitivity of 86% and specificity of 78% in distinguishing the subjects. Correlation coefficients of the mean BIS values and respiratory distress index (RDI) were not significant.

Conclusion: Measures derived from BIS were able to differentiate SDB from normal subjects in the sample population.

0616
Studying The Effects Of Depression In Patients With Obstructive Sleep Apnea
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Introduction: Obstructive sleep apnea (OSA) and mood disorders often have overlapping symptomatology. OSA may be a risk factor for depression. Fatigue, excessive daytime sleepiness, insomnia, poor memory and concentration are the neuro-vegetative features common in these disorders. Our objective was to compare the sleep architecture of OSA patients with and without depression.

Methods: A retrospective chart review was completed of all (N=107) OSA patients evaluated in Sleep Clinic during 1998-2004. Forty-two men and thirty-five women underwent an overnight polysomnography, filled out questionnaire and Epworth scale. Patients were divided into two groups (i) Obstructive Sleep Apnea with depression (N=47), mean age 42.6 (SD ± 5.7), BMI, mean 30.74 (SD ± 6.9), and mean RDI 24.8 (SD ± 19.2). (ii) Obstructive Sleep Apnea without depression (N=60), mean age 42 (SD ± 6.2), BMI 30.1 (SD ± 8.1) and mean RDI 22.2 (SD ± 20.3). Depression was self-reported and patients were on antidepressant medications.

Results: Patients with obstructive sleep apnea and depression when compared with the group without depression showed: Increased REM (rapid eye movement) latency (p<0.006), increased stage-I sleep (p=0.004), decreased stage-III sleep (p<0.025), increased anxiety (p<0.0000005), increased caffeine use (use of 6 or > cups of coffee or coke per day) (p<0.032), more females (p<0.008), increased miscarriage (p<0.005) and smoking (p<0.015). There were no statistically significant difference between the two groups in stage-IV sleep, arousal index, RDI (respiratory distress index, defined as ≥5 apneas per hour), Epworth scale, snoring, fatigue, headaches, insomnia, oxygen desaturation, sleep efficiency, total sleep time, education level, family history, job status and marital status.

Conclusion: Patients with Obstructive Sleep Apnea and depression when compared with patients with OSA without depression, have more fragmentation of sleep. Patients with depression were also found to have increased incidence of anxiety disorders. We also found significantly more miscarriages among females with OSA and depression though the number of patients is small further studies are needed to investigate the possibility of OSA being a risk factor for miscarriage. Physicians evaluating patients for mood disorders should suspect sleep disorder, especially if the treatment is drug resistant or if they are multiple risk factors for OSA.

0617
Sleep Apnea Screening Questionnaire: Validation Of A Model Used In Central Maryland.
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Introduction: While some sleep apnea screening tools show promise in predicting the presence of sleep apnea, most questionnaires show disappointing correlation with polysomnographic results, and in general are poor predictors of OSA severity. The purpose of our study was to develop a tool that should ideally be simple, easy to implement, have educational value, and widespread applicability in community and clinical settings. Most previously developed questionnaires have been directed at snoring, witnessed apneas, daytime somnolence and obesity. We find in our analysis that certain phrasings and presentation of these questions can have better predictive value than others when using polysomnography (psg) as the bench mark.

Methods: Our 5-question survey was distributed in several primary care and cardiology waiting rooms. Of patients referred for suspicion of OSA, 918 of these were evaluated for our study, having been referred to four different sleep labs participating in the survey analysis. Results of psg of all 918 pts were used to stratify patients into categories of normal as well as mild, moderate and severe OSA. The results of survey questions were evaluated with respect to their ability to predict these categories.

Results: Our initial screening statistical analysis, using chi-square
method showed that 3 out of 5 questions have statistically significant p-values for differentiating apnea-hypopnea index (AHI) 0-5 and AHI>15. The three questions with significant p-values included our snoring survey (<0.005), our query regarding pauses in breathing during sleep (<0.005), and our obesity screen (<0.005). It was also noted that our question regarding obesity correlated directly to BMI among study patients, suggesting that this question can replace the actual BMI calculation.

Conclusion: Our questionnaire provides a concise, easy, educational survey that shows statistically significant ability to differentiate between non-OSA patients and those with AHI >15. Although medical conditions related to OSA, other than HTN, did not show significant predictive value, we maintain them in the survey to heighten patients’ awareness of the relationship between apnea and these conditions. We present our Sleep Apnea Risk Questionnaire, further analysis of our data, as well as suggestions for scoring modifications based on these results.

0618
A Novel Strategy For Treating Upper Airway Obstruction (UAO) With Transnasal Insufflation (TNI)
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Introduction: Snoring and obstructive sleep apnea reflects different degrees of upper airway obstruction during sleep. We investigated whether inspiratory flow limitation (IFL) can be alleviated by insufflation of air via a small bore nasal cannula. Five subjects (BMI 25.6±2.6, Age 30.8±8.8) with mild degrees of sleep disordered breathing (NREM AHI 8.7±6.9, REM AHI 9.1±2.6) were studied. We hypothesized that TNI will: (1) abolish mild UAO, and will (2) stabilize ventilation during sleep. Methods: Compressed air which was heated (29-31 degrees C) and humidified (90% rel. humidity), was delivered through a modified nasal cannula (ID 4mm, ED 5mm) at 10 and 20 lpm intermittently during periods of IFL. Maximal inspiratory flow, tidal volumes, esophageal pressure swings, and end-expiratory supraglottic pressures were compared between baseline and TNI conditions.

Results: TNI stabilized the breathing pattern in all subjects. IFL was abolished with 10 lpm in one and 20 lpm in four individuals. Breathing pattern at 20 lpm was associated with an increase in end expiratory supraglottic pressure of 1.8±0.7 cm H20 (p=0.02), and a decline in esophageal pressure swings from 11.0±3.8 to 5.5±2.6 cm H20 (p=0.01). Tidal volumes increased from 447.3±209.0 to 557.3±141.1 ml/s (p=0.18), maximal inspiratory flow increased from 293.8±139.4 to 393.1±152.1 ml/s (p=0.07), and minute ventilation increased from 5.6±3.9 to 7.2±1.8 lpm (p=0.34).

Conclusion: TNI significantly improved upper airflow dynamics and breathing patterns during sleep. These findings suggest that TNI may provide effective and comfortable treatment for patients with milder degrees of upper airway obstruction (snoring and obstructive hypopnea).

0619
Sleep Disordered Breathing In An Inpatient Setting
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Introduction: Population based epidemiologic studies have shown there to be a high prevalence of undiagnosed obstructive sleep apnea (OSA) and significant morbidity associated with even mild OSA. Little is known about the prevalence of sleep disordered breathing (SDB) in hospitalized patients. We performed a retrospective study of hospitalized patients who underwent polysomnograms.

Methods: We reviewed the medical records and polysomnograms of 100 patients who were admitted to one of the Johns Hopkins University Hospitals between January 2003 and September 2004. Patients with a total sleep time (TST) < 2 hours or patients studied with an open tracheostomy were excluded from further review. Means are expressed with standard deviations.

Results: All of the requests for polysomnograms originated from general medicine or medical subspecialty staff. 6/100 (6%) were excluded from further review. Referral forms showed 70% were obese, 25% had CHF, 15% had COPD. Mean age was 55 years (+/- 13); 46% were male. TST = 3.5 hrs +/- 1.2; sleep efficiency = 75% +/- 17; Stage 1 = 32% +/- 25; Stage 2 = 53% +/- 23; stage 3/4 = 4% +/- 8; REM = 11% +/- 10. SDB (defined as AHI >10) was present in 75%; 95% of SDB studies showed OSA (>50 obstructive events). The average low SaO2 = 89% (NREM); 82% (REM); 58% of patients were on O2 during the study. 6% were noted to have an arrhythmia during the study.

Conclusion: There is a high prevalence of SDB in patients referred for inpatient sleep testing. Although this may be due to a selection bias on the part of the referring physician, it is likely that there remains a significant number of patients in whom the diagnosis is missed because it is not considered. The impact of undiagnosed SDB in this population is unknown and deserves further study.

0620
Self-Identified Sleep Apnea Is Associated With Subjective Sleepiness
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Introduction: It is unclear why some patients self-identify a sleep problem while other patients’ sleep problem is first identified by a living partner. We tested the hypothesis that self-identified patients have more subjective sleepiness than partner-identified patients in a cohort of newly diagnosed sleep apnea patients. We also sought to identify other differences between self-identified and partner-identified patients. Methods: We studied newly diagnosed sleep apnea patients in a prospectively designed cross-sectional analysis of the Seattle Sleep Cohort. On the evening of initial diagnostic polysomnography, all patients answered a question about who initially suspected their sleep problem and completed the Epworth Sleepiness Scale, other sleep measures, and a health questionnaire. Comparison between self- and partner-identified patients were made with chi-square test, t-test, and multivariate logistic regression.

Results: The cohort consisted of 102 consecutive patients who indicated either a self-identified (n=50) or a partner-identified (n=52) sleep problem. The self-identified group was younger (47 v 41 years, p<0.01), more commonly female (54 v 29%, p<0.05), and sleepier (Epworth Sleepiness Scale 11 v 8, p<0.05). Self-identification remained associated with greater sleepiness on multivariate regression, after adjusting for age and sex (p<0.05).

Conclusion: Among patients newly diagnosed with sleep apnea, those who first identified their sleep problem themselves are, on average, sleepier than those whose partner first identified their sleep problem. We hypothesize that self-identified patients may be more motivated to comply with treatment, and if so, it may be related to their motivation to improve their symptoms.

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0621
Acoustic Sleep Fragmentation Is Associated With Increased Expression Of Apneas In Healthy Young Adults
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Introduction: In healthy adults, occasional apneas and hypopneas are associated with sleep onset and REM sleep and acoustic sleep fragmentation is associated with respiratory pattern changes even when generalized EEG arousal is absent. The frequency of disordered breathing events increases during recovery from sleep deprivation in patients with sleep apnea syndrome. Here, we tested the impact of acoustic sleep fragmentation and sleep deprivation on the expression of apneas and hypopneas in healthy adults.

Methods: Two women and 3 men aged 20 to 40 years underwent laboratory polysomnography (PSG) on 4 occasions at 1 week intervals. The first recording served as an acclimatization night. Subsequently, in random order, a repeat baseline PSG, a fragmentation PSG (80 dB, 0.5 s, 3 KHz tone bursts via ear bud headphones), and a recovery PSG following 24-hour sleep deprivation were completed.

Results: As expected, acoustic fragmentation and sleep deprivation produced opposite changes in sleep architecture. Stage 1 sleep increased from 3.1% to 5.8% (p = 0.04 by Fisher's PLSD) during fragmentation and decreased to 1.9% (p = 0.01) during recovery sleep. Stage 4 sleep decreased from 3.6% to 0.28% (p = 0.01) during fragmentation and increased to 10.3% (p = 0.004) during recovery sleep. REM sleep was unchanged by fragmentation, but increased from 16.5% to 24.2% during recovery sleep (p = 0.006). No significant changes in sleep efficiency or number of awakenings were observed. The number and frequency of disordered breathing events was unaffected by sleep deprivation, but sleep fragmentation was associated with an increase in the number of apneas from 2.6 ± 1.2 to 12.7 ± 1.8 (p = 0.003). These included both central and obstructive events that were immediately associated with sleep onset following transient arousal.

Conclusion: Sleep fragmentation can be associated with increased disordered breathing events even in healthy young adults.

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0622
Cardiologists Knowledge And Attitudes About Obstructive Sleep Apnea: A Survey Study
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Introduction: Recent data suggest that Cardiologists do not commonly report the diagnosis of obstructive sleep apnea (OSA), despite an established association with cardiovascular diseases (CVD). This study was designed to assess whether Cardiologists’ knowledge and attitudes about OSA are contributing factors to this observation.

Methods: A previously validated questionnaire, “Obstructive Sleep Apnea Knowledge and Attitudes” Questionnaire (OSAKA), was modified and used to assess Cardiologists knowledge and attitudes about OSA. Twenty knowledge items, specifically about the relationship between OSA and CVD, were added to the original questionnaire. The modified questionnaire is composed of 38 knowledge items, 5 attitude questions and demographics of the respondents. This was mailed to 518 Cardiologists nationwide (USA). One-way analysis of variance tested the significance of differences in knowledge, grouping by age, gender, and years in practice.

Results: To date, 60 (12%) of 518 Cardiologists have responded. Demographics: 50 (83%) males, mean age 50 +/- 9 years, and mean years in practice 17+/-.11. Mean scores: 76%/+-13 on the 18 original questions from the OSAKA questionnaire and 79% +/-7 on the additional 20 questions. On the attitude portion of the questionnaire, 46 (77%) felt that OSA was a very important or extremely important clinical disorder; 32 (53%) felt confident identifying patients at risk for OSA and 10 (17%) felt confident managing patients with OSA. There was no statistically significant difference in scores with regards to knowledge about OSA based on age, gender or years in practice. There was a significant correlation between Cardiologists’ knowledge and confidence in identifying patients at risk for OSA (r=0.3 p=0.02).

Conclusion: Cardiologists appear knowledgeable about OSA and its association with CVD. However, there appears to be a lack of confidence in identifying and managing patients with OSA. The latter may indeed be an important factor contributing Cardiologists’ low rate of reporting OSA.

0623
CPAP Use Predicts Change In Depressive Symptoms 3 Months Post-Treatment In Obstructive Sleep Apnea (OSA)
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Introduction: Obstructive Sleep Apnea (OSA) has been associated with depressed mood. In the present study, we aim to determine whether Continuous Positive Airway Pressure (CPAP) treatment reduces depressive symptoms associated with OSA.

Methods: Data on the first 112 patients (mean age 52.7 ± 11.1 years, 36 women, mean AHI 40.4 ± 23.4) completed through three months from a clinical trial examining treatment adherence in patients with OSA were examined. Participants were medically and psychiatrically healthy, diagnosed with moderate to severe OSA by overnight polysomnography, judged by their sleep physician to be CPAP responders, and choose CPAP as their treatment. The BDI-II was administered as part of a neuropsychological assessment battery at baseline (prior to CPAP initiation) and at 3 months post-CPAP initiation. Total BDI-II scores were considered as well as factors scores representing the cognitive and somatic dimensions of depression. Objective CPAP adherence was measured by covert monitoring via Respironics SmartCard™ technology.

Results: Linear regression was used to determine the degree to which CPAP use predicted BDI-II scores at 3-month follow-up, over and above depression score at baseline. Baseline BDI-II scores predicted depression at 3-month follow-up (R2=.37; p<.001). Average nightly CPAP use accounted for an additional 3.6% of the variance in 3-month BDI-II scores (p=.01). Regarding factor scores, CPAP use accounted for a unique 5.7% of the variance in somatic factors (p<.005), but did not contribute significantly to cognitive factors (R2=.38; p>.05).

Conclusion: Nightly CPAP use is predictive of a change in depressive symptoms from baseline to 3-months. These changes appear to be related more to an improvement in somatic than cognitive symptoms. These findings may reflect that OSA is more likely to affect somatic than cognitive depressive symptoms. However, the study sample endorsed relatively few cognitive symptoms, which could also explain this trend.

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Category J—Sleep Disorders—Breathing

0624 Endothelial Dependent Vascular Dilation Is Abnormal In Patients With Obstructive Sleep Apnea
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Introduction: Respiratory events in OSA can disturb sleep and produce oxygen desaturations. Intermittent hypoxemia and sleep fragmentation provoke heightened sympathetic activity and may impair vascular function. We investigated flow and nitroglycerin-mediated (FMD and NMD, respectively) vascular dilation in patients with moderate to severe OSA.

Methods: We recorded polysomnograms from eight male subjects (mean age = 57 ±7.8) with symptomatic OSA and measured FMD and NMD in brachial artery using high-resolution vascular ultrasound with a 10-MHz linear-array transducer. The right brachial artery diameter (BAD) was measured at baseline, and then a pneumatic tourniquet was placed around the forearm and inflated to a pressure of 200 mm Hg for 5 minutes. BAD measurements were repeated at 15 seconds, then at every minute for 5 minutes following cuff deflation and following administration of 0.4 mg of sublingual NTG. The FMD was expressed as a percentage change of diameter after reactive hyperemia relative to the baseline scan. Likewise, the NMD was expressed as a percentage change of diameter after NTG administration relative to the baseline scan.

Results: Mean [SD] ESS was 14 [7], mean [SD] AHI was 61 [42], and lowest O2 saturation was 74% [16%]. Brachial artery diameter (mm) at baseline, 1 minute post hyperemia, and 3 minutes post NTG were 0.45 [0.05], 0.45 [0.03], and 0.5 [0.04] mm. Baseline and post NTG diameters were significantly different (p <0.01). The FMD and NMD were 2% [10%] and 13% [11%], respectively (p<0.005).

Conclusion: Endothelial dependent vascular function is impaired in subjects with moderate to severe OSA. Further studies will evaluate the effect of therapeutic intervention to determine if this is a reversible alteration in vascular function.

0625 Randomized Multicenter Trial To Improve Compliance In Non-Adherent OSA Patients Using CPAP Vs Novel Bi-Level Positive Airway Pressure (NB-PAP)
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Introduction: At last years APSS, we reported our first phase success rate from a problem-directed, comprehensive protocol directed at improving CPAP compliance in OSA patients previously non-adherent with CPAP therapy. Only 37% of patients achieved targeted optimal objective meter readings of ≥4 hrs/day during phase 1 using education and several other conventional methods. We hypothesized that a second phase therapy with either re-titrated CPAP or NB-PAP will achieve additional increase in compliance rated by %patients with mean daily meter reading ≥4 hrs/day.

Methods: When phase 1 interventions proved suboptimal after 14 days by objective meter reading, consenting patients had repeat therapeutic polysomnography (PSG). After successful re-titration PSG, the patient was randomly assigned to continue with CPAP or initiate NB-PAP (BiFlex Respironics, Inc. Murrysville PA). This device was double blindly set to deliver either CPAP or NB-PAP and the 2 groups of patients were followed up at 30 and 90 days.

Results: To date, 87 patients (63% male) with previously diagnosed OSA and non-adherence to CPAP therapy underwent repeat PSG and entered phase 2. Overall mean age, BMI, and baseline AHI were 52.4+12 years, 33.3±7.5 kg/m2, and 37.8±26 events/hr and the 2 groups did not differ in baseline findings. The %patients adherent to CPAP vs. NB-PAP therapy at 30(43 vs. 44 pts) and 90 days (35 vs. 37 pts completed with only 2 dropouts) were 33% vs. 45% (p=0.083) and 32% vs. 54% (p=0.046) respectively, significantly favoring NB-PAP by 90 days.

Conclusion: These results confirm a relatively low improvement of <40% after a conventional comprehensive protocol directed at improving CPAP compliance in OSA patients previously non-adherent with CPAP therapy. Subsequent retitration resulted in improved therapeutic compliance with some patients but significantly better results warrants consideration of NB-PAP in such difficult patients.

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0626 The Neglected Spectrum Of REM Obstructive Sleep Apnea
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Introduction: Rapid eye movement related obstructive sleep apnea (REM-OSA) is an underestimated clinically distinct form of obstructive sleep apnea. It is often overlooked, as it is associated with lower overall apnea-hypopnea indices (AHI). As a result, patients may not receive appropriate treatment and may continue to be symptomatic. We sought to define the characteristics of this group of patients and their response to treatment.

Methods: Overnight polysomnography (PSG) records were reviewed from September 2003 to May 2004. Patients who met criteria for REM OSA were identified, defined as mild OSA with Total AHI <15, REM AHI <10, REM AHI>10 and REM AHI/ NREM AHI >2. Obstructive apnea was defined as a ≥90% reduction in airflow for more than 10 seconds in the presence of continued respiratory effort. Hypopneas were defined as a reduction in the amplitude of the nasal pressure transducer signal below 50% of baseline level during sleep, lasting for more than 10 seconds and associated with an EEG arousal or oxygen desaturation ≥3%.

Results: Of 482 overnight PSGs reviewed, 72 (15%) met the criteria for REM-OSA. Female: male ratio of REM OSA was 1:3.1:1. Age was 46 ± 12 years (Mean ± SD). The most common symptoms reported by patients in this category included excessive daytime sleepiness 65 (90%), snoring 64 (88%), witnessed apneas 26 (36%), repeated nocturnal awakenings 12 (16.6%) and fatigue 5 (6.9%). The most common coexisting medical conditions included hypertension 22 (30.5%), hypothyroidism 14 (19.4%) and depression 10 (13.8%). The Total AHI was 7.8 ± 3.7, NREM AHI 4.6 ± 3.1, REM AHI 26 ± 13.5 (mean ± SD). Of 72 patients, 56 (77.8%) received treatment, 54 with CPAP, one patient underwent gastric bypass and one patient underwent tonsillectomy. In the group who received CPAP therapy, follow-up was available for 42 patients. 40 reported significant improvement in their symptoms. 4 patients were unable to tolerate CPAP. 16 patients (22.2%) did not receive any treatment except for conservative management including advice on weight loss. Follow-up was available for 13 of these patients and all continued to be symptomatic.

Conclusion: These data confirm previous observations that REM-related OSA is common and higher in women. These patients are symptomatic and identification of this cohort is important as treatment has a significant favorable impact. The frequent co-existence of hypertension, depression and hypothyroidism with REM-OSA merits further study.
Introduction: The pattern of hypoxic exposure may determine the magnitude of hemodynamic and biologic responses, which are clinically relevant to patients with Sleep-Disordered breathing. Nitric oxide (NO), a potent vasodilator, is produced by (NOS), of which inducible NOS (iNOS) is one isofrm. Different responses to IH and CH may reflect differences in iNOS expression. Purpose: 1) To compare blood pressure (BP) and heart rate (HR) responses to daily exposure (X 3 days) of IH vs. CH (comparable total hypoxic exposure time); 2) To examine the relation between BP and HR responses and iNOS exposure under the IH and CH exposure conditions.

Methods: On each of 3 consecutive days, 10 normal males had six 10-min. hypoxic exposures (oxyhemoglobin saturation, SpO2: 80-90%), exposures were separated by 10 min. of normoxia. Subjects also had 3 consecutive days of CH (60 min/day; SpO2: 80-90%). IH and CH exposure blocks were separated by at least 7 days. BP, HR, and SpO2 were recorded during the 5 min. prior to and the last 5 min. of each daily IH and CH exposure. Venous blood for iNOS mRNA (PAXgene used to stabilize cellular RNA) was obtained before IH and CH exposure on day 1, and 2 hrs. after the last exposure on day 3. Analyses reflected a within-subjects repeated measures design.

Results: HR, systolic and diastolic BP were significantly (p<0.05) increased from baseline- to end-exposure on each day, regardless of IH or CH. There was a significant negative correlation (r<0.01) between both diastolic and mean BP with iNOS at the end of the day 3 IH session.

Conclusion: Hypoxic stress reflected by IH and CH is associated with significant, but comparable changes in BP. However, the negative correlation between BP and iNOS in conjunction with IH, but not CH, exposure suggests that the former may elicit a compensatory biologic response.

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Introduction: Sleep-related breathing disorders (SRBD) demonstrate a high degree of coincidence with cardiac diseases. Effective treatment of sleep apnea results in improvement of cardiovascular function and prognosis. Therefore a widespread screening for SRBD in this patient group is desirable. We evaluated an algorithm to detect apneas using TransThoracic-Impedance (TTI) changes recorded additionally in a Holter ECG.

Methods: 180 outpatients (79% male, mean age 55.5 years) were recorded with the Holter ECG system with integrated TTI-recording (CM3000, getemted-Teltow, Germany) within the routine diagnostics. Simultaneously a standard polygraphy with a validated sleep apnea screening system (ApnoeScreen, JAEGER, Germany) was done. We compared blinded the findings from the automatic impedance analysis (I-AHI) with the results from standard polygraphy (AHI), determining the correlation index and the sensitivity and specificity of this new method for screening of sleep apnea.

Results: In the apnea monitoring conducted, 46 of the patients studied demonstrated an apnea hypopnea index (AHI) >10/h (prevalence 25.5%). For 37 of these 46 patients automatic analysis of the impedance signal disclosed an I-AHI >10/h (sensitivity 80%). Only 10 out of 134 patients without SRBD were false-positive (specificity 93%).

Conclusion: Automatic detection of SRBD by means of transthoracic-impedance-recording, integrated into a Holter ECG system is feasible. This new additional method shows a good sensitivity for detection of sleep apnea and has a high specificity to debar SRBD in this examined patients. Further studies are warranted to evaluate this system in everyday life.

Efficacy And Safety Of Armodafinil 150 Or 250 Mg As Adjunct Therapy For Residual Excessive Sleepiness And Fatigue Associated With Obstructive Sleep Apnea/Hypopnea Syndrome

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Introduction: Residual excessive sleepiness may be observed in patients with obstructive sleep apnea/hypopnea syndrome (OSA/HS) despite stable nasal continuous positive airway pressure (nCPAP) therapy. Modafinil is a racemic compound. Armodafinil, the enantiomer of modafinil with the longer half life, was investigated as adjunct therapy for improving daytime wakefulness in patients with OSA/HS who experience excessive sleepiness despite adequate nCPAP therapy.

Methods: This 12-week, randomized, double-blind, multicenter study enrolled OSA/HS patients with an Epworth Sleepiness Scale (ESS) score ≥10 on adequate nCPAP therapy. Patients received armodafinil 150 or 250 mg once daily or placebo. Assessments were done at baseline and weeks 4, 8, and 12. The Maintenance of Wakefulness Test (MWT) was performed at 2-hour intervals. Clinical Global Impression of Change (CGI-C), ESS, Brief Fatigue Inventory (BFI), and tests of cognitive function from the Cognitive Drug Research System were also assessed. MWT (mean sleep latency of first 4 naps) and CGI-C were primary measures (combined doses vs placebo). nCPAP use, nighttime polysomnography, and adverse events were evaluated.

Results: 392 patients (armodafinil, n=262; placebo, n=130; mean age, 49.5 yr; mean BMI, 36.7 kg/m2) received study medication. Armodafinil significantly improved wakefulness (MWT) at final visit vs placebo (baseline, 25.9 and 26.4; final visit, 26.6 and 25.3, respectively; p=0.0077). Armodafinil significantly improved clinical condition (CGI-C) compared with placebo (final visit, 72% vs 37% rated as improved, respectively; p=0.0001). At final visit, armodafinil significantly improved subjective wakefulness (ESS) vs placebo (baseline, 15.3 and 15.9; final visit, 9.9 and 12.5, respectively; p<0.0001) and reduced fatigue (BFI; mean change, -1.2 vs -0.6; p=0.0067). Clinical benefit was observed at week 4 and was sustained until final visit. Differences versus placebo in quality of episodic memory, speed of memory, and attention were not statistically significant. Armodafinil did not adversely affect nCPAP use or nighttime sleep. Adverse events reported in ≥5% of patients who received armodafinil were headache, nausea, insomnia, dizziness, and anxiety.

Conclusion: For patients with OSA/HS and excessive sleepiness, armodafinil improved patients' ability to sustain wakefulness, overall clinical condition, and subjective wakefulness, and reduced fatigue. Armodafinil was well tolerated.

This study was sponsored by Cephalon, Inc., West Chester, PA.
0633
Prescription Methamphetamine In Narcolepsy: Frequency, Cognitive And Behavioral Effects
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Introduction: To determine from a referral center data base, the frequency of methamphetamine (MAmph) trial/subsequent prescription and effects on alertness, cognition and mood.

Methods: Retrospective analysis of 60 subjects (42 male, mean age 42 years) meeting criteria for narcolepsy who underwent acute trials of psychostimulants for: frequency of MAmph treatment trials, acute effects on alertness and cognition, and if sustained use, for maintenance of alertness & cognitive benefit and effects on mood. Instruments employed: Sleep study/polysomnography, Epworth Sleepiness Scale, sleep log, HLA typing, pupillometry; Rey Auditory Verbal Learning Test (AVLT), Letter Cancellation Test (LCT), Digit Span (DS), Conners' Continuous Performance Test (CPT), Test of Variables of Attention (TOVA), Wisconsin Card Sorting Test (WCST); Minnesota Multiphasic Personality Inventory (MMPI).

Results: 11 of the 60 subjects (18%) underwent acute MAmph trials (mean test dose 10 mg) usually because of incomplete response to other psychostimulants (8 male, mean age 45 years). Acutely improved cognition: AVLT-3, LCT-10, DS-3, CPT-7, TOVA-6, WCST-3. Acutely improved alertness-9. None acutely worsened cognitively. 8 continued MAmph >6 months (mean dose 30 mg/d). None of these lost cognitive or alertness benefit. Pre-MAmph Rx: MMPI-depression 11, anxiety 5. Post-MAmph Rx: none worsened mood, 5 less depression, 1 increased obsession. No treated patient had family or personal substance abuse history, no case of MAmph abuse was observed.

Conclusion: In select otherwise refractory narcolepsy subjects, MAmph may be an effective alternative for cognition/alertness.

Investigator sponsored trial grant from Ovation Pharmaceuticals, Inc.

0634
Cataplexy Emotional Trigger Questionnaire (CETQ) Can A Brief Patient Survey Identify Cataplexy In Patients With Narcolepsy?
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Introduction: Cataplexy is considered pathognomonic of narcolepsy but is difficult to diagnose. This study extends upon a previous 55-questionnaire administered to narcolepsy-cataplexy and control groups (Sleep 2001;24:A327). We postulated that it could be reduced to 5 questions without compromising the high degree of sensitivity and specificity.

Methods: Questions were: 1. Have you ever experienced sudden muscle weakness when you laugh? If yes, during your episodes of muscle weakness: 2. Can you hear? 3. Does your speech ever become slurred? 4. Is your head affected? 5. Is your whole body affected? Narcolepsy participants had cataplexy diagnosed by a sleep specialist and an MSLT showing a mean latency <8 minutes and 2 SOREMPs. The control group was patients with confirmed OSA. Sensitivity, specificity, the area under the receiver-operating characteristic (ROC) curve (AUC), positive predicted values (PPV), and negative predicted values (NPV) were computed for each question individually along with appropriate 95% confidence intervals.

Results: 78 narcolepsy with cataplexy and 78 OSA participants completed the questionnaire. The mean age for narcolepsy subjects was 53.5 ±18.4 years compared to 58.8 ±10.7 years for controls (p=0.158). There were 45 (58%) women in the narcolepsy group versus 28 (36%) in the controls (p=0.006). Question 1 had a sensitivity of 0.94 (95% CI: 0.86,0.98) and a specificity of 0.99 (95% CI: 0.93,1.0) with an AUC of 0.96 (95% CI: 0.93,0.99). The NPV was ≥ 0.99 for all questions and the PPV was 0.79 (95% CI: 0.55,1.0) for question 1 and 0.79 (95% CI: 0.54,1.0) for question 2 assuming a prevalence of 5%.

Conclusion: Question one discriminates patients with cataplexy from controls with excellent sensitivity and specificity. The addition of the other 4 questions did not improve specificity, AUC, PPV, or NPV. This single question provides a brief practical tool that could improve the clinical recognition of cataplexy.

The Department of Psychiatry and Psychology, Mayo Clinic College of Medicine, Rochester, funded this study

0635
Sodium Oxbyate, Alone And In Combination With Modafinil, Produces Significant Improvements In Sleep Architecture In Narcolepsy
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Introduction: A placebo-controlled, double-blind, double-dummy study measured the efficacy of sodium oxybate, alone and in combination with modafinil, for the treatment of excessive daytime sleepiness (EDS) in narcolepsy patients. Overnight polysomnograms (PSGs) measured changes in sleep architecture associated with these drug treatments.

Methods: This trial enrolled narcolepsy patients currently using modafinil for the treatment of EDS. During the 8-week double-blind treatment phase of the study, patients were randomized into 4 treatment groups: sodium oxybate + placebo modafinil, placebo sodium oxybate + modafinil, sodium oxybate + modafinil, or placebo sodium oxybate + placebo modafinil. The dose of sodium oxybate was 6 g nightly for the first 4 weeks, then 9 g nightly for the remainder of the trial. Patients receiving modafinil remained on their usual dose. Overnight PSGs were performed at the beginning and end of the double-blind phase of the trial. The intent-to-treat population consisted of 222 subjects.

Results: Patients receiving sodium oxybate, modafinil, or both medications combined, experienced significant improvements in EDS; however, only those patients receiving sodium oxybate, either alone or combined with modafinil, demonstrated positive changes in nocturnal PSGs. These improvements included increased NREM sleep, Stage 3 and 4 sleep and delta power (for each, p < 0.001 compared to placebo-treated patients) and nightly awakenings were significantly decreased (p = 0.008 and p = 0.14, respectively). Sodium oxybate, alone or in combination with modafinil, was not associated with an increase in sleep disordered breathing or evidence of respiratory depression as measured by blood oxygen saturation.

Conclusion: In contrast with other agents used for the treatment of EDS in narcolepsy, sodium oxybate produces significant improvements in the quality of nocturnal sleep in this patient population. Sodium oxybate may be effective monotherapy for the treatment of narcolepsy.

This study was sponsored by Orphan Medical, Inc.
0636
Screening For Autoantibodies Against Lateral Hypothalamic Neurons In Human Narcolepsy
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Introduction: Human sporadic narcolepsy is thought to be an autoimmune disorder, although this theory has not been proven. As narcolepsy is characterized by deficient hypocretin neurotransmission, the hypothalamic hypocretin neurons are a likely target for a putative autoimmune attack. We used immunohistochemistry to screen for circulating antibodies against hypothalamic neurons in narcoleptic patients.

Methods: We collected serum from 76 narcoleptic patients (45 males, age: 45.6±15.6 years) and 111 control subjects (45 males, age 35.4±12.3 years). Immunohistochemistry was performed, using standard protocols, on freshly dissected formalin-fixed hypothalamic sections from 2 subjects, who died of non-neurological disease. In short, hypothalamic sections were incubated with patient or control serum at a dilution of 1:400 overnight at room temperature. Subsequently, sections were incubated with biotinylated goat-anti-human-IgG for one hour, and labeled with ABC-Elite kit (Vector) for 30 minutes, stained with 3,3′-diaminobenzidine as chromogen, and counterstained with Harris hematoxylin. Of every 25 slides, one was stained with rabbit-anti-hypocretin-1 1:5000 to identify the area of interest.

Results: As expected, hypocretin-1 cell bodies and multiple bead-like varicosities were mainly located in the perifornical area of the lateral hypothalamus. The sera of two narcoleptic patients showed consistent staining of neuronal cell bodies and bead-like fibers in the lateral and tuberal hypothalamus. However, 2 control subjects were also found to have circulating antibodies staining neurons in the perifornical hypothalamus. The number of positive cells that stained using the control sera was higher than the neurons stained with the patients sera, and the controls did not stain fibers.

Conclusion: We did not find disease-specific antibodies against hypothalamic neurons in narcoleptic patients. A small percentage of patients have autoantibodies recognizing neuronal components, but this is also the case in healthy controls. As of yet, there is no direct evidence supporting the autoimmune hypothesis for narcolepsy.

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0637
Studies Of Humoral Immunity To Preprohypocretin In HLA DQB1*0602 Positive Narcoleptics With Cataplexy
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Introduction: Canine models for narcolepsy have mutations of the hypocretin (orexin) receptor 2 gene and preprohypocretin knock out murine lines exhibit narcoleptic-like behaviors. Human narcolepsy with cataplexy is associated with HLA DQB1*0602 and reduced hypocretin levels in cerebrospinal fluid (CSF) suggesting an autoimmune diathesis. We tested the hypothesis that HLA DQB1*0602 positive narcoleptics with cataplexy have antibodies against human preprohypocretin and its cleavage products.

Methods: Serum samples were donated by 41 HLA DQB1*0602 positive narcoleptics with cataplexy and 55 controls. CSF samples were donated by 19 narcoleptics and 13 controls. We tested for antibodies to preprohypocretin and hypocretin 1 and 2, and the N-terminal leader and the C-terminal tail peptides of preprohypocretin using immunoprecipitation assays (IPA), Western blots, and immunofluorescence (IF) microscopy of Chinese Hamster Ovarian (CHO) cells expressing preprohypocretin.

Results: There was no evidence for antibodies to preprohypocretin or its cleavage products in subjects with narcolepsy using IPAs, Western blots, and IF staining of preprohypocretin producing CHO cells. Although, the IPA using CSF and the C-terminal peptide showed a significant difference, it was opposite that hypothesized.

Conclusion: The hypothesis that HLA DQB1*0602 positive narcoleptics with cataplexy have antibodies against human preprohypocretin or its cleavage products was not supported.

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ation of sodium oxybate therapy at a dose of 6 g nightly as well as subjects in previous studies where treatment was initiated at a dose of 4.5 g nightly.

This study was sponsored by Orphan Medical, Inc.

0639
Weight Loss In Narcolepsy With Sodium Oxybate
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Introduction: Narcolepsy is often associated with increased body weight. Several studies have shown that this is most likely due to impaired energy homeostasis rather than lack of activity. Sodium oxybate has efficacy in many narcolepsy symptoms. The purpose of this study was to evaluate the effects of sodium oxybate on weight in patients with narcolepsy.

Methods: Charts of all patients with narcolepsy who had been using sodium oxybate for at least 3 months were reviewed. Patients in whom anticitaplexy medications were added or withdrawn or wake-promoting medications added after the start of sodium oxybate were excluded from further analysis. In the remainder, pre-sodium oxybate and most recent on-sodium oxybate weight and body mass index (BMI) were compared using Student t-tests. Sodium oxybate dose and duration of therapy was also noted.

Results: A total of 17 patients with narcolepsy using sodium oxybate in whom medication changes had not been made were identified. Of these 17, 6 (35%) were women; the mean age was 43 (±16.6) years. The mean pre-sodium oxybate weight was 182.1 (±33.3) pounds and the BMI was 27.6 (±4.0). The most recent on-sodium oxybate weight was 171.7 (±31.2, p<0.05) and BMI was 26.0 (±3.5, p<0.05). The average weight loss was 10.4 pounds, whereas the maximum was 41 pounds. The mean dose of sodium oxybate was 7.0 (±1.8) grams/night and the duration of therapy was 10.7 (±7.2) months.

Conclusion: This study suggests that treatment of patients with narcolepsy with sodium oxybate can result in significant weight loss.

0640
Hypocretin Receptor Expressions In Hypocretin Neuron Ablated (Orexin/Ataxin-3 Transgenic) Narcoleptic Mice
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Introduction: This study aimed to examine influences of postnatal ablation of hypocretin/orexin neurons on hypocretin receptor 1 (HCRTR1) and HCRTR2 gene expression in 8-week and 27-week-old orexin/ataxin-3 transgenic (TG) narcoleptic mice.

Methods: HCRTR gene expressions in the cortex (Cx), hypothalamus (Hyp) and pons (Ps) in wild type (WT) and TG mice (8-week and 27-week-old, n=10-12 for all 4 groups) were analyzed by the quantitative RT-PCR method.

Results: In WT mice, the expression of both HCRTR1 and 2 were the highest in the Hyp, followed by the Ps and Cx in both age groups. The 27-week-old WT mice showed a significant increase in the HCRTR2 mRNA expression for Cx (p<0.01), Hyp (p<0.02), and Pos (p<0.01) compared to the 8-week-old WT mice, while no age-dependent change was observed in the HCRTR1 expressions. In the TG mice, similar distributions and age-dependent changes of HCRTR expression were observed. Increases in HCRTR2 expression in 27-week-old TG mice were, however, less prominent compared to those in WT, and the difference between WT and TG (ratio of HCRTR2 expression over respective 8-week-old group) was statistically significant for Ps (p=0.006) and Hyp (p=0.033). The relative declines in HCRTR2 gene expressions in TG mice (compared to WT) were about 20%.

Conclusion: HCRTR expression was not altered in 8-week-old TG mice at the time when 90% of hypocretin neurons are selectively eliminated, but a significant decrease in HCRTR2 expression was observed in 27-week-old TG mice. The decrease is, however, small (20%) and is not likely to be functionally significant. These results are rather consistent with the recent outcomes by Mieda et al, that hypocretin supplements (either genetically and pharmacologically) rescue narcolepsy phenotype in aged TG mice. Examining the HCRTR expression in hypocretin ligand deficient narcoleptic (sporadic) dogs and humans is useful in evaluating the effectiveness of hypocretin supplements in these conditions.

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0641
The Anticatatplectic Effect Of Milnacipran, A New Serotonin Noradrenaline Reuptake Inhibitor, On Human And Canine Narcolepsy
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Introduction: Conventionally, cataplexy of narcolepsy has been treated with tricyclic antidepressants including clomipramine and imipramine. However, their use is often limited by their side effects such as orthostatic hypotension, tachycardia, dry mouth, constipation, and sleepiness. In this study, we assessed the anticatatplectic effect of milnacipran, a new serotonin noradrenaline reuptake inhibitor(SNRI), on human and canine narcolepsy.

Methods: In the study on human narcolepsy, 7 cataplectic subjects who replaced from clomipramine to milnacipran because of side effects were enrolled. From each subject, the informed consent on the participation in this study was obtained. The change of frequency of cataplexy and side effect before and after drug replacement was investigated. In the study on canine narcolepsy, four genetically narcoleptic Doberman pinschers were studied. The food-elicited cataplexy test was used to assess the anticatatplectic effect of milnacipran. The effect was measured by both the dose-response and the time course study, and the significance of anticatatplectic effects was evaluated using Friedman's nonparametric analysis of variance(ANOVA). In addition, Pearson's correlation was used for regression analysis between the dose producing 50% of maximal effect(ED50) which was estimated by the result of previous dose-response study and the 50% inhibiting constant(IC50) of various antidepressants.

Results: In the study on human narcolepsy, the mean dosage of clomipramine and milnacipran were 24.3±6.7mg/day(mean±SD) and 30.7±13.7mg/day, respectively. There was no significant difference between the frequency of cataplexy observed with clomipramine and milnacipran were 24.3±6.7mg/day(mean±SD) and 30.7±13.7mg/day, respectively. The relative declines in HCRTR2 gene expressions in TG mice (compared to WT) were about 20%

Conclusion: In our current study, milnacipran effectively reduced cataplexy with a low incidence of side effects in human narcoleptic subjects.

Category K—Sleep Disorders-Narcolepsy
Category K—Sleep Disorders-Narcolepsy

In addition, milnacipran significantly reduced cataplexy in narcoleptic dogs. Venlafaxine, another SNRI, has become the first choice for treatment of cataplexy. Especially in the case with severe side effects by tricyclic antidepressants, milnacipran should also be good for treatment of cataplexy.

0642
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-cataplexy (NC) is now established. What remains to be established is whether the deficiency is partial or complete. The role(s) of hct-1 in other disorders of excessive daytime sleepiness (EDS) is less well understood. We report on CSF Hcrt levels in a sample of patients with disorders of EDS specifically Monosymptomatic Narcolepsy (MN) and Primary Hypersomnia (PH).

Methods: We set out to measure CSF hct-1 in this sample of patients with narcolepsy-cataplexy (NC), in monosymptomatic narcolepsy (MN) and primary hypersomnia (PH) Radioimmunoassay. CSF samples were analyzed by RIA. The solid-phase assay (Maidment and Evans, 1991) provided an IC50 of 3.8 (0.7) fmol and a limit of detection of 0.2 fmol.

Results: NC: n = 31 (F = 21, M = 10) ESS mean score of 18.4, MSLT analysis provided a mean sleep latency of 3.9 minutes. All but two of the patients were HLA DQB1*0602 positive; Hcrt-1 was detectable in all the samples tested with a mean CSF hct-1 of 4.4 fmol/ml, (Range of 9.4; minimum 0.7; maximum 10 fmol/ml) . MN: n = 6 (F = 4, M = 2); ESS mean = 17.6; MSLT mean SL of 5.4 minutes. Two patients were HLA DQB1*0602 positive; Hcrt-1 was detectable in all the samples with a mean of 21.7 fmol/ml (Range of 53, minimum 1.7; maximum 57.3) PH: n = 13 (F = 3, M =10); Mean ESS = 14; Mean SL of 9.7 minutes. 4 patients were HLA DQB1 * 0602 positive; Mean CSF hct-1 was 24.2 fmol/ml (Range of 40; minimum 7; maximum 47)

Conclusion: Our early results confirm the previous findings that hct-1 is deficient in patients with NC and indicate that there may be a graded deficiency of hct-1 in disorders of excessive daytime sleepiness.

0643
Escitalopram In The Treatment Of Narcolepsy - First Experience
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Introduction: Usual pharmacological treatment of REM sleep-related phenomena consists in antidepressant drugs, although no drug against cataplexy is registred in the Czech Republic. Escitalopram is a novel selective serotonin reuptake inhibitor.

Methods: Seven outpatients (4 men and 3 women, mean age 44.4 SD=16.6 years) suffering from narcolepsy and at least weekly occuring cataplexy were treated with 5 mg or 10 mg of escitalopram a day. None of them had any major OSA, RLS or other sleep influencing diseases. Two patients received for stimulants (methylphenidate and modafinil) over a long period of time.

Results: One patient discontinued escitalopram because of delayed ejaculuation. No other side effects were reported. Another patient failed to comply with the therapy for unknown reasons. These two noncompliant patients were excluded from the final evaluation. Three patients received 5 mg a day and two 10 mg. The mean number of cataplexies per week was 7.2 (8.0) before and 0.5 (0.7) during the cure. In-treatment cataplexies occurred only in two subjects (2?, P=0.038). The mean number of spells of hypnagogic hallucinations, sleep paralysis, involuntary naps as much as the score on the Epworth sleepiness scale remained unaltered while the group were treated with escitalopram. There were also no changes in subjective night sleep quality, wakefulness, concentration or mood rated on a 4-degree scale.

Conclusion: Escitalopram proved to have antcataplectic effects in this small-scale open-label study.

0644
Screening Of HLA DQB1*0602 Positive Narcoleptics’ Serum For Immunoreactivity To Rat Hypothalamus Protein Extract Using Elisa
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Introduction: Human narcolepsy with cataplexy is associated with HLA DQB1*0602 carrier status and reduced hypocretin levels in cerebrospinal fluid (CSF) suggesting an autoimmune diathesis involving hypocretin secreting cells. We tested the hypothesis that human narcoleptics’ IgG reacts to proteins expressed in the rat hypothalamus since this is where hypocretin secreting cells are anatomically located.

Methods: Forty five narcoleptics with cataplexy who carried the HLA DQB1*0602 allele donated serum for this research and they were compared to 57 non-narcoleptic controls. Four Sprague-Dawley rat hypothalamami, which were homogenized in saline and then defilipified, were the source of the protein for this experiment. ELISA plates were coated with 250 ng protein extract/well based upon optimization with antisemur reactive to the carboxy-terminal region of the preprohypocretin polypeptide. Narcoleptic and control sera were tested in duplicate using doubling dilutions ranging from 1:40 to 1:2560. Results were averaged and compared by t test. We analyzed data by group and after stratifying for age, gender and control HLA status.

Results: Custom antisemur to the carboxy-terminal region of preprohypocretin produced a detectable signal on ELISA using this protein preparation. However, no significant differences were observed at any titer when comparing the narcoleptic and control samples for the entire group, and when the results were stratified by age, gender, and control HLA type.

Conclusion: We found no evidence of immunoreactivity of narcoleptic serum to rat hypothalamus using this screening ELISA approach. Explanations include the possibility that 1) there were no antibodies present in sera of patients with narcolepsy, 2) the immunogenic epitopes were lost with isolation of the proteins from rat hypothalamus using this approach, 3) this screening approach is too insensitive to detect low titer serum antibodies or low abundance epitopes that exist, 4) cell mediated immunity is etiologic for narcolepsy, or 5) narcolepsy does not have an autoimmune etiology.

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A Case-Control Study Of The Environmental Risk Factors For Narcolepsy

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Introduction: There is a general consensus that the etiology of narcolepsy involves both genetic and environmental risk factors. However, there has only been one previous case-control study on environmental risk factors, which focused exclusively on the dichotomous assessment of psychological stressors that occurred within one year prior to onset. This study sought to examine the effect of a variety of environmental risk factors throughout the lifespan prior to onset.

Methods: Cases (n=63) were recruited through the Stanford Center for Narcolepsy. All were HLA-DQB1 *0602 positive, met conventional MSLT criteria, and reported typical cataplexy. Controls (n=63) were non-related family members of cases and local community members. Controls were frequency matched on current age to minimize recall bias and reported on events prior to the age of 20 since this is the median age of cataplexy onset. The procedure entailed mailing a self-administered questionnaire that assessed the frequency and age of each risk factor. Portions of this questionnaire (The Narcolepsy Environmental Triggers Survey) were previously assessed for reliability and validity while other portions were derived from published recommendations on the questionnaire assessment of environmental risk factors.

Results: A small minority of the infectious diseases that were examined carried a significant risk. These were flu infections (OR=1.8, p<0.05) and unexplained fevers (OR=3.9, p<0.05). Several of the psychological stressors that were examined carried a significant risk. These included major changes in sleeping habits (OR=2.0, p<0.01), which replicates previous research, and childbirth (OR=2.7, p<0.05). Interestingly, total stressors were only a significant risk factor if they occurred before the age of 10 (OR=1.2, p<0.05).

Conclusion: These findings indicate the importance of environmental risk factors in the etiology of narcolepsy. The timing of these risk factors may also be significant given the risk associated with exposure prior to an age where puberty typically begins and given the post-pubertal onset of narcolepsy.

Data made available by the Stanford Center for Narcolepsy. Research supported by a gift to the University of Southern Mississippi Foundation by Robert and Peggy Wallace of Northport, New York.

The Relationship Between Psychiatric Disorders And Cerebropinal Fluid Hypocretin Levels In Narcolepsy

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Introduction: Hypocretin neurons project to brainstem nuclei where they modulate monoamines including norepinephrine, serotonin, and dopamine. These neurotransmitters play an important role in psychiatric disorders. Our aim was to compare the frequency of psychiatric disorders in narcolepsy patients with normal and low CSF hypocretin levels. We hypothesized that normal hypocretin levels would be associated with a higher frequency of some psychiatric disorders.

Methods: All patients diagnosed with narcolepsy at Mayo Clinic Rochester tested for CSF hypocretin were evaluated. Patients with a history of excessive daytime sleepiness with definite cataplexy, and/or a mean sleep latency of <8 minutes and 2 or more sleep onset rapid eye movement periods on MSLT without other untreated sleep disorders were included. Patient histories were reviewed for the presence of physician diagnosed psychiatric disorders.

Results: Of 48 narcolepsy patients tested for CSF hypocretin, 29 had low (<110 um/L) and 19 had normal hypocretin levels (>110 um/L). Cataplexy was present in 26 (90%) of those with low hypocretin and 8 (42%) of those with normal levels. Psychiatric diagnoses occurred more frequently in the normal (16/19) versus low (14/29) hypocretin group (p=0.016). Attention deficit hyperactivity disorder (ADHD) and anxiety disorders were more frequent in the normal than the low hypocretin group (6/19 versus 0/29 for both disorders, p=0.002). No differences were noted with other psychiatric diagnoses, including affective and psychotic disorders.

Conclusion: Psychiatric diagnoses, specifically ADHD and anxiety disorders, occur more frequently in narcolepsy patients with normal hypocretin levels. It is uncertain whether this finding is due to a protective effect of low hypocretin (possibly related to reduced monoamine activity), or to a higher frequency in patients with the variant of narcolepsy associated with normal hypocretin levels. More research is needed to evaluate this relationship.

Supported by Mayo Piscopo Funds

Gray Matter Changes In Young Narcoleptic Patients

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Introduction: Recently, narcolepsy has been suggested to be caused by the hypocretin deficiency. Structural changes in hypothalamus, where hypocretin producing neuron is located, have also been suspected in patients with narcolepsy. However, previous voxel-based morphometry (VBM) studies on narcolepsy have not replicated consistent results. The objective of the current study was to explore gray matter changes in young adults with narcolepsy using 3 Tesla magnetic resonance (MR) imaging.

Methods: Ten patients with narcolepsy and 15 age- and sex-matched healthy comparison subjects were recruited. Subjects older than 35 year were excluded to prevent potential confounding aging effects. Subjects with cormobid sleep disorders or psychiatric/medical disorders were also excluded. All narcoleptic patients had cataplexy and the HLA allele DQB1 *0602. MR images were acquired using 3 Tesla GE whole body system. VBM analysis was conducted for the comparison of gray matter densities between groups. In addition, grey matter densities in voxel of interest (VOI) at hypothalamus were calculated.

Results: Lower gray matter densities in the right thalamus and the right cerebellum in patients with narcolepsy, relative to healthy comparison subjects, were found on VBM analysis (all p<0.001). Gray matter density of VOI at hypothalamus were also decreased in patients with narcolepsy (p<0.05).

Conclusion: The current finding suggests that young adults with narcolepsy had the structural changes of thalamus and cerebellum, which are closely related with sleep-wake cycle and REM sleep. To a lesser degree, probably due to a small sample size, we found decrease of hypothalamic gray matter densities in young adults with narcolepsy.
**0648**

**Cataplexy And Frequency Of HLA-DQB1*0602 In Korean Narcoleptics**


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**Introduction:** Cataplexy, a sleep disorder characterized by excessive daytime sleepiness, hypnagogic hallucination, sleep paralysis, abnormal REM sleep and cataplexy has been known to be highly associated with the HLA DR2 and DQB1*0602. This study was designed to investigate the frequency of HLA-DQB1*0602 in the Korean narcolepsy patients, and to compare clinical features and frequency of DQB1*0602 of the narcolepsy patients with or without cataplexy.

**Methods:** The subject were 111 narcoleptic patients (mean age: 30.3 ± 14.7, 67 men and 44 women) who were confirmed by PSG and MSLT as well as clinical history and symptoms at the Catholic University of Korea, St.Vincent’s Hospital Sleep Disorders Clinic. Patients who were co-morbid with other hypnorsomnic sleep disorders such as sleep apnea or periodic limb movements during sleep were excluded. All patients have done HLA typing for the presence of DQB1*0602. Clinical variables were examined by semi-structured interview for narcolepsy patients.

**Results:** 1) Characteristic symptoms of narcolepsy were investigated as follows: excessive daytime sleepiness(100%), cataplexy(82%), hypnagogic hallucination(54.1%), sleep paralysis(57.7%). 2) Cataplexy-positive narcoleptics experienced more frequent hypnagogic hallucinations(P=0.002) and sleep paralysis(P=0.003). 3) In cataplexy-positive patients, compared with cataplexy-negative patients, manifested decreased sleep latency(2.1 ± 1.9 min. VS 3.0 ± 1.8 min.) and increased frequency of SOREMPs(3.1± 1.2 VS 2.9[*plusmn* 1.1]) but these differences were not statistically significant by MSLT. 4) The positivity of HLA-DQB1*0602 of all narcoleptic patients were 92 subjects(82.9%). In cataplexy-positive patients, compared with cataplexy-negative patients, the positivity of HLA-DQB1*0602 was found to be significantly increased(89.0% VS 55.0%).

**Conclusion:** Significant differences of clinical symptoms and frequency of HLA-DQB1*0602 between cataplexy-positives and cataplexy-negatives suggest that cataplexy-positive narcoleptics would be more etiologically homogenous group than cataplexy-negative group.

**0649**

**Basal Metabolic Rate And Autonomic Regulation At Rest In Human Narcolepsy**

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**Introduction:** Obesity is recognised as an associated symptom of narcolepsy. Human and animal studies suggested a lower basal metabolic rate or disturbed autonomic balance as its cause. We investigated both explanations.

**Methods:** Basal metabolic rate was measured in 15 male, medication free narcolepsy patients and 15 healthy controls matched for age, sex and BMI. Subjects lied prone, at rest but awake. Oxygen uptake (VO2) and carbon dioxide expiration (VCO2) were measured with an open-flow indirect calorimeter for 30 minutes in the morning while subjects were sober for at least 10 hours. Basal metabolic rate was calculated using the Weir equation. Blood pressure and ECG were continuously measured using a Finometer and ECG electrodes. Heart rate variability was quantified using the standard deviation of beat intervals.

**Results:** Basal metabolic rate did not differ significantly between patients and controls (t-test, p=0.54). Narcoleptic patients did have significantly more variation in heart rate (t-test, p=0.04). Diastolic and systolic blood pressures showed the same significantly increased variation (t-test, p=0.02).

**Conclusion:** We found no evidence for a lower basal metabolic rate in narcolepsy, but an increased variability of blood pressure and heart rate.

**0650**

**Nightly Administration Of Sodium Oxybate Is Effective For The Treatment Of Excessive Daytime Sleepiness In Narcolepsy**

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**Introduction:** As mounting evidence suggests the nightly administration of sodium oxybate to patients with narcolepsy is associated with improvements in excessive daytime sleepiness (EDS), the following placebo-controlled, double-blind study measured the efficacy of sodium oxybate, alone and in combination with modafinil, for the treatment of EDS in narcolepsy patients.

**Methods:** Narcolepsy patients currently using stable doses of modafinil for the treatment of EDS were enrolled. During the 8-week double-blind phase of this study, patients were randomized to receive sodium oxybate + placebo modafinil, placebo sodium oxybate + modafinil, sodium oxybate + modafinil, or placebo sodium oxybate + placebo modafinil. The sodium oxybate dose was 6 g nightly for the first 4 weeks, then 9 g nightly for the final 4 weeks. Except those receiving placebo, patients remained on their usual dose of modafinil. The primary measure of efficacy was the change in EDS as measured with the Maintenance of Wakefulness Test (MWT) while secondary measures included changes in Epworth Sleepiness Scale (ESS) scores and patient reports of weekly sleep attacks. The intent-to-treat population consisted of 222 patients.

**Results:** In patients receiving sodium oxybate alone, there was no difference in MWT scores compared to patients receiving modafinil alone (p < 0.001, p = 0.006 compared to placebo), suggesting the two were equally efficacious; however, combined drug therapies resulted in significant improvement in MWT scores (p < 0.001). Significant improvements in ESS and the frequency of weekly sleep attacks were only demonstrated in groups receiving sodium oxybate alone and in combination with modafinil (for each, p < 0.001) as were the investigator rated improvements in disease severity (p = 0.002, p = 0.023, respectively).

**Conclusion:** The results of this study indicate the sodium oxybate is an effective treatment for EDS associated with narcolepsy.

This research was supported by Orphan Medical, Inc.

**0651**

**Loss Of Hypocretin/Narp Neurons In Human Narcolepsy**

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**Introduction:** Previously, we have reported that human narcolepsy is linked to an approximately 90% loss of neurons immunostaining for the peptide hypocretin. It is not known whether this loss in the hypothalamus results from a failure of hypocretin synthesis or from a loss of the hypocretin synthesizing neurons. Narp (neuronal activity-regulated pentraxin) has been found to colocalize with virtually all hypocretin neurons in the lateral hypothalamus of the rat brain. Narps have also been found in...
other areas of the rat brain including the paraventricular and supraoptic nucleus of the hypothalamus, the habenula, hippocampus, basolateral nucleus of the amygdala and the lateral vestibular nucleus.

Methods: We investigated the distribution of Narp in normal and narcoleptic human post-mortem brain tissue using immunohistochemistry with an antibody to Narp. We also performed a colocalization study using hypocretin-1 and Narp antibodies in normal human hypothalamus.

Results: We found that Narp is present in the lateral hypothalamic area (LHA), the dorsomedial hypothalamic area (DMH), the dorsal hypothalamic area (DHA), and the posterior hypothalamic area (PHA) of the normal human and that it colocalizes with hypocretin in these areas. In the narcoleptic human brain, Narp stained cells are decreased by 89% in the LHA, DMH, DHA and PHA. Narp stained cells were also found in the paraventricular (Pa) and supraoptic (SO) nuclei of the normal human hypothalamus but were unaltered in the Pa and SO of the narcoleptic.

Conclusion: This study further supports the hypothesis that narcolepsy is caused by a loss of the actual hypocretin neurons and not by altered production or metabolism of the peptide hypocretin.

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0652 Sodium Oxybate Therapy For Narcolepsy Improves Patient Quality Of Life

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Introduction: Promising results of an open-label pilot study with sodium oxybate for the treatment of narcolepsy included improvements in sleep architecture, daytime sleepiness and cataplexy, prompting a larger, double-blind, placebo-controlled study. As no placebo-controlled sodium oxybate studies have yet evaluated changes in quality of life (QOL) in patients with narcolepsy, this study measured changes in this important outcome, while assessing the efficacy of this treatment for excessive daytime sleepiness and other symptoms.

Methods: In this double blind, placebo-controlled trial (N = 209), patients with narcolepsy/cataplexy weaned from any prior antidepressants, then randomized to receive 4.5, 6 or 9 g sodium oxybate or placebo in 2 equally-divided doses taken at bedtime and 2.5 to 4 hours later for 8 weeks. Patients receiving 6 and 9 g doses were titrated to their final dose. Efficacy measures included PSGs, MWTs and daily diaries. The Functional Outcomes of Sleep Questionnaire (FOSQ), the measure of QOL, was administered upon enrollment, following the baseline period, and after 4 and 8 weeks of treatment.

Results: Compared to placebo, patients randomized to receive 9 g sodium oxybate nightly demonstrated significant improvements in the FOSQ Total score as well as the General Productivity, Vigilance, Activity Level, and Social Outcome subscales (p<0.05), but not Intimacy/Sexual Relationships. The 6 g dose produced similar results with the exception of the General Productivity subscale. Active treatment was not superior to placebo for the 4.5 g dose for the FOSQ Total and all subscale scores.

Conclusion: Sodium oxybate, previously shown to improve narcolepsy symptoms as excessive daily sleepiness and cataplexy, at nightly doses of 6 and 9 g is also highly effective for elevating many aspects of daily functioning enhancing QOL in patients with narcolepsy.

This study was sponsored by Orphan Medical, Inc.

0653 Attenuated Amphetamine Induced Locomotor Sensitization In Hypocretin/Orexin-Deficient Narcoleptic Mice

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Introduction: Amphetamine abuse is very rare among narcolepsy patients who receive it chronically. To experimentally determine whether hypocretin/orexin-deficient narcolepsy is resistant to amphetamine abuse, we compared amphetamine-induced locomotor sensitization between preproorexin knockout (KO) and their littermate wild type (WT) mice, and between orexin/ataxin-3 transgenic (TG) narcoleptic and their littermate wild type mice.

Methods: Preproorexin KO (n=8; N8, C57BL/6-129SvEv backcrossed to C57BL/6) and orexin/ataxin-3 TG mice (n=8; N8, C57BL/6-DAB backcrossed to C57BL/6) and respective WT littermates (n=8 for each group) were used. Locomotor sensitization of amphetamine was assessed using a home cage monitoring system equipped with horizontal infrared red lights. Each mouse received saline (day -2, -1, -0) and d-amphetamine (2mg/kg, i.p.) injections from day 1 to 9 at ZT 4, and locomotor activity was monitored for 4 hours. On day 14, 21 and day 24, d-amphetamine challenges (2mg/kg, i.p.) and on 18 day and 26, saline challenges were applied and locomotor activity was monitored for 4 hours.

Results: Two-mg/kg amphetamine increased locomotor activity on day 1 in all groups (about 200% of the respective baselines). In WT mice, this effect was significantly enhanced (379 to 456%) during chronic amphetamine treatment, and similar enhancements were observed at amphetamine challenges even after the session of the chronic treatments. Additionally, saline injection challenges also increased locomotor activity in WT mice (201%). In contrast, an increase in locomotor activity was attenuated during the chronic 2mg/kg amphetamine session in both KO and TG narcoleptic mice (140 to 375%). Furthermore, only small increases in locomotor activity were observed at the saline challenges (130%) in these animals.

Conclusion: Both KO and TG narcoleptic mice are less responsive in developing amphetamine-induced locomotor sensitization, and the locomotor sensitization experiments are typically used to evaluate the susceptibility to stimulant abuses. The attenuated amphetamine-induced locomotor sensitization in these narcoleptic mice may indicate the resistance of the psychostimulant abuse in hypocretin deficient narcoleptics and that the hypocretin neurotransmission may be one of the critical factors for development of stimulant abuse.

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0654 Cholecystokinin Activates Orexin (Hypocretin) Neurons Through A CCKA Receptor

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Introduction: The human sleep disorder narcolepsy is accompanied by a loss of orexin production due to specific destruction of orexin neurons suggesting the importance of orexin neurons in the maintenance of arousal. However, little is known about the regulation of orexin neurons. Here we revealed the effect of sulfated octapeptide cholecystokinin (CCK-8S) on the activity of orexin neurons to apply electrophysiological and calcium imaging technique to orexin neurons.
Category K—Sleep Disorders-Narcolepsy

Methods: The transgenic mice which express a calcium sensing protein, cameleon, in orexin neurons were used for Ca2 imaging of orexin neurons. While the transgenic mice which express green fluorescent protein in orexin neurons were used for electrophysiological studies. Peptides affect the activity of orexin neurons were identified by Ca2 imaging. Further electrophysiological study using slice patch clamp revealed detail mechanism the action of peptides. All drugs were applied by bath application at room temperature. Immunohistochemical study showed the expression of the receptor on the orexin neurons.

Results: The Ca2 imaging study revealed that CCK-8S (10 nM) application increased intracellular calcium concentration in orexin neurons in a concentration dependent manner. In voltage clamp mode, CCK-8S induced an inward current in orexin neurons. A reversal potential of CCK-8S-induced current was near 0 mV suggesting an involvement of non-selective cation channel in this response. A CCKA receptor agonist lorglumide inhibited CCK-8S-induced current. On the other hand, a CCKB receptor selective agonist CCK-4 had little effect on orexin neurons suggesting that CCKA receptor is involved in this response. Immunohistochemical study showed CCKA receptor-immunoreactivity was observed on the orexin neurons.

Conclusion: CCK-8S activates orexin neurons through the CCKA receptor and an activation of the non-selective cation channels. An activation of orexin neurons by CCK might have an important role in the regulation of feeding behavior and sleep/wakefulness regulation.

0655

HLA Expression In Narcoleptic Hypothalamus

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Introduction: Narcolepsy is a sleep disorder that affects 1 in 2000 people. Its main symptoms include excessive daytime sleepiness, loss of muscle tone in response to emotional stimuli (cataplexy), and other abnormalities of rapid eye movement (REM) sleep. Narcolepsy is tightly associated with HLA-DQB1*0602, suggesting an autoimmune etiology. How HLA-DQB1*0602 and its possible role as an antigen presenting molecule in and outside the brain mediated narcolepsy and a potential destruction of hyporetin cells is unknown.

Methods: Postmortem frozen hypothalamic tissue were dissected and anterior and posterior parts collected separately. Six-8 control and 6-7 narcolepsy samples were used for the experiment. Total RNA was prepared from the collected tissue and cDNA was synthesized by Superscript II reverse transcriptase with random hexamer. Using quantitative real time PCR system, we simultaneously PCR-amplify each HLA transcript and internal control (GAPDH) with TaqMan probe, and calculated relative expression level of HLA-DRA, DRB1, DQB1 and related genes.

Results: HLA expression is detectable in the hypothalamus. DRB1 and DQB1 expression level was higher in narcolepsy versus controls in anterior or hypothalamus (and only marginally in the posterior hypothalamus). DRA expression, a non polymorphic HLA gene, was similar in both groups in both anterior and posterior hypothalamus. Further study is required to elucidate the role of individual HLA haplotypes in the observed changes.

Conclusion: We previously showed that the immune related transcripts including HLA class II were up-regulated in the anterior hypothalami of narcoleptic patients. Our results suggest a direct HLA involvement and immune abnormalities in the hypothalamus of narcoleptic patients. The finding of changes in the anterior but not posterior hypothalamus is surprising but concordant with our published prior postmortem data.

0656

The MSLT And MWT Sleep Latency Measure Is Not Related To Eventual Therapeutic Wake Promoting Agent Dosage

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Introduction: There is little data on the predictive value of the sleep latency measure of the MSLT and MWT in determining the eventual therapeutic wake promoting agent dosage that a patient will subsequently have to take. The aim of this study is determine whether eventual therapeutic dosage range of wake promoting agents can be predicted using the MSLT and MWT.

Methods: Study was a retrospective review of 20 patients diagnosed with Narcolepsy/Cataplexy by a consultant neurologist (8 men, 22 women, median age: 39, mean latency to diagnosis: 13.4 years) over a 12-month period. Each patient underwent a standard MWT (20min, 1 epoch of sleep, protocol) and MSLT as part of the assessment process. Patients were drug free at testing. Case notes were reviewed after a period of 6 months after testing. Patients on successful peak therapeutic wake promoting agents as detailed in case note reports were analysed. The medication regime was graded as low, moderate or high dosage based on pharmacological data and compared to the retrospective MSLT and MWT data using the Kendall rank correlation test.

Results: Mean MSLT time of 2.6mins and a mean MWT time of 5.7mins. Both data sets had a non-normal distribution before and after log transformation as determined by the Shapiro-Wilk test for non-normality (MWT: W=0.7907208, p=0.000475, MSLT: W=0.8259677, p=0.001683). Kendall's rank correlation between the MSLT and dosage grade, adjusted for ties, normalised statistic (Z) = 1.57024, two sided P = 0.1164. For the MWT and dosage grade, adjusted for ties, the normalised statistics (Z) = 0.4227569, two sided P = 0.6725. The null hypothesis of mutual independence is not rejected in both results.

Conclusion: Preliminary results suggest that neither the sleep latency parameter of the MSLT or MWT is mutually dependent upon the subsequent dosage of therapeutic wake promoting agents. Therefore we can conclude that the sleep latency measure of the MSLT and MWT does not predict eventual therapeutic medication dosage.

0657

Health-Related Quality Of Life In Patients With Narcolepsy: A Prospective Cohort Study

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Introduction: Though health related quality of life (HRQoL), measured by the SF-36, was demonstrated to be a valid prognostic measure in narcolepsy, no prospectively designed survey investigated the clinical course of the disease. Cross-section designed studies disclosed that most scales were impaired. Two clinical factors (excessive daytime sleepiness (EDS) and the disease duration inversely) determine this impairment. To disclose the evolution of HRQoL of patients with narcolepsy and the role of the state of mood as influencing factor, we performed a five-year prospective cohort study.

Methods: Fifty-four adults with narcolepsy (mean age 49 years; 77% men) from the sleep center of the Department of Neurological Sciences of Bologna, self-administered the 36-Item Short Form (SF-36) and the Zung’s depression scale in 1999 and 2004.

Results: Sex and age standardized score of role functioning-physical (RP), general health (GH), vitality (VT), social functioning (SF), role functioning-emotional (RE) and mental health (MH) were lower than the Italian
norm in the two observations (RP from -0.78 to -0.70, GH from -0.33 to -0.32, VT from -0.62 to -0.64, AS from -0.82 to -0.76, RE from -0.71 to -0.60, MH to -0.33 to -0.40). By means of multiple linear regression some of the variance of these scores (R2 from 0.35 to 0.67) were explained by sleepiness, measured by Epworth sleepiness scale (inverse correlation), state of mood (inverse correlation), disease duration (direct correlation).

Conclusion: This study, to our knowledge the first with a prospective design, disclosed that 1) RP, VT, SF and RE were the most impaired SF-36 scales in patients with narcolepsy; 2) the HRQoL profile was stable across five years of evolution of the disease; 3) together with subjective sleepiness and disease duration the mood state of patients seems to play a relevant role in influencing HRQoL. These findings strongly suggest the need for additional cognitive and behavioural therapies in narcolepsy.

0658
Rebound Cataplexy Following The Cessation Of Antidepressant Therapy In A Population Of Narcolepsy Patients
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Introduction: The abrupt cessation of antidepressant medications used for the treatment of cataplexy is associated with rebound cataplexy. Although a well-known phenomenon, information describing rebound cataplexy is derived from case reports. To date, no attempt has been made to describe rebound cataplexy in a population of narcolepsy patients following cessation of antidepressant drug therapy. A study measuring changes in cataplexy following the nightly administration of sodium oxybate provided an opportunity to describe rebound cataplexy in narcolepsy patients discontinuing antidepressant medications.

Methods: Prior to entering the double-blind treatment phase of the study, patients with narcolepsy/cataplexy were slowly weaned for safety reasons from antidepressant medications during a 21-day withdrawal period followed by a washout period lasting 5 days or 5 times the half-life of the discontinued drug, but not exceeding 18 days; however, an additional 2 weeks were permitted for withdrawal from fluoxetine. The washout period was followed by a 14-21 day baseline period, after which patients received 4.5, 6 or 9 g sodium oxybate or placebo nightly for 8 weeks. Of 226 patients enrolled in the trial, 71 were discontinued from antidepressant medications. This study was conducted in accordance with the ethical principles delineated in the Helsinki Declaration, revised 1997.

Results: The 71 patients using antidepressants provided a median of 17.8 weekly cataplexy attacks upon trial entry, increasing to 41.4 at the end of the washout period, decreasing to 39.5 at the end of the baseline period; however, at the end of the 8-week double-blind phase of the trial, the 67 patients completing the trial reported a mean of only 7.4 weekly cataplexy attacks. Patients receiving sodium oxybate displayed a dose-related decrease in weekly cataplexy attacks.

Conclusion: Gradual withdrawal from antidepressant therapy in resulted in significant rebound cataplexy in narcolepsy patients.

This study was sponsored by Orphan Medical, Inc.

0659
The Significant Placebo Effect Observed During Sodium Oxybate Clinical Trials May Result From Improved Sleep Hygiene
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Introduction: The importance of appropriate sleep hygiene in the treatment of sleep disorders, including narcolepsy, has been long advocated; however, the benefits of sleep hygiene are difficult to demonstrate. The following trials provided an opportunity to describe improvements in the symptoms of placebo-treated narcolepsy patients.

Methods: In an initial placebo-controlled study with 136 narcolepsy/cataplexy patients, subjects were randomized in blinded fashion to receive 3, 6 or 9 g sodium oxybate or placebo nightly for 4 weeks. The effect of sodium oxybate on weekly cataplexy attacks was measured using patient daily diaries. In a second placebo-controlled study with 228 narcolepsy/cataplexy patients, subjects were randomized in blinded fashion to receive 4.5, 6 or 9 g sodium oxybate or placebo nightly for 8 weeks. The effect of sodium oxybate on weekly cataplexy attacks was again measured using patient daily diaries.

Results: At the end of the first trial, 3, 6 and 9 g doses of sodium oxybate caused a median change in cataplexy of 49, 49 and 69%, respectively, while placebo-treated patients reported a 28% decrease. At the end of the second trial, 4.5, 6 and 9 g doses of sodium oxybate caused a median change in cataplexy of 57, 65 and 85%, respectively, while placebo-treated patients reported a 21% decrease. In both trials, the decrease in cataplexy was statistically significant compared to baseline. Placebo-treated patients also demonstrated less dramatic improvements in other narcolepsy symptoms.

Conclusion: The patients in these studies achieved substantial improvements in narcolepsy symptoms with appropriate drug therapy; however, we believe the structure that participation in these clinical trials added to patient lifestyle was also responsible for some improvement in patient symptoms, supporting the hypothesis that sleep hygiene may have a positive influence on narcolepsy symptoms.

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0660
The Prevalence Of SOREMPs In The General Population
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Introduction: Two or more sleep onset REM periods (SOREMPs) on a multiple sleep latency test (MSLT) has been used as one of the criteria for the diagnosis of narcolepsy and is thought to be specific to this disorder. However previous studies have shown the prevalence of SOREMPs in healthy volunteers and apnea patients to be higher than expected. The present study determined the prevalence of 2 or more SOREMPs in a representative sample and investigated potential associations with other sleep-related variables.

Methods: A population based sample of 333 subjects were assessed by nocturnal polysomnography and daytime MSLT (5 naps), and an additional 206 subjectively-sleepy people were also assessed (TOTAL=539). Sample demographics were comparable to the 2000 census. Epworth Sleepiness Scale (ESS) scores were also determined. Groups were formed based on a median split of each sleep variable (ESS, MSLT, total sleep time) for comparisons of SOREMPs in each group.

Results: Prevalence of 2 or more SOREMPs was 3.9%. Only MSLT was a discriminator for the presence of 2 or more SOREMPs (short latency=6.3%, long latency=1.9%, p<0.05). Amongst the subjects who had an MSLT≥5 minutes 9.5% had ≥2 SOREMPs.

Conclusion: The overall prevalence of two or more SOREMPs in the general population is 3.9%. Interestingly, of the variables assessed (MSLT, ESS and TST), objective sleepiness on the MSLT was the only measure significantly associated with ≥2 SOREMPs. Therefore subpopulations with excessive sleepiness (e.g. Shift workers, young adults, apnea patients) are likely to have a greater prevalence of SOREMPs.

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Introduction: Narcolepsy with cataplexy usually commences between 10 and 30 years of age. A study of French and Canadian narcoleptics suggested a bimodal age of onset with an earlier peak at 14-7 years and a later peak at 34.5-36 years (Neurology 2001;57:2029-2033). The aim of our study was to investigate the age of onset of narcolepsy with cataplexy in a large U.S. narcolepsy registry. We hypothesized that we would not find a bimodal distribution.

Methods: The Mayo Narcolepsy Registry was used to determine the age of onset of the disorder in patients with narcolepsy and definite cataplexy. Onset was taken as the age of occurrence of the first symptom, either sleepiness or cataplexy. Cases of secondary narcolepsy were excluded. 

Results: The age of onset could be determined in 295 patients. The distribution was skewed to the right but was not bimodal. The median age of onset was 16.0 years. The 25th percentile was 12.5 years, 75th percentile 25.7 years, and 90th percentile 33.4 years. The minimum age of onset was 4.0 years and the maximum 56 years. Age of onset did not differ between those patients who were HLA DQB1*0602 positive (111/135) and those who were negative (24/135). Gender and % HLA positivity were not significantly different between the groups with onset ≥30 and <30 years.

Conclusion: 90% of narcoleptics with cataplexy have disease onset before 33 years with median onset 16 years. Narcolepsy can start at an older age with a small percentage showing onset as late as 56 years. However, we did not confirm the presence of a bimodal distribution and % HLA positivity was the same for the groups of younger and older onset. The different results from the French and Canadian study may reflect different genetic populations.

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Effects On Daytime Sleepiness Of Combination Low-Dose Methamphetamine HCL And Modafinil In Narcolepsy

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Introduction: Narcolepsy is a chronic, often debilitating disorder characterized by excessive daytime sleepiness (EDS) and, commonly, sleep attacks. The mainstay of treatment is the use of stimulant medication to decrease EDS. Modafinil and methylphenidate are currently widely used. Methamphetamine HCL (Desoxyn), introduced in the 1930s, is well known to sleep specialists. Some patients are not adequately treated with single agents so we evaluated the efficacy of combination therapy.

Methods: Ten patients 18-64 years old who met ICSD criteria, on a stable dose of modafinil were treated in crossover fashion with methamphetamine HCL 5 mg BID and 10 mg BID for one week with a one-week washout between treatments. Subjects underwent overnight polysomnography and Maintenance of Wakefulness Testing (MWT) at baseline and at the end of each treatment period.

Results: MWT results were significantly improved with methamphetamine HCL relative to baseline at 5 mg (15.9 ±1.0 mins; < 0.002) and at 10 mg (16.4 ±1.1 mins; < 0.001) compared to baseline (10.9 ±1.0 mins). There was no significant difference between the two treatment doses. Latency to persistent sleep was increased over baseline at 10 mg (22.6 ±3.6 mins vs. 10.1 ±3.4 mins; < 0.022) but not at 5 mg. no values were clinically problematic. Total sleep time decreased from baseline for the 5 mg and 10 mg, by 10 and 20 minutes, respectively. Subjective efficacy of both doses was also seen on the ESS at 5 mg (11.7 ±1.2; p< 0.04) and 10 mg (8.2 ±1.3; p< 0.001) compared to baseline (15.5 ±1.2).

Methamphetamine HCL was well tolerated with no subject withdrawals from the trial and minimal adverse events.

Conclusion: Methamphetamine HCL was effective in improving objective and subjective measures of daytime alertness in narcoleptic patients taking a stable dose of modafinil.

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Idiopathic Narcolepsy-Cataplexy Responsive To Plasmapheresis

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Introduction: The HLA association and loss of hypocretin neurons in human narcolepsy suggest a possible autoimmune etiology. Recent reports suggest therapeutic effects of immunotherapies when applied close to symptom onset. We report a case of late-onset idiopathic narcolepsy-cataplexy in a 60 year-old woman, with transient response to plasmapheresis instituted within 2 months of presentation.

Methods: The clinical course and treatment response in a patient with a delayed diagnosis of narcolepsy-cataplexy are described.

Results: Perplexing sleep attacks and severe, intermittent muscle weakness brought on by emotions and occurring spontaneously, progressed rapidly over a 2 week-period. Physical examination, laboratory work, MRI and EEG were unrevealing and she was eventually hospitalized for rapid progression of muscle weakness (75 attacks/day). A right apical lung lesion was identified on CT, leading to a workup for paraneoplastic syndrome. Comprehensive antibody testing was negative, and although the lesion was found to be PET-negative, it was resected and found to be benign. In the midst of this workup and without a clear diagnosis, a trial of exchange plasmapheresis was performed [8 U (250 cc) 5% albumin/day x 5 days] with dramatic (80%) improvement in muscle weakness. Three days later however, symptoms recurred. An additional course of plasmapheresis was performed as an outpatient, with favorable effects, but was interrupted due to a catheter infection. At this point, the diagnosis of narcolepsy was considered and confirmed by MSLT (MSL 1.85 min, 2 SOREMPs) and HLA-DRB1*1501 positive typing. She was initially treated with antidepressants and stimulants, but was switched to sodium oxybate, with more complete attenuation of symptoms.

Conclusion: This is the first reported case of narcolepsy-cataplexy responding to plasmapheresis. Given previous reports using IVIg, our case further supports a possible immune-mediated mechanism for narcolepsy.
0665
A New Tool To Measure Insomnia: The Sleepmed Insomnia Index (SMI)
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Introduction: 80 million Americans suffer with some degree of insomnia. Insomnia causes impairment of daytime function, mood, quality of life, and functional status. The SleepMed Insomnia Index (SMI) is a new tool to provide clinical measurement of a subject’s severity of insomnia.

Methods: A total of 543 adults (ages 31-63 years) presenting to the sleep clinic for evaluation were administered the SMI. Sleep disorders were established by clinician’s assessment and diagnostics: insomnia(90), obstructive sleep apnea (OSA) on CPAP(158), OSA not on CPAP(127), narcolepsy(39), idiopathic hypersomnia(66), restless legs syndrome(20), fibromyalgia(12), depression(5), pain(4), and other(22). There were 50 normal controls with no history of medical, psychiatric, or medication related abnormalities. The SMI is a 10 item questionnaire administered to patients at their clinic visit and to normal controls. Questions are scored on a scale of 0(no problem with sleep) to 4(big problem with sleep). Totals range from 0-40 with higher scores indicating more severity.

Results: Mean scores with standard deviations for the groups were insomnia 31(5), OSA on CPAP 12(8), OSA not on CPAP 17(9), narcolepsy 17(9), idiopathic hypersomnia 13(8), restless legs syndrome 17(9), fibromyalgia 21(10), depression 24(10), pain 31(12), other 13(8), and control 5(3). Mean scores for the insomnia group were 31 and 31 generally below 20. SMI scores above 20 are, therefore, felt to be indicative of an insomnia component. ANOVA revealed that there were significant differences in scores between diagnostic groups and normal controls (p<0.001).

Conclusion: SMI is a useful measure as a screening tool for sleep disorders and differentiates as well as quantitates an insomnia component. This is a new tool to provide clinical measurement of a subject’s severity of insomnia.

0666
Sleepmed Insomnia Index(SMI) As An Outcome Measure In Treated Insomnia
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Introduction: This is a retrospective study to examine the use of the SMI in evaluating treatment outcomes in patients with idiopathic insomnia. A standard tool to measure insomnia outcomes would enhance the ability of a clinician to successfully assess and manage subjects with insomnia. Outcome measures should select a range of variables including sleep, mood, and quality of life. SMI is a simple, quick ten question self-administered tool to assess in general, patient insomnia symptoms.

Methods: A total of 17 adult subjects were administered the SMI. Each subject was judged to have an isolated diagnosis of insomnia using ICSD criteria. The subject was treated with zolpidem and was asked to complete the questionnaire first assessing sleep with drug therapy (at present). Each subject was administered the Epworth Sleepiness Scale (ESS). Subjects also completed the questionnaire assessing sleep off drug therapy. There were 50 normal controls with no history of medical, psychiatric or medication related abnormalities.

Results: SMI scores for the 17 subjects were compared on drug, off drug, and with ESS on drug. Ages ranged from 31-63. Mean scores with standard deviations on zolpidem 12(7); off zolpidem 34(5); and ESS 5(3). ANOVA revealed that there were significant differences (p<0.001) between groups. SMI mean score for normal subjects was 5(3). Statistical analysis with t-tests comparing SMI scores between groups and normal controls was significant (p<0.001).

Conclusion: The SleepMed Insomnia Index is a tool that provides assessment of patient outcomes in the management of insomnia. Zolpidem produced significant improvement in insomnia symptoms. Patients treated with zolpidem did not experience hypersomnolence as measured by ESS.

0667
Behavioral Insomnia Therapy For Fibromyalgia: Final Report
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Introduction: Fibromyalgia (FM) is a debilitating condition characterized by widespread pain, fatigue, low mood, and sleep disturbance. FM therapies have largely ignored the sleep complaints associated with this condition. This trial tested the efficacy of cognitive behavioral insomnia therapy (CBT) with FM patients.

Methods: Enrollees (45 women, 2 men; MAge = 48.6±8.2 yrs.) met ARC criteria for FM and had insomnia > 1 month, ≥ 60 minutes of total wake time (TWT) per night, and no primary sleep disorders or other psychiatric medically-based sleep problems. Baseline assessment included sleep logs (2 weeks), actigraphy (1 week), and questionnaires (pain, mood, health status). Enrollees then completed 6 weeks of CBT (n = 18) therapy, a sleep hygiene (SH) treatment (n = 18), or continued with their standard FM care (SC; n = 11). Measures taken at baseline were repeated immediately after treatment and again 6 months later.

Results: Forty-one patients completed therapy and 20 completed follow-up. ANCOVAs showed significant effects for log measures of TWT (F [2, 39] = 6.63, p = .003) and sleep efficiency-SE (F [2, 39] = 6.50, p = .004), actigraphic measures of sleep latency (F [2, 34] = 3.9, p = .03), and measures of mood (F [2, 39] = 3.21, p = .05), pain (F [2, 37] = 3.81, p = .03), and general mental health (F [2, 29] = 5.96, p = .007). A posteriori comparisons showed CBT out-performed SC whereas SH did not. Sleep log (TST ≥ 6½ hours + TWT < 60 minutes + SE ≥ 85%) and actigraphic (TST ≥ 6½ hours + TWT < 45 minutes + SE ≥ 85%) indicators of clinical improvement showed a significantly greater % of CBT patients were rated improved after treatment than were those in the other two groups.

Conclusion: CBT improves sleep and other symptoms of FM patients.
the Sleep Matrix. Seventeen adults with insomnia by ICSD criteria on/off zolpidem were scored. Twenty-two normal controls with no history of medical, psychiatric, or medically related abnormalities were scored.

**Results:** Means with standard deviations of untreated primary insomnia were SMI 34(5) and ESS 7(4). On zolpidem means were SMI 12(7) and ESS 5(3). Normals were SMI 4(4) and ESS 5(3). T-tests comparing SMI scores of normals with patients both on/off zolpidem were significant (p<0.001). Zone plots into the matrix positioned the untreated insomnia group in the following regions: insomnia(14), sleepiness with sleep disruption(3). Zone plots for the normal controls were: normal(19), sleepy(1), and nonsleepy with nonrestorative sleep(2). Zone plots for patients on zolpidem were: normal(7), nonsleepy with nonrestorative sleep(8), sleepy with nonrestorative sleep(1) and insomnia(1). Group outliers for the expected regions based on the means in the matrix were minimal.

**Conclusion:** Zones of the two dimensional matrix quickly quantitate a patient’s sleep complaint. The Sleep Matrix is a visual screening tool that can be used as a sleep vital sign, characterizing severity of a sleep disorder, degree of sleep disruption, and residual daytime sleepiness. This may allow the clinician to determine diagnostic and treatment options as well as decide upon the need for referral. Our patients with idiopathic insomnia had normal ESS results.

**0669**

**What Beliefs About Sleep Discriminate Those With Insomnia From Good Sleepers?**

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**Introduction:** A previous study showed the Dysfunctional Beliefs about Sleep (DBAS) scale could be used to discriminate between older insomnia sufferers and age-matched normal sleepers. The present study re-evaluated the DBAS for discriminative value using an expanded age range (20 - 79 years old; M = 48.42; SD = 16.88).

**Methods:** The 30-item DBAS was administered to a sample meeting insomnia criteria on a structured sleep disorders interview (N = 102) and gender-matched, non-complaining normal sleepers (N = 106), who were screened for medical, psychiatric and other sleep disorders that could affect sleep.

**Results:** To identify items that differentiated insomniacs from normal sleepers, analyses of variance (ANOVA) were conducted on each of the 30 items of the DBAS. There was a statistically significant difference between insomniacs and normals on 16 items. To determine what items most strongly discriminated between those with and without insomnia, the 16 items with statistically significant ANOVAs were entered into a multiple stepwise regression equation. Six of the sixteen items were retained in the regression analysis, accounting for approximately 41.9 % of the variance. To test for group and gender effects, ANOVAs were conducted on the DBAS-6, DBAS-10, DBAS-16 and DBAS-30; all four ANOVAs revealed a statistically significant group effect, only the DBAS-10 demonstrated a significant gender effect, and there were no significant interactions. The effect sizes were greater for the 6- and 16-item DBAS than the 30- or 10-item DBAS (eta squared = .34, .25, .17, and .12 respectively). Internal consistency was highest for the 30-item version (Cronbach’s alpha = .816), followed by the DBAS-16 (.808), the DBAS-10 (.723), and DBAS-6 (.629).

**Conclusion:** This study found that a 16-item DBAS was most useful for discriminating insomnia sufferers from good sleepers, and demonstrated good internal consistency.
Results: Results of the formative evaluation process suggest that implementing BSM programs in medical settings can be challenging, yet are well received by sleep physicians and patients alike. Pilot study results are consistent with other studies evaluating the effectiveness of other short-term, multi-component, cognitive-behavioral treatment interventions for insomnia. In this study, each of the 3 patients exhibited visually significant improvement in their PSQI scores.

Conclusion: The primary goal of the current study was to investigate and describe the process of implementing and evaluating a BSM program in pre-existing sleep center to facilitate the development of similar programs in other sleep disorders centers. Although the increasing need for BSM treatment is well documented in the literature, few sleep disorders centers offer this treatment option. Implementing CBT insomnia programs in medical settings can be challenging and typically involves several intertwined steps. These steps include, but are not limited to, developing the treatment program, working collaboratively with sleep center staff to implement the proposed program, establishing referral sources, and educating medical staff and the community about BSM. The study suggests that many primary care physicians are unaware of the efficacy of CBT for insomnia and may not readily refer patients for such services. The study suggests a need for extensive community and medical education regarding the efficacy and patient receptiveness to CBT for insomnia.

0672 Changes In POMS, GDS, And Epworth In Response To Light Treatment For Insomnia In Older Adults
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Introduction: Dysphoric mood and daytime sleepiness frequently accompany insomnia. In testing light treatment efficacy in older insomniacs, we hypothesized: 1) greater mood and sleepiness improvement with bright light (10,000 lux, BRIGHT) compared to dim light (<30 lux, DIM); 2) baseline (BL) mood/sleepiness measures predict sleep improvement at end of 12-week treatment (END).

Methods: 51 community-dwelling primary insomnia subjects (36 women/15 men; mean age=63.6±7.1 y; mean education=16.2±2.3 y) completed questionnaires at BL and END. Epworth Sleepiness Scale (ESS) assessed sleepiness; Geriatric Depression Scale (GDS), depression; Profile of Mood States (POMS), tension-anxiety (T) and depression-dejection (D) dimensions. Subjects completed 7 days of wrist actigraphy at BL and END. Mood and sleepiness were analyzed within light conditions at BL and END using paired comparisons (Wilcoxon signed-rank); we also conducted between-group comparisons (Mann-Whitney U) BRIGHT (N=37) vs DIM (N=14) on these measures. Correlations (Mann-Whitney U) were performed between BL mood/sleepiness and END-BL change in sleep variables.

Results: There were no BL age, education, mood, sleepiness, sleep variables between-group differences. BRIGHT END scores declined on GDS (3.8 ± 2.8 to 2.1 ± 2.9***), ESS (7.1 ± 4.8 to 5.1 ± 3.8***), POMS-D (5.3 ± 6.0 to 2.8 ± 5.2**), POMS-T (6.0 ± 4.5 to 3.0 ± 2.8**). In DIM only ESS declined (8.9 ± 2.9 to 7.1 ± 4.1**). BRIGHT at END showed greater reductions than DIM for GDS and POMS-T***. In testing predictive value of BL measures, BL POMS-T positively correlated with END gain in Sleep Efficiency (SE)*** and negatively with Wake After Sleep Onset (WASO)*; POMS-D negatively with WASO* and Sleep Latency* positively with SE*; ESS positively with Time In Bed* and Total Sleep Time*. DIM BL mood/sleepiness and END sleep measures did not correlate. *p<0.05, **p<0.01, ***p<0.001.

Conclusion: Greater mood/sleepiness improvement in BRIGHT vs. DIM at END suggest light intensity contributes to mood/sleepiness amelioration. Worse BL mood/sleepiness predicted greater sleep improvement for BRIGHT but not DIM. These findings raise the possibility that mood/sleepiness improvement is a main effect of bright light. The question remains if improved mood/sleepiness results from improved sleep with higher light intensity or the converse. Subjects scored below pathological range on all mood/sleepiness measures. The findings suggest minimal dysphoria/ sleepiness indicators predict bright light treatment response.

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0673 Family Incidence As A Predisposing Factor Of Insomnia
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Introduction: Although a family history of insomnia is often reported by individuals with insomnia, data regarding this possible predisposing factor are sparse, and derived from relatively small convenience samples. Our objective was to examine family incidence of insomnia in a large population-based sample.

Methods: Participants were French-speaking adult residents of the province of Quebec who took part in a longitudinal study on the natural history of insomnia. Of the initial sample, 997 individuals completed several self-report questionnaires. Of those, 36 were excluded because they reported another sleep disorder. The final sample comprised 961 adults (aged 18-83, M = 43.9; 60% women). Respondents were categorized into three sleep/insomnia subgroups using an algorithm based on DSM-IV and ICD-10 diagnostic criteria for insomnia: 1) good sleepers (n= 444); 2) insomnia symptoms (n= 266); 3) insomnia syndrome (n= 251). Family incidence was measured by two questions asking whether any member of the family had a current sleep problem or had experienced one in the past.

Results: A total of 38.3% reported having at least one first-degree relative (parents, siblings, children) with current or past insomnia, while 25.8% reported at least one of the parents with an insomnia history. The respondent's mother was the family member most frequently afflicted by insomnia (20.1%), followed by sisters (11.5%). Family incidence rates for first-degree relatives by subgroups were: good sleepers: 32.9%; insomnia symptoms: 40.6%; insomnia syndrome: 45.5%. Family incidence rates for parents only were: 19.6%, 28.6%, and 30.7% respectively. Good sleepers were further divided into two subgroups according to whether they had reported insomnia in the past (n = 71) or not (n = 373). Those with a past history of insomnia reported a higher family incidence than those who did not, both for first-degree relatives (50.7% vs. 29.5%) and for parents only (28.2% vs. 18.0%).

Conclusion: Results suggest that a family history of insomnia is more frequent among individuals with insomnia than good sleepers. The observation that insomnia is more frequent among mothers and sisters is consistent with the higher prevalence of insomnia among women.

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0674 Morningness / Eveningness And CBT For Insomnia
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Introduction: Misalignment of the circadian rhythm with the external environment is estimated to account for 5-10% of insomnia cases. Little
is known about the effects of circadian rhythm on the efficacy of cognitive behavioral therapy for insomnia (CBT-I). This study explores the relevance of circadian tendencies to CBT-I treatment in a sleep disorders clinic patient sample.

**Methods:** 569 patients (age >18 years) attending group CBT-I completed the following measures: Composite Scale (CS; Smith et al., 1989) to assess circadian rhythms, Dysfunctional Beliefs and Attitudes About Sleep (DBAS), Beck Depression Inventory (BDI), Insomnia Severity Index (ISI), and items adapted from Seligman’s Consumer Reports Survey. Higher CS-scores correspond to more morningness. The sample was subdivided into morningness (MOR, 20%), eveningness (EVE, 7%), and intermediate (INT, 73%) subgroups, based on validated CS cutoff scores.

**Results:** CS scores were negatively correlated with the severity of sleep-onset insomnia, and positively correlated with the severity of sleep-maintenance and early morning insomnia (p<.05). CS scores were negatively correlated with participants’ perceptions of the negative consequences of poor sleep (ISI impact-component, r(157)=−.21, p<.01; DBAS factor1; and factor2 r(576)=−.16, p<.05). CS was significantly correlated with depression severity (BDI, r(520)=−.75, p<.0001). BDI scores were significantly correlated with maintenance insomnia (r(110)=.24) in the INT but not MOR or EVE groups. Satisfaction with treatment was significantly correlated with CS (r(270)=−.14, p<.05).

**Conclusion:** Morningness was associated with lower treatment satisfaction. The proportion of the morning types found in the clinic sample was twice that found in a normative college-aged sample. Increased eveningness was associated with greater depression symptom severity and dysfunctional beliefs about sleep. The results suggest that tailoring CBT-I for specific circadian rhythm subtypes might enhance treatment outcome. This includes adding strategies for delaying the circadian phase of patients with morningness tendencies and addressing depressive symptoms and dysfunctional cognitions for insomniacs with eveningness tendencies.

**0675**

**Sleep Maintenance Insomnia And Nasal Flow Limitation; A Randomized Treatment Study**

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**Introduction:** How should subjects be treated who present with sleep-maintenance insomnia and have upper airway flow limitation during polysomnography (PSG)?

**Methods:** Thirty patients (18 women) who complained of sleep-maintenance insomnia and whose PSG demonstrated an apnea-hypopnea index (AHI) <5 and SaO2 >92% but had a respiratory disturbance index (RDI) ≥5, were randomized with stratification into two treatment groups. All subjects had clinical interviews, ENT & orthodontic evaluations, 15 days of sleep logs, sleep questionnaires, Beck’s depression inventories, and cephalometric X-rays. Initial treatment: group A: 90 minutes/week for 8 weeks of cognitive-behavior therapy for insomnia and sleep clinic follow-up; group B: surgical (ENT or orthodontic) treatment of upper airway problems. Both groups then crossed-over after reevaluation of symptoms. Surgeries considered after specialized consultation (groups A, B): Adenotonsillectomy with: -Radiofrequency (RF) of turbinate n=10 (5.5) -Uvulo-flap with turbinate treatment n=7 (3.4) -Nasal septoplasty n=5 (3.2) -RF base of tongue n=2 (1.1) Septoplasty with RF turbinate treatment n=3 (1.2) Uvulo-flap with maxillo-mandibular distraction osteogenesis n=3 (2.1)

**Results:** At enrollment, 24 subjects complained of sleep maintenance problems, while 6 had sleep onset and maintenance insomnia. All subjects finished phase 1 of their treatment. Both groups reported improvement of nocturnal sleep and daytime activities. Group A: complaints of sleep onset insomnia were eliminated; but all reported persistence of awakenings during sleep despite better acceptance of these sleep disturbances, and persistence of daytime fatigue. All subjects then crossed over to phase 2. Group B: all subjects reported disappearance of daytime fatigue and longer total sleep time; 7 reported complete elimination of sleep problems post surgery and refused phase 2, 8 subjects (3 sleep-onset insomniacs, 5 subjects with persistent early awakenings) underwent phase 2.

**Conclusion:** Anatomical abnormalities of the upper airway may lead to chronic sleep-maintenance insomnia, that can be controlled by upper airway surgery.

**0676**

**Nocturnal Interleukin-6 (IL-6) And Leptin Excretion In Patients With Primary Insomnia**

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**Introduction:** There is increasing evidence that besides many hormones the functioning of the immune system and the sleep wake cycle are correlated and influence each other reciprocally. In the present study we investigated whether there is a difference in evening/nocturnal Interleukin-6 production and secretion of the peptide Leptin in patients with primary insomnia (PI) compared to healthy controls (HC).

**Methods:** IL-6 and Leptin excretion were studied in 11 patients with PI (age: 42.5 ± 10.1 years; 9 females, 2 males) and 11 age- and gender matched HC. Patients were drug-free for at least 7 days prior to the study. Insomnia duration was 7.1 ± 1.6 years. The PSQI score averaged 11.7 ± 2.9. All healthy controls had PSQI values below 5. All subjects slept for 3 nights in the sleep laboratory with blood sampling in the third night from 19.00 hours in the evening to 9.00 hours in the morning. IL-6 and Leptin were measured every two hours.

**Results:** Comparing polysomnographic data for all 3 nights with ANOVA, the following differences were found: sleep efficiency was significantly decreased (p < 0.05), sleep latency was significantly increased (p < 0.05), total sleep time decreased (p < 0.05) and total REM density increased (p < 0.05) in PI compared to HC. Leptin excretion did not differ between healthy controls and primary insomniacs at any of the measurement points. IL-6 excretion was significantly enhanced in patients at 3.00 a.m., 5.00 a.m. and 7.00 a.m. (p < 0.05 at each measurement point).

**Conclusion:** In a sample of 11 PI patients we did not find any differences with respect to Leptin excretion during the night. In contrast, IL-6 excretion was significantly increased during the night, indicating a dysfunction of the immune system in patients with primary insomnia.

**0677**

**Therapeutic Alliance And Patient Expectations As Predictors Of Outcome In Group CBT For Insomnia**

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**Introduction:** With growing evidence for the efficacy of cognitive-behavioral therapy for insomnia (CBT-I), it is important to identify patient and therapist attributes that may contribute to treatment outcome. This study examined the role of the therapeutic alliance and patients’ expectations about the efficacy of treatment in predicting treatment outcome.

**Methods:** Participants were 39 men and 47 women participating in group-CBTI. Patients’ perceptions of the therapeutic alliance were assessed following the first session with items from the Group Therapy Session Report (GTSR). Patients’ treatment expectations were assessed at...
the end of session 2. The GTSR has two conceptual subscales: "Directive" (average of 4 items: active, confrontive, critical, and directive) and "Friendly" (average of 4 items: receptive, supportive, tolerant, and understanding). During the last (7th) session, patients completed an adaptation of Seligman's Consumer Reports Survey by rating the extent to which treatment helped alleviate insomnia (1 item) and improve daytime functioning (average of 7 items: energy, productivity, coping, enjoyment, helpfulness, self-esteem/confidence, and mood).

**Results:** 87% of the participants attended at least 3 of the first 6 sessions, but outcome data were available for only 46% of the initial sample. Those with post-treatment data had expectation and alliance ratings similar to those without it and not different from those who attended at most 3 sessions. A regression analysis, with expectation and the Directive and Friendly GTSR subscales as predictors, revealed that only therapist directiveness predicted improvement in insomnia ($\text{beta}=0.58$, $p<0.001$, $R=0.60$). Similarly, therapist directiveness was the only predictor of improvement in daytime functioning ($\text{beta}=0.53$, $p<0.01$, $R=0.44$).

**Conclusion:** In the context of group CBT-I, patients' perception of the therapist as directive was positively associated with clinical improvement. Although therapist's directiveness might be detrimental in some forms of general psychotherapy, it is possible that a friendly-directive style is well suited for group CBT-I.

**0678**

**A Pilot Study Examining The Utility Of The Cognitive-Behavioral Model Of Insomnia In Early Stage Breast Cancer Patients**

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**Introduction:** Insomnia is a common and distressing issue reported by breast cancer patients. The main purpose of this pilot study was to investigate the utility of the cognitive-behavioral model in understanding insomnia in breast cancer patients. The hallmark of the cognitive-behavioral model is its assertion that dysfunctional sleep-related cognitions and poor sleep hygiene developed in reaction to sleep disturbance can serve to maintain and exacerbate insomnia after precipitating factors occur. The secondary purpose of this study was to investigate associations between insomnia and breast cancer symptoms, mood disturbance, and quality of life.

**Methods:** Participants were 38 women with early stage breast cancer. 20 patients met criteria for insomnia and 18 did not meet criteria for insomnia, as determined by the Structured Interview for Sleep Disorders (SIS-D). Participants completed a series of questionnaires assessing dysfunctional sleep-related cognitions, poor sleep hygiene, mood disturbance, and quality of life. They also completed standard sleep logs that also assessed breast cancer symptoms (pain, fatigue, and number of hot flashes) daily for 7 days.

**Results:** Results indicated that the breast cancer patients with insomnia reported significantly higher levels of dysfunctional sleep-related cognitions ($p<0.009$) and poor sleep hygiene ($p<0.001$) than patients without insomnia. Patients with insomnia also reported significantly higher levels of daily pain ($p<0.01$), daily fatigue ($p<0.001$), anxiety ($p<0.001$), and depressive symptoms ($p<0.001$) and lower levels of quality of life ($p<0.001$). There were no group differences in number of hot flashes ($p=0.17$).

**Conclusion:** Considering the heightened level of dysfunctional sleep-related cognitions and poor sleep hygiene in the insomnia group, these findings suggest that early stage breast cancer patients with insomnia may benefit from cognitive-behavioral interventions for insomnia. These findings also indicate that insomnia is associated with poorer clinical status and overall quality of life.

**0679**

**Double-Blind, Placebo-Controlled Outpatient Clinical Trial Of Ramelteon For The Treatment Of Chronic Insomnia In An Elderly Population**

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**Introduction:** Ramelteon is a novel highly selective MT1/MT2 receptor agonist being studied for the treatment of insomnia. This study evaluated the efficacy of ramelteon in elderly patients with chronic insomnia.

**Methods:** A total of 829 elderly patients (aged 63-94 years, mean, 72.4 years; 341 men, 488 women) with chronic primary insomnia (defined by DSM-IV-TR) were randomized to receive double-blind ramelteon 4 mg, 8 mg, or placebo every night for 5 weeks. There was a 7-night single-blind placebo lead-in period, and a 7-night single-blind placebo run-out period (to evaluate possible rebound insomnia and withdrawal effects). Patients completed sleep diaries and Benzodiazepine Withdrawal Symptom Questionnaire (BWQS). Least square means were calculated for comparison analyses. The primary endpoint was patient-reported sleep latency for Nights 1-7 (Week 1).

**Results:** Six hundred ninety-three patients completed the trial. Patients treated with ramelteon reported statistically significant reductions in sleep latency at Week 1 compared to those treated with placebo (4 mg: 70.2 vs. 78.5 min; $p=0.008$; 8 mg: 70.2 vs. 78.5 min; $p=0.008$). Similarly, total sleep times at Week 1 were longer with ramelteon 4 mg (313.9 min vs 324.6; $p=0.004$) and 8 mg (313.9 vs 321.1 min; $p=0.055$). Ramelteon-treated patients (4 mg and 8 mg groups combined) experienced statistically significant reductions in sleep latency vs. placebo at Week 1 ($p=0.009$), Week 3 ($p=0.013$) and Week 5 ($p<0.001$). Sleep quality, number of night-time awakenings, and ease of falling back to sleep were not significantly different between ramelteon and placebo. Rebound insomnia did not occur, and no withdrawal effects were observed. Adverse event rates were similar for all treatment groups.

**Conclusion:** Elderly patients with chronic insomnia reported statistically significant reductions in time to fall asleep, with no rebound insomnia or withdrawal effects, over 5 weeks of treatment with ramelteon.

Funded by Takeda Pharmaceuticals.

**0680**

**Double-Blind, Placebo-Controlled Polysomnography And Outpatient Trial To Evaluate The Efficacy And Safety Of Ramelteon In Adult Patients With Chronic Insomnia**

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**Introduction:** Ramelteon is a novel selective MT1/MT2 receptor agonist being studied for the treatment of insomnia. This study evaluated the efficacy of ramelteon in patients with chronic insomnia.

**Methods:** In this 35-night double-blind study, 405 patients (mean age, 39.3 years) with primary insomnia (defined by DSM-IV-TR) took ramelteon 8 or 16 mg or placebo every night. Patients were evaluated in the sleep laboratory on Nights 1-2, 15-16, 29-30, and 36-37 using polysomnography (PSG) and a post-sleep questionnaire, and at home all other nights using a sleep diary. Placebo was given on Nights 36-37 to
evaluate possible rebound insomnia and withdrawal effects.

**Results:** A statistically significant reduction in mean latency to persistent sleep was observed with ramelteon 8 and 16 mg vs. placebo, as measured by PSG: Nights 1-2 (32.2 and 28.9 vs. 47.9 minutes; P<.001), Nights 15-16 (32.6 and 27.9 vs. 45.5 minutes; P<0.001), and Nights 29-30 (31.5 and 29.5 vs. 42.5 minutes, P=0.003). On Nights 1-2, ramelteon resulted in statistically significant improvements in total sleep time (394.2 and 397.6 vs. 375.2 minutes; P<0.001) and sleep efficiency (82.3 and 83.4 vs. 78.3%; P<0.001). Subjective results were supportive of PSG data. No rebound insomnia or withdrawal effects were observed. Adverse event rates were similar for all treatment groups.

**Conclusion:** Ramelteon 8 and 16 mg resulted in a statistically significant reduction in latency to persistent sleep in patients with chronic insomnia, with no rebound insomnia or withdrawal effects.

Funded by Takeda Pharmaceuticals.

**0681 Efficacy And Tolerability Of Indiplon-IR In Elderly Patients With Primary Insomnia**

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**Introduction:** The efficacy and tolerability of the immediate release (IR) formulation of indiplon, a GABA A potentiator, was evaluated in elderly patients with primary insomnia.

**Methods:** Patients ages 65-80 years old (N=358) who met DSM-IV criteria for primary insomnia, and who reported a latency to sleep onset (LSO) ≥45 min and total sleep time (TST) ≥6.5 h on ≥3 nights/week were enrolled. Following a 2-week, single-blind, placebo lead-in period, patients were randomized to 2 weeks of double-blind treatment with indiplon-IR 5mg, 10mg or placebo. Patients completed daily sleep logs which included LSO, TST; wake after sleep onset (W ASO); number of awakenings (NA), and sleep quality. Discontinuation effects were evaluated using the Benzodiazepine Withdrawal Symptom Questionnaire (BWSQ).

**Results:** Compared to placebo, both indiplon-IR doses significantly reduced mean LSO during both weeks (5mg: 34.6±1.8 and 32.7±2.0; 10mg: 30.4±1.6 and 31.2±1.9; placebo: 47.7±2.5 and 40.2±2.4; p < .0001 to .01). TST, NA and sleep quality were also significantly better during both weeks with both doses as compared to placebo (all p < .001). WASO was reduced in the 10mg group at both time points (p < .0001 and p=.011). Low percentages of patients discontinued treatment due to adverse effects 10mg: 8.4%; 5mg: 5.0%; placebo: 0.8%). There were no differences among groups on the BWSQ.

**Conclusion:** In elderly patients with primary insomnia, indiplon-IR 5mg and 10mg, improved subjective measures of sleep induction, maintenance, and quality during both study weeks. Both doses were tolerated well by the vast majority of patients.

Research supported by Pfizer, Inc. and Neurocrine Biosciences.

**0682 Long Term Efficacy And Tolerability Of Indiplon-IR In The Treatment Of Chronic Insomnia: Results Of A Double-Blind, Placebo-Controlled 3-Month Study**

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**Introduction:** The efficacy and tolerability of the immediate release (IR) formulation of indiplon was evaluated in a 3 month study of chronic insomnia patients.

**Methods:** Patients (N=702; 61% female; mean age, 46 years) who met DSM-IV criteria for chronic primary insomnia of at least 3 months duration, and who reported time to sleep onset (TSO) >45 min and total sleep time (TST) <6.5 h over ≥3 nights/week, were enrolled. Following a 3 week, single-blind, placebo lead-in period, eligible patients were randomized to 3 months of double-blind treatment with indiplon-IR 10mg, 20mg, or placebo. Subjective assessments included TSO (primary endpoint), TST, number of awakenings after sleep onset (NAASO), wake time after sleep onset (WASO), sleep quality, Insomnia Severity Index (ISI), and global improvement. Discontinuation effects were evaluated using the Benzodiazepine Withdrawal Symptom Questionnaire (BWSQ).

**Results:** Treatment with indiplon-IR resulted in significant improvement relative to placebo at all time-points on the TSO. The TSO means at month 1 were: 10mg (34.0 ± 1.3 mins), 20mg (33.0 ± 1.3 mins), and placebo (48.7 ± 1.9 mins; p<0.0001 for both comparisons); efficacy was sustained through month 3, with TSO means of 10mg (29.7 ± 1.6 mins); 20mg (31.6 ± 1.7 mins), placebo (41.9 ± 2.3 mins) (p<0.001 for both comparisons). Indiplon-IR resulted in significant improvement in TST, WASO, sleep quality, ISI, and global improvement at all assessment time-points. In the subset of patients who continued indiplon treatment up to 6 months, TSO improvement achieved in the first month was sustained, with no evidence of tolerance. Both doses of indiplon-IR were well-tolerated. There was no evidence of withdrawal symptoms on the BWSQ.

**Conclusion:** Long term treatment with indiplon-IR resulted in significant and sustained efficacy in sleep onset and sleep maintenance parameters in patients with chronic insomnia, with no evidence of withdrawal upon abrupt discontinuation.

Financial support provided by Neurocrine Biosciences, Inc, and Pfizer Inc.

**0683 Efficacy And Safety Of Indiplon-IR In Adults With Chronic Insomnia Characterized By Prolonged Nighttime Wakefulness With Difficulty Returning To Sleep**

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**Introduction:** To date no medication has been shown to effectively manage prolonged nighttime awakenings in insomnia patients. The objective of this study was to evaluate the efficacy and tolerability of immediate release (IR) indiplon using an “as needed” dosing strategy in response to prolonged nighttime awakenings.

**Methods:** Adult outpatients (N=260; 71% female; age, 46 years) were enrolled who met DSM-IV criteria for primary insomnia, with average total sleep time (TST) <6.5 h, and >8 nights in past month with prolonged awakenings (> 60 mins duration). Following a 2-week placebo lead-in period, patients were randomized to 4 weeks of double-blind treatment with indiplon-IR 10mg, 20mg, or placebo, administered once per night on a PRN basis, provided >4 hours sleep time were available. The primary endpoint was latency to sleep onset post-dosing (LSO-pd). Secondary endpoints included subjective assessment of total sleep time (TST-pd).
Next day residual effects were evaluated by a 100-mm Visual Analog Scale (VAS) rating of sleepiness.

**Results:** Both doses of indiplon-IR significantly improved LSO-pd at all time-points, with an LSO-pd (averaged over 4 weeks) on indiplon-IR 10mg of 36.5 min (p=0.0023) and on indiplon-IR 20mg of 34.4 min (p<0.0001) compared to placebo (45.2 min). The 4-week average sTST-pd was higher on indiplon-IR 10mg (253 min) and 20mg (278 min) compared to placebo (229 min; p<0.01 for both comparisons). VAS ratings showed no evidence of next day sleepiness with either dose of indiplon-IR. Indiplon-IR was well-tolerated.

**Conclusion:** Chronic insomnia patients with middle of the night awakenings showed significant and sustained improvement in sleep parameters using as needed dosing with indiplon-IR, taken after a prolonged awakening. Indiplon-IR was well-tolerated using this dosing strategy, with no next-day residual effects.

Financial support provided by Neurocrine Biosciences, Inc, and Pfizer Inc.

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**0685**
**Efficacy And Tolerability Of Indiplon-MR In Elderly Patients With Chronic Insomnia: Results Of A Double-Blind, Placebo-Controlled, 2-Week Trial**
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**Introduction:** The efficacy and tolerability of the modified release (MR) formulation of indiplon, a novel GABA-A receptor potentiator with selectivity for receptors containing the α1 sub-unit, was evaluated for the treatment of elderly insomnia patients with sleep maintenance difficulties.

**Methods:** Elderly patients, ages 65-85 years old (N=229) who met DSM-IV criteria for primary insomnia of ≥3 months duration, and who reported a total sleep time (TST) ≥ 6.5 hours and wake time after sleep onset (WASO) ≥45 mins on ≥4 nights/week, were randomized to 2 weeks of double-blind treatment with indiplon-MR 15mg or placebo. Subjective assessments included TST (the primary endpoint), time to sleep onset (TSO), WASO, total wake time (TWT), number of awakenings after sleep onset (NAASO); and patient-rated and investigator-rated global scales. Patient ratings of daytime drowsiness and daytime functioning were also evaluated.

**Results:** TST was significantly improved on indiplon-MR treatment relative to placebo at week 1 (377 ± 4 mins vs. 328 ± 4 mins; p<0.0001) and week 2 (373 ± 5 mins vs. 337 ± 5 mins; p<0.0001). TSO was also significantly improved on indiplon-MR treatment relative to placebo at week 1 (22.0 ± 1.0 mins vs. 34.9 ± 1.8 mins; p<0.0001) and week 2 (21.2 ± 1.2 mins vs. 31.0 ± 1.7 mins; p<0.0001). Efficacy of indiplon-MR treatment was also significant at both weeks 1 and 2 on all secondary sleep maintenance endpoints (WASO, NAASO, TWT). Significant improvements were also observed at both study weeks in sleep quality ratings, and in patient- and investigator global ratings. Indiplon-MR was not associated with any residual daytime drowsiness or impairment in functioning relative to placebo. Indiplon-MR was well-tolerated.

**Conclusion:** In elderly patients with chronic insomnia, indiplon-MR 15mg was well-tolerated and effective in inducing and maintaining sleep.

Financial support provided by Neurocrine Biosciences, Inc, and Pfizer Inc

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**0686**
**Improvements In Daytime And Nocturnal Symptoms In Relation To Cognitive Changes Following CBT For Insomnia**
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**Introduction:** Cognitive distortions have been hypothesized to play a role in the perpetuation of insomnia. Previous research has found that reductions in dysfunctional beliefs and attitudes about sleep (DBAS) are associated with improved sleep following cognitive-behavior therapy for insomnia (CBTI). However, the relationship between these cognitive changes and improvements in daytime symptoms of insomnia remains unexplored. This study explores the relationship between changes in DBAS, changes in nocturnal and daytime symptoms of insomnia, and treatment satisfaction among patients who received CBTI.
Methods: Analyses were conducted on 315 adult patients who were enrolled in group-CBTI and completed the following measures at both baseline and last session: DBAS Scale and the Insomnia Severity Index (ISI). Two additional post-treatment measures were collected during the final session: the Helpful Components Questionnaire and overall treatment satisfaction.

Results: Pre- to post-changes on the DBAS Scale were significantly correlated with improvements in daytime symptoms on the ISI (r = .35, p < .01) but not with pre- to post improvement in nocturnal symptoms on the ISI (r = .19, p = .14). Similarly, overall treatment satisfaction was significantly correlated with improvements in daytime symptoms (r = .39, p < .01) but not with improvements in nocturnal symptoms (r = .22, p = .07). Self-ratings on the helpfulness of cognitive components were significantly correlated with improvements in daytime symptoms (r = .42, p < .001) and sleep onset (r = .26, p < .05), but not with other nocturnal symptoms.

Conclusion: The findings indicate that cognitive changes are more strongly associated with improvements in daytime symptoms of insomnia than improvements in sleep. By helping patients change thoughts and beliefs about catastrophic consequences of poor sleep, CBTI addresses a core concern of insomniacs and contributes to reductions in daytime symptoms of insomnia.

0687 Correlates Of Health-Related Quality Of Life In Primary Insomnia

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Introduction: Insomnia is often associated with daytime fatigue, impairments of functioning, and with mood disturbances. Recent studies have shown that quality of life (QoL) is lower for people suffering from insomnia compared to good sleepers. The present study aimed at examining the role of conditioned factors in insomnia and the mechanisms of change associated with improvements in QoL.

Methods: The sample included 169 participants (mean age = 52, 60% women) meeting DSM-IV criteria for persistent primary insomnia. Of those, 45 were taking hypnotics on a regular basis, and for an average of 13 years. Mean insomnia duration was 17 years. Participants completed baseline assessment which included three nights of polysomnography (PSG), daily sleep diaries, and several self-report questionnaires such as the SF-36, the Multidimensional Inventory of Fatigue, and the Insomnia Severity Index. Variables were divided into four areas, hypothesised to be related to QoL: sleep, insomnia severity, fatigue, and other daytime impairments.

Results: Pearson correlation coefficients showed that health-related QoL was associated with insomnia severity, hypnotic use, and daytime impairments.

Conclusion: These results suggest that subjective insomnia severity, as well as its daytime consequences and fatigue are associated with QoL, but sleep per se may not. Interestingly, it appears that insomniacs taking hypnotic medications on a regular basis have lower QoL scores, even if they report equivalent insomnia severity to those who do not use hypnotics. Further studies should be conducted to replicate these findings and to evaluate if treating insomnia improves quality of life via the improvement of these correlates.

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0688 Are Psychophysiological Insomniacs Sleeping Better Away From Home?

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Introduction: Stimulus-control therapy for insomnia, which is based on the Classical Conditioning paradigm seeks to strengthen the association between the bedroom environment and sleep-inducing stimuli. According to ICSD criteria for psychophysiological insomnia, conditioned arousal to the bedroom or sleep-related activities is one of the indicators of learned sleep-preventing associations. As such it is expected that individual sleeping poorly at home may actually sleep better away from home. However, clinical evidences suggest that some patients, otherwise meeting the criteria for psychophysiological insomnia, sleep poorly outside their home as well. The present study aimed at evaluating self-reported sleep status in order to assess the presence of conditioned arousal to one’s own bedroom.

Methods: Data from the present study are derived from four treatment studies in which participants underwent comprehensive clinical sleep evaluations including the Insomnia Diagnostic Interview. Data from 250 participants (mean age = 47.9, 60% women) all meeting DSM-IV criteria for persistent primary insomnia, and suspected to have psychophysiological insomnia, are reported. Mean insomnia duration was 15.8 years (SD = 12.3), insomnia severity was moderate with an Insomnia Severity Index mean score of 17.4 (SD = 3.8). The Insomnia Diagnostic Interview included questions pertaining to sleep quality in which participants were asked if their sleep was better, the same, or worse, while away from home; and whether they slept better, the same, or worse on weekends.

Results: Results showed that 9.0% of the sample reported sleeping better while away from home, 34.3% reported unchanged sleep, and 56.7% reported that their sleep was worse. Sleep quality over the week-end was reported as better by 26.4% of participants, 68.4% reported no change, and 4.0% reported worsened sleep. These percentages were significantly different (X2(2, 250)= 79.4 and 162.3, ps < .0001, respectively).

Conclusion: The majority of the sample (91%) did not meet one of the two conditions described in the ICSD criteria indicating that patients show conditioned arousal to their bedroom. These results raise some questions about the clinical validity of this feature for psychophysiological insomnia. Additional research would be useful to better understand the role of conditioned factors in insomnia and the mechanisms of change underlying stimulus control.

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0689 Psychological Factors Predisposing to Insomnia: Comparison of Good Sleepers, Individuals With Insomnia Symptoms and Individuals With an Insomnia Syndrome

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Introduction: A three-factor model, including predisposing, precipitating, and maintaining factors, is usually proposed to explain the development of insomnia. However, few studies have documented and empirically validated the hypothesized predisposing factors. The objective of this study was to compare good sleepers, individuals with insomnia symptoms...
and individuals with an insomnia syndrome on several psychological variables presumed to predispose to insomnia.

**Methods:** Data from the present study are derived from an epidemiological study assessing the prevalence, incidence, and natural course of insomnia over a 2-year period. A random sample of 2000 French-speaking adults from the province of Quebec took part in an initial telephone survey. From the initial pool, 997 individuals completed several self-report questionnaires. Of those, 36 were excluded because they reported another sleep disorder. The final sample thus comprised 961 participants; they were categorized into three sleep/insomnia subgroups using an algorithm based on DSM-IV and ICD-10 diagnostic criteria for insomnia: 1) good sleepers (n = 444); 2) insomnia symptoms (n = 266); 3) insomnia syndrome (n = 251). End-point variables included demographics, psychological and personality factors, and stress and arousability.

**Results:** There was a higher proportion of women (66%) in the syndrome subgroup (p=0.04). No other group differences were observed on demographics. A higher proportion of individuals reported a past episode of insomnia (49%) and a parent history of insomnia (33%) in the syndrome subgroup relative to the other two groups (p=0.001). Regarding psychological variables, the same pattern of findings was observed on seven variables including arousability, stress perception and emotion-oriented coping strategies; depression and anxiety symptoms; and neuroticism and extraversion personality traits. Individuals with an insomnia syndrome had higher scores on these variables than individuals with insomnia symptoms, which in turn had higher scores than good sleepers.

**Conclusion:** Psychological factors seem paramount in predisposing individuals to insomnia. Longitudinal follow-ups are being conducted to assess the relative contribution of these variables in the development and natural course of insomnia.

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**0690**

**Insomnia Complaints And Repressive Coping Among Black And White Americans**

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**Introduction:** This study assessed whether racial differences in sleep complaints and durations are mediated by differences in repressive coping.

**Methods:** A total of 1274 women were recruited (White=28%; Black=72%; mean age and BMI: 59.36 ±6.53yrs and 29.36 ± 5.59kg/m2, respectively). In a semi-structured interview, we assessed repressive coping with the Index of Self-Regulation (ISE). High ISE scores represented greater defensiveness/repressive coping. Sleep complaints were assessed with the sleep disorder subscale of the Comprehensive Assessment and Referral Evaluation.

**Results:** Of the sample, 70% reported arthritis, 38% respiratory conditions, 53% hypertension, and 46% heart diseases; 11% were current smokers and 24% were social drinkers. Spearman correlations showed that women with high ISE scores reported less insomnia complaints [rs = -0.41, p < 0.001], greater sleep satisfaction [rs = 0.28, p < 0.001], slept longer [rs = 0.20, p < 0.001], and had better sleep quality [r = 0.35, p < 0.001]. Based on Fisher’s exact test, the percentage of Whites reporting insomnia complaints was greater than that of Blacks [74% vs. 46%; χ² = 87.67, p < 0.0001]. Moreover, Black race correlated to higher scores on self-regulation [rs = -0.44, p < 0.001], less insomnia complaints [rs = 0.26, p < 0.001], greater sleep satisfaction [rs = 0.20, p < 0.001], and earlier rise time [rs = 0.18, p < 0.001] and bedtime [rs = 0.17, p < 0.001]; Blacks tended to sleep longer [rs = -0.10, p = 0.04] and to have better sleep quality [rs = -0.11, p = 0.02]. Controlling for ISE, the magnitude of the relationship of race to insomnia and sleep satisfaction was significantly reduced [rs = 0.09, p < 0.001; rs = 0.10, p < 0.01, respectively].

**Conclusion:** Results suggest that Blacks may be experiencing better and longer sleep. The relationship of race to insomnia complaints and sleep satisfaction is jointly dependent on the degree of repressive coping, suggesting that Blacks report less insomnia complaints due to a greater ability to regulate emotions. It may be that Blacks cope with sleep problems within a positive self-regulatory framework, allowing them to better deal with sleep-interfering psychological processes to stressful life events and to curtail dysfunctional sleep-interpreting processes. It is of interest to ascertain whether self-reported and physiologically monitored sleep patterns differ greatly among those showing divergent repressive coping styles.

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**0691**

**A Comparison Of Regional Cerebral Metabolism Across Waking And NREM Sleep Between Primary Insomnia And Major Depression**

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**Introduction:** Depression and primary insomnia share some, but not all, clinical and epidemiologic features suggesting that there may be both common, as well as disparate, neurobiological mechanisms underlying the two disorders. Functional neuroimaging studies have identified the changes in brain function that occur across waking and NREM sleep in healthy subjects and independently, in depressed and insomnia subjects.

**Methods:** Twenty-five depressed subjects (18 women and 7 men, mean age +/- s.d. = 35.7 +/- 10.4 years), 10 DSM-IV diagnosed primary insomnia subjects (6 women / 4 men, mean age +/- s.d. = 33.5 +/- 10.6 years) and 28 healthy subjects (18 women and 10 men, mean age +/- s.d. = 34.1 +/- 9.5 years) received waking and NREM sleep [18F]-FDG PET assessments.

**Results:** Insomnia subjects, but not depressed subjects, showed elevated whole brain metabolism across waking and NREM sleep. Insomnia subjects showed greater waking metabolism in the frontal pole and in the ventral prefrontal cortex. Both areas showed greater reductions in metabolism from waking to NREM sleep than in depressed patients. Within sleep, insomnia subjects showed increased metabolism in the brainstem, anterior cingulate and midbrain arousal structures. Depressed patients showed an elevated metabolism in a ventral and posterior emotional neural network that persisted into sleep.

**Conclusion:** Increased waking metabolism in prefrontal cortex in insomnia patients may be associated with their cognitive hyperarousal, whereas waking hypofrontality in depressed patients may be associated with their cognitive impairments. Increased metabolism during sleep in insomnia patients in the brainstem, anterior cingulate and midbrain structures may be responsible for their increased physiological arousal, whereas the increased arousal in depressed patients may be due more to an increased metabolism in a ventral and posterior emotional neural network.

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0692
Assessment Of Daytime Sequelae Of Poor Sleep: The Insomnia Impact Questionnaire (IIQ)
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Introduction: Distress over negative daytime sequelae of poor sleep is usually why patients seek treatment. Existing validated insomnia questionnaires assess global distress about poor sleep and daytime impact. Assessment of specific aspects of daytime impairments, as they are perceived by insomniacs, has not received much attention. Our aim was to develop a questionnaire that evaluates specific negative effects of insomnia and to classify them into empirically based dimensions.

Methods: The IIQ consisted of 65 symptoms and adverse effects of poor sleep, pooled based on the authors’ experience with concerns expressed by clinic patients. Patients who were enrolled in a group cognitive-behavioral therapy for insomnia rated each item on a 5-point Likert scale (0=not at all, 1=little, 2=somewhat, 3=much, 4=very much) the extent to which they experience each problem due to insomnia.

Results: 155 IIQs were subjected to a principle components analysis with varimax rotation and item factor loading criterion of ≥0.5. The emerging 4 factors (% of total variance explained; Cronbach’s alpha reliability coefficient) are: Cognitive Ineffectiveness (20.6%; 0.97), Emotional Distress (10.5%; 0.95), Physical Distress (9.2%; 0.84), and Fatigue (6.6%; 0.88). Subscale scores (means ± SD), derived by averaging all items that loaded on each factor, were Fatigue 2.1±1.1 (4 items), Emotional Distress 1.9±1.0 (18 items), Cognitive Ineffectiveness 1.8±0.9 (20 items), and Physical Distress 1.5±0.9 (8 items). Fatigue subscale was not correlated with the Epworth Sleepiness Scale (r=0.09; p=0.24). The severity of insomnia, based on the mean of the 3 insomnia items on the Insomnia Severity Index, was not significantly correlated with Physical Distress or Fatigue, but was significantly correlated with Cognitive Ineffectiveness (r=0.17; p=0.04) and Emotional Distress (r=0.19; p=0.02).

Conclusion: The IIQ identified 4 dimensions of adverse impact of insomnia and demonstrated high internal consistency. Findings suggest that fatigue is unique from that of sleepiness and is the most severe impact of insomnia. The IIQ may be a useful tool for treatment planning and for assessing clinical significance of insomnia treatment.

0694
Does Insomnia Kill?
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Introduction: We investigated the prevalence, associated factors, and hazard ratios for endorsement of sleep complaints in a large population-based study.

Methods: The Atherosclerosis Risk in Communities (ARIC) Study is a prospective, population-based study of cardiovascular disease. We applied multivariable regression analysis to 13563 ARIC participants to predict the likelihood of endorsing the symptoms of difficulty falling asleep, waking up repeatedly, awakening tired and fatigued, and combinations of these symptoms by age, sex, alcohol intake, smoking, diabetes, heart disease, menopausal status, use of hypnotics, hypertension, depression, educational level, Body Mass Index, respiratory symptoms, and pulmonary function status. We also predicted the Hazard Ratios (HR) of death at 5-7 year follow-up by endorsement of these complaints and by use of hypnotics controlling for the covariates listed. We defined insomnia as either a complaint of sleep onset or sleep maintenance coupled with a complaint of nonrestorative sleep.

Results: Predictors of insomnia were depression (OR 5.04, 4.58-5.53) and heart disease (OR 1.88, CI 1.66-2.13). After controlling for depression and other covariates, complaints of insomnia were not associated with an increased Hazard Ratio for death (HR 1.01, 0.85-1.21), nor was use of any hypnotic.

Conclusion: After controlling for important confounders, neither insomnia nor use of hypnotics was associated with an increased risk of death in 5-7 years of follow-up.

0695
Guidelines For The Diagnosis And Management Of Insomnia In Primary Care: A Consensus Report Produced By GPS And Sleep Specialists
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Introduction: The purpose of the study was to assess whether persons with and without sleep complaints differed regarding subjective and objective effort expenditure.

Methods: Participants were 42 female (mean age=22.81 years; range=18-32) and 26 male (mean age=22.11 years; range=18-41) undergraduate students who completed a sleep diary for seven days prior to assessment. The assessment included the Stanford Sleepiness Scale (SSS), The Profile of Mood States (POMS), a reaction time task and a math addition task. The Math Effort Task (MET) and a task choice question measured objective effort. Subjective effort questions asked "...how much of that maxi-


**Introduction:** Two national surveys (Studio Morfeo 1 and Studio Morfeo 2) conducted in Italy by the Italian Association of Sleep Medicine (AIMS) have shown that GPs have the clinical skills to identify insomnia and provide appropriate management. However, they have limited time to formulate a diagnosis and initiate a therapeutic solution. A set of functional guidelines can be useful to overcome this constraint.

**Methods:** A panel of sleep experts and GPs prepared 300 statements to achieve a Consensus on the diagnosis and management of insomnia in primary care. After a series of meetings, 38 statements were selected and submitted for voting to a group of 665 GPs.

**Results:** The statements that received significant percentages of agreement (p < 0.0001) were: 1. Insomnia can be managed by the GP (94%). 2. Insomnia must be always diagnosed when the patient complains spontaneously and treated even when not openly required by the patient (59%). 3. Insomnia must always be searched for and treated in the presence of psychiatric or severe medical disorders (89%). 4. Insomnia should always be searched for in the presence of mood disorders (94%). 5. The cause of insomnia should be searched for the diagnostic and therapeutic management (95%). 6. It is preferable to use hypnotic drugs with short elimination half-life (97%). 7. For safety reasons, it is preferable to use non-benzodiazepine hypnotics. Benzodiazepine hypnotics must be used under specific diagnostic circumstances (89%). 8. Non-benzodiazepine hypnotics should be preferred in cases of depression (83%). 9. Hypnotics pills (no drops) should be always preferred (81%). 10. The evolution of insomnia and its treatment must be regularly controlled (87%). 11. When ineffective, the prescribed dose of hypnotic drug must not be increased (65%), and therapy shall be modified or diagnosis re-assessed (87%). 12. Self-prescription must be discouraged and avoided (95%).

**Conclusion:** To our knowledge this is the first Consensus on insomnia produced in collaboration between GPs and sleep specialists. GPs are overwhelmed by daily practice in manifold clinical fields. In order to provide a rapid and effective management of insomnia, GPs need to have at their disposal acceptable and easy-to-apply guidelines.

The Consensus was supported by an educational grant provided by Sanofi-Aventis Italy. The present report was carried out on behalf of the Progetto Morfeo Committee.

**0696**

**The GABA<sub>δ</sub> Agonist Gaboxadol Improves Subjective And Objective Sleep Quality In Elderly Subjects**

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**Introduction:** The selective extrasynaptic GABA<sub>δ</sub> agonist gaboxadol was demonstrated to increase sleep maintenance and intensity in rats and young subjects. Moreover, a recent study using an afternoon nap model, confirmed that gaboxadol consolidates sleep and promotes slow wave sleep (SWS). Ageing is associated with marked decreases in sleep maintenance and SWS, which, at least partially, may be responsible for the high prevalence of insomnia in elderly. In the present double-blind, placebo-controlled study we investigated the effects of repeated gaboxadol administration on nocturnal sleep in aged subjects.

**Methods:** Ten healthy subjects (age range 63-78 years, 4 females), without sleep complaints, slept in the sleep laboratory of the Max-Planck-Institute during two randomized study periods. Each period consisted of 4 consecutive nights. On nights II, III and IV, 30 min before bedtime (<11 pm), the subjects ingested placebo during one and 15 mg gaboxadol hydrochloride during the other study period. Throughout these nights polysomnographic recordings were made. Questionnaires assessing subjective sleep quality were completed shortly after rising (<7 am). Data were analyzed with repeated measures ANOVA using log-transformed values.

**Results:** Compared with placebo, gaboxadol significantly shortened subjective sleep latency, on average from 28.5 ±14.3 to 18.1 ± 8.6 min, and increased self-rated sleep quality and intensity. Gaboxadol significantly improved sleep efficiency, on average from 78.2 ±6.7 to 83.3 ± 6.7 %, which was related to decreases in intermittent wakefulness. Furthermore, gaboxadol increased stage 2 and SWS. In line with the latter, EEG spectral analysis showed that gaboxadol enhanced slow wave activity. All these effects were stable throughout the study period.

**Conclusion:** The present study shows that gaboxadol reverses the typical age-related sleep changes and thus, effectively improves sleep quality in elderly subjects. Moreover, the data suggests that gaboxadol does not rapidly produce tolerance toward its hypnotic action.

Research was supported by Lundbeck.

**0697**

**Physiological Reactivity Of Insomniacs Participating In Written Emotional Disclosure: Salivary Cortisol And Respiration**

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**Introduction:** The aim of the current study is to measure physiological arousal during written disclosure.

**Methods:** Ten insomniacs (6 female) meeting DSM-IV criteria for insomnia participated in a writing task. The average age of the participants was 36.6 (4 Caucasian, 6 African-American). Six experimental (emotional disclosure) and 4 control (neutral time management topic) participants completed the task. Salivary cortisol was measured before and immediately after each writing session using a salivette technique (Salimetrics, Inc.; State College, PA). Participants wore the Vivometrics LifeShirt (Ventura, CA) for continuous ambulatory monitoring of heart rate, respiratory rate, rapid shallow breathing, change in end-expiratory lung volume, and activity level for one baseline and 4 writing sessions.

**Results:** Salivary cortisol levels of experimental participants increased significantly during writing on day 3 only (p = .0001). An index of change in end-expiratory lung volume differed significantly from baseline for experimental but not control subjects on days 3 and 4 of writing (p = .05 and .04 respectively). Rapid shallow breathing tended to be higher for experimental subjects than controls on day 3 of writing (p = .06), this difference became significant on writing day 4 (p = .05). Importantly, groups did not differ in their perception of the credibility of the intervention for application as an insomnia treatment (Credibility Scale by Borkovec & Nau, 1979).

**Conclusion:** In the current study individuals participating in a written emotional disclosure task secreted higher levels of salivary cortisol than controls on one of four writing days, but had significantly greater levels of rapid shallow breathing changes on 2 of 4 writing days. Change in end-expiratory lung volume differentiated the groups on 2 of 4 writing days as well. This report is based on preliminary data from a study that aims to include a total of 40 insomniacs. Further analyses include group comparisons at baseline, and 1- and 2-month follow up periods on sleep quality (PSQI), physical health (SF-36), and mood (PANAS-X). Physiological arousal during writing will be analyzed as a possible moderator of these effects.
The Effect Of Light Exposure During Daytime To Night Sleep In Elderly Subjects
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Introduction: To clarify the effects of daytime light exposure to the function of the autonomic nervous during sleep in elderly subjects, we evaluated the relationship of heart rate variability, subjective insomnia and daytime light exposure.

Methods: The subjects consisted of 40 subjects, 10 young men, 10 young women, 10 elderly men and 10 elderly women. The measurement was performed for 24 hours from the time when the subjects get up in the morning until the next morning. All subjects were instructed to keep normal daily activity as always. Light exposure meter was fixed on the metopic region near eyes of each subject. Power spectral analysis of heart rate variability was performed by using Mem/Calc, and the power of the low frequency (LF: 0.04 - 0.15Hz) and high-frequency (HF: 0.15 - 0.4Hz) components, LF to HF ratio and the slope of Power spectral density (PSD) were calculated. Sleep and wake were determined by using Actigraph. This study was approved by local ethical committee.

Results: In elderly subjects, the increase of HF during sleep did not observed, but decrease of LF to HF ratio and increase of slope during sleep were observed. In elderly subjects, we divided into two groups, nine subjects with insomnia and eleven subjects without insomnia. Compared with the subjects without insomnia, the light exposure during daytime was not significantly different. The increase of HF and decrease of LF/HF during early sleep was significantly correlated to light exposure in the morning in elderly subjects without insomnia (HF: Spearman r=0.862, p=0.002, LF/HF: Spearman r=-0.767, p=0.016). However, this was not observed in elderly subjects with insomnia.

Conclusion: The results of the study suggested that the increase of light exposure during daytime might be related with the superiority of parasympathetic nerve activity during nighttime in elderly subjects without insomnia. However, this was not observed in elderly subjects with insomnia, and this revealed that factors other than light exposure amount might be involved.

0699
Cognitive Behavioral Therapy For Hiv-Related Insomnia
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Introduction: Sleep disruption is a significant problem among HIV+ individuals, with rates of sleep complaints reported to be as high as 73% to 100%. Difficulties noted include increases in sleep onset latency, frequent awakenings, reduced total sleep time and sleep architecture alterations. These sleep difficulties have also been associated with problems in daytime functioning. Even though sleep disruption is commonly reported in HIV, little data exist on treatments to improve sleep. This pilot study is designed to explore the effectiveness of a cognitive-behavioral intervention (CBT) for insomnia on subjective sleep of HIV-infected individuals.

Methods: Five HIV+ participants (ages 36-49) with complaints of insomnia of at least 6 months’ duration were recruited to participate and screened via structured interviews. Baseline assessment included several questionnaires and sleep diaries (1 week) that were completed prior to beginning a 6-week treatment protocol. Treatment included components of psychoeducation, stimulus control, sleep restriction and sleep hygiene guidelines. Upon treatment completion they again completed questionnaires and sleep diary.

Results: Matched-sample t-tests were performed on sleep diary data. Mean changes between baseline and post-treatment in sleep efficiency percent (SE), total sleep time (TST) and wake after sleep onset (WASO) were compared. Mean changes in SE and WASO were significant (t = 4.9, p <.01 and t = 3.5, p <.05, respectively). Mean baseline SE was 73.7 (s.d. = 5.0) whereas post-treatment SE mean was 90.2 (s.d. = 3.5), WASO baseline mean was 79.3 minutes (s.d. = 31.0); WASO post-treatment mean was 28.1 minutes (s.d. = 6.0).

Conclusion: While the data comprise a small sample, they are compelling. The changes observed are consistent with findings in the literature of other primary and secondary (HIV-negative) insomnia populations. These preliminary findings suggest that CBT may be an effective intervention strategy to reduce insomnia symptoms in HIV-positive individuals.

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0700
Hypnotic Taper With Or Without Self-Help Treatment Of Insomnia
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Introduction: Cognitive-behavioral therapy (CBT) has been shown effective to facilitate hypnotic discontinuation in the context of insomnia treatment. However, such structured intervention may be time-consuming and is not always readily accessible. This study aimed at comparing the efficacy of a minimal intervention focusing on a hypnotic taper schedule, used alone or combined with a self-help treatment for insomnia.

Methods: Preliminary data from 37 chronic hypnotic users are reported (25 women, mean age = 56, SD = 12). The taper intervention comprised two medical visits and eight weekly phone follow-ups aimed at guiding participants to comply with their individualized medication withdrawal schedule. CBT self-help booklets described stimulus control, sleep restriction, cognitive strategies, and sleep hygiene elements.

Results: Twenty-nine participants used benzodiazepine hypnotics and eight used zopiclone. Mean duration of hypnotic use was 13 years (SD = 9). Mean weekly hypnotic use decreased in both conditions, from a nearly nightly use to less than once a week use. At post-treatment, participants who received CBT gained approximately 7% of sleep efficiency (from 67 to 74%) while those who did not lost 3% (from 64 to 61%). Total wake time decreased by 56 min among CBT participants (from 169 to 115 min) and increased by 19 min among those receiving the taper schedule alone (from 170 to 189 min). Total sleep time remained relatively stable throughout withdrawal in both CBT (361 to 355 min) and taper (316 to 311 min) conditions.

Conclusion: Preliminary findings suggest that a brief intervention providing a systematic withdrawal schedule might be sufficient in helping chronic users stop their hypnotic medication. However, the addition of a self-help treatment focusing on insomnia produced greater sleep improvement relative to the taper condition alone. Follow-ups are being conducted to evaluate the long-term impact of these interventions.

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0701
Chronic Insomnia And Health Care Utilization
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Introduction: Chronic insomnia is associated with high frequency of medical and psychiatric comorbidities. This study explored the pattern of health care utilization among clinic patients whose chief complaint was chronic insomnia.

Methods: We surveyed Stanford Sleep Disorders Clinic patients enrolled in a cognitive-behavioral group treatment program for insomnia. 350 patients completed a Health Service Utilization Questionnaire pre-treatment. The questionnaire provided retrospective data on the number and type of medical (MED) and mental health (MH) outpatient visits in the past 2 months.

Results: 82% of the patients had MED visits, 44% had MH visits, and 42% had both in the past 2 months. On average, patients made 3.66.2 MH visits, 87% were taking prescription medication for insomnia. Of those treated by medication, 46% were on medication for >6 months, 46% reported that medication helped a lot, and 35% reported medication helped a little. Of those who were treated by a MH provider, 54% were treated for >6 months, and 75% thought treatment was at least somewhat helpful for the specific problem they sought help for. In contrast, MH care was not perceived as very helpful for ameliorating insomnia; 6.2% reported it helped a lot, 28.4% reported it was somewhat helpful, and 54.3% said it made no difference. The Beck Depression Inventory (BDI) score was significantly correlated with the total number of health care visits (r=0.350, p<0.001).

Conclusion: Patients with chronic insomnia sought medical and mental health care at high frequency; the higher the distress level (BDI), the more health care visits. A substantial percentage of patients were taking medications prescribed for sleep for >6 months at the time they presented at a sleep disorders clinic. Although the majority of patients reported medication helped them sleep, their seeking treatment at a sleep clinic suggests that their insomnia remained insufficiently controlled.

0702
Safety Of Zolpidem And Zaleplon In Chronic Insomnia
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Introduction: There has been much concern regarding the safety of long term treatment of insomnics with hypnotics. Most such drugs are recommended to be prescribed for only a few weeks. The present study attempted to treat chronic insomnia patients with two popular hypnotic agents and evaluate the incidence of side effects, both short term and long term.

Methods: A retrospective chart review of 198 female patients and 154 male patients was performed at Cape Fear Valley. All patients had undergone evaluation, diagnosis and treatment for sleep disorders in the Department of Sleep Medicine. Mean age was 50.12 years. Patients received ICSD Axial diagnoses and polysomnography as necessary. 307 patients received Zolpidem and 57 received Zaleplon. Dosing of Zolpidem ranged from 5-30 mg. Dosing of Zaleplon ranged from 5-20 mg. The patients were assigned to Zolpidem or Zaleplon based upon clinical judgement and past medication history and response to medications. The duration of treatment is shown in the table below.

Results: Zolpidem # of patients 185 35 11 20 1 10 1 18 21 24 >24 Zaleplon # of patients 44 8 3 1 1 Months on Drug 3 6 9 12 15 18 21 24 >24 Side effects were reported in a total of five patients. Three patients reported sleepiness and agitation the next day after taking Zolpidem. One patient experienced hallucinations following dosage with 20 mg. Zolpidem was reduced to 5 mg. H.S. with no reoccurrence. One patient experienced depression on Zolpidem, and it was tapered and discontinued.

Conclusion: Both Zolpidem and Zaleplon have a low incidence of associated side effects in long term use.

0703
Hyperarousal Behavioural Trait, Sufficient Sleep Index And Health Related Quality Of Life
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Introduction: Knowledge concerning the extent to which hyperarousal behaviour trait interferes with habitual sleep in association with health related quality of life (HRQOL) in patients with coronary artery disease, is lacking. Our objectives were to assess hyperarousal behavioural trait and habitual sleep related to sufficient sleep index (SSI) and sleep quality. Furthermore, we wished to ascertain which variables best predicted HRQOL in patients with coronary artery disease.

Methods: This descriptive, comparative and predictive study included 203 women [63.3 (SD 9.6) years] and 424 men [62.4 (SD 10.8) years] with coronary artery disease. The Swedish version of the Hyperarousal behavioral trait scale, the Upplapa sleep Inventory, the SF-36 scale and actigraphy recordings were used.

Results: The mean value (SD) for the hyperarousal behavior trait scale (H-scale) was 31.1 (9.7), for introspective 7.4 (3.4), reactivity 2.7 (2.0) and extremeness 2.6 (2.9). The scores were also higher than those reported in the general Swedish population. The total score on the H-scale was significantly higher in women than in men (p<0.0001) and for 74 patients, the total score on the H-scale corresponded with that reported in insomniacs (score > 39.9). Mean (SD) value for SSI% was 89.9% (SD 16.2), for sleep quality 2.5 (1.2). Women reported significantly lower SSI% and significantly worse sleep quality (p<0.0001) and perceived significantly worse daytime distress, due to poor sleep, than men. Actigraphy showed that those with SSI <85% had significantly lower sleep efficiency (%) assessed during three nights, compared with those with SSI of between 85 and 100%. Those who had reported worse sleep quality had significantly lower objective sleep efficiency during two nights of seven. Using a stepwise multiple regression, preliminary analysis demonstrated that worse sleep quality, increased reactions to external factors, and diabetes predicted poorer HRQOL outcome.

Conclusion: These findings support that lower SSI and sleep quality, partly due to Hyperarousal behavioral trait are important factors for HRQOL.

This research was supported by grants from the Swedish Research Council (VR) and the Medical Research Council of Southeast Sweden (FORSS).

0704
The Basel Survey On Sleep Behavior And Vasospastic Syndrome: Evidence For An Association Of Sleep Onset Insomnia With Peripheral Vasoconstriction
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Introduction: Sleep Onset Insomnia (SOI) frequently occurs in psychiatric disorders but also in the general population. The primary Vasospastic Syndrome (VS) is a functional disorder of vascular regulation in otherwise healthy subjects (leading symptom: cold hands and feet). In controlled laboratory studies we have shown a close relationship between digital vasoconstriction and long sleep onset latency. The aim of the Basel Survey is to assess whether SOI is associated with VS in the general population.

Methods: In a random population sample of Basel-Stadt, 2800 subjects (age: 20-40 years) were asked to complete a questionnaire on sleep behavior and VS (response rate: 73% in women, N=1001; 62% in men, N=809). ANOVA and backward stepwise regression analysis were performed. Values of SOI and VS were based on questionnaire-derived scores.

Results: In comparison to men, women showed similar score values for SOI (w: 3.23±0.07 sem, m: 3.26±0.07; n.s.), but higher values for VS (w: 4.61±0.10, m: 2.15±0.07; p<0.0001). SOI and VS showed a similar pattern of gender dependency which differs however in women and men: While women have highest values in the youngest age group (20-24yr) and lowest values in the oldest age group (36-40), men’s values do not significantly vary with age, neither the values for SOI, nor those for VS. Multivariate analysis controlling for BMI, gender, age, stress rating and smoking revealed VS as the most significant predictor for SOI. In contrast to SOI, the timing of sleep (onset, offset, mid point and duration) shows different gender and age dependency and VS revealed no predictive value for these variables.

Conclusion: Women exhibit more problems with cold extremities (VS) than men, especially in younger age groups. VS is associated with SOI but not with timing of sleep. Therefore, a thermophysiological approach to SOI may provide a successful treatment concept.

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0705

Analysis Of The Treatment Effect Of Eszopiclone On Sleep Parameters That Affect Next Day Function In The Elderly

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Introduction: The relationship between nighttime sleep and daytime function is unclear. Studies have shown that insomnia patients treated with the non-benzodiazepine eszopiclone (ESZ) demonstrated improvements in sleep onset, sleep maintenance, and next day function (NDF). This analysis assessed the correlation between nighttime sleep and NDF, and the percent of the treatment effect (PTE) on the NDF attributable to the effect of ESZ on sleep.

Methods: Analyses were performed on data from a randomized, double-blind, placebo-controlled, parallel-group study of patients (age 64-85) with primary insomnia who received ESZ 2mg (n=79) or placebo (n=80) nightly for 2 weeks. Pearson correlation coefficients between three NDF parameters (daytime alertness, ability to function, physical well-being) and several patient-reported sleep parameters (sleep quality [SQ], total sleep time [TST], wake time after sleep onset [WASO], and sleep latency [SL]) were calculated. To assess PTE, two statistical models were used. Model 1 had treatment as the only explanatory variable for NDF improvements (estimated treatment effect β1). In Model 2, both treatment and the post-dose sleep parameters were explanatory variables (estimated effect β2). PTE was calculated as follows: PTE=100(β1-β2)/β1. PTEs >100% were set to 100%.

Results: In both groups for all nights combined, NDF correlated highly with SQ (r=0.5), and modestly with TST (r=0.3), WASO and SL (r=0.2; p<0.0001 for all). With regard to daytime alertness, the PTE was 57%, 45%, 29%, and 27% for subjective measures of SQ, WASO, TST and SL, respectively. For ability to function, the PTE was 55%, 48%, 31%, and 32%, respectively. For physical well-being the PTE was 54%, 47%, 28%, and 29%, respectively.

Conclusion: In this analysis, SQ, WASO, TST and SL correlated with NDF. The treatment effect of ESZ on NDF was largely explainable by improvements in SQ and WASO, with TST and SL affecting improvements to a lesser degree.

Support for this study provided by Sepracor Inc.

0706

Sedative Hypnotics Employed To Treat Patients With And Without Insomnia Complaints In The National Ambulatory Medical Care Survey: 2000-2002

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Introduction: Pharmaceutical treatments are available for patients with a complaint of insomnia. These treatments often vary by patient and physician characteristics. This study describes the use of several medications commonly used to treat sleep disorders as reported in the National Ambulatory Medical Care Survey (NAMCS).

Methods: Data was obtained from the 2000, 2001 and 2002 NAMCS. Descriptive analyses were utilized to examine medications (i.e., trazolam, temazepam, flurazepam, zolpidem or zaleplon, trazadone, and diphenhydramine) commonly used to treat individuals with a complaint of insomnia. Patient level weights were utilized to derive US national population estimates. Given the complex stratified survey design, Rao Scott and Wald Chi-square tests were used to assess statistically significant differences within groups.

Results: Across all age groups, patients with a complaint of insomnia were most often prescribed zolpidem or zaleplon (60.8%) followed by trazadone (17.5%). However, patients under 18 years of age were more likely to be given diphenhydramine than any other medication. For all patients taking a medication commonly used to treat sleep complaints, psychiatrists were more likely to prescribe zolpidem (52.5%), while family/general practice physicians (32.2%), general internists (43.2%) and other specialists (25.1) were more likely to prescribe zolpidem or zaleplon. Additionally, for this group, patients’ age 18-44 years were more likely to be taking trazadone (34.7%) than zolpidem or zaleplon (28.4%) relative to other age groups.

Conclusion: Newer sleep agents such as zolpidem or zaleplon are the most commonly prescribed medication across the majority of physician types, gender and age groups. This study provides an important descriptive look at those who are taking medications commonly used to treat sleep disorders.

0707

A Dose-Response Efficacy And Safety Study Of Eszopiclone In The Treatment Of Primary Insomnia

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Introduction: This study evaluated the efficacy and safety of eszopiclone 3 mg and zolpidem 10 mg vs placebo in adults with primary insomnia.

Methods: Multicenter, double-blind, placebo-controlled, 6-way

Category L—Sleep Disorders-Insomnia

Return to Author Index

Return to Key Word Index

A237

SLEEP, Volume 28, Abstract Supplement, 2005
crossover study. Patients (N = 65; 21-64 years old) received 2 nights of treatment with placebo, eszopiclone 1, 2, 2.5, or 3 mg, and zolpidem 10 mg in random order. Visits were separated by a 3-7 day washout. Efficacy parameters assessed were latency to persistent sleep (LPS), sleep efficiency, wake time after sleep onset (WASO), wake time during sleep (WTDS) and number of awakenings (NAW), as measured by polysomnography (PSG). Patient-reported sleep parameters including quality, depth and morning sleepiness were assessed using questionnaires.

**Results:** By PSG, all active treatments reduced LPS (P ≤ 0.0001) and increased sleep efficiency (P ≤ 0.05) compared with placebo. Only eszopiclone 3 mg significantly reduced WASO, WTDS and NAW, relative to placebo (P ≤ 0.05). By patient-report, all active treatment groups except for eszopiclone 1 mg had improved sleep quality and depth relative to placebo (P < 0.05). Morning sleepiness was significantly improved with eszopiclone 2.5 and 3 mg vs placebo, but not with lower doses of eszopiclone or with zolpidem. Adverse events reported in more than 4% of patients following eszopiclone 3 mg or zolpidem 10 mg were dizziness (eszopiclone: 4.7%, zolpidem: 10.9%, placebo: 4.8%), somnolence (eszopiclone: 4.7%, zolpidem: 9.4%, placebo: 0%); headache (eszopiclone: 9.4%, zolpidem: 9.4%, placebo, 9.5%); unpleasant taste (eszopiclone: 7.8%, zolpidem: 0%, placebo 1.6%) and hallucinations (eszopiclone: 0%, zolpidem: 4.7%, placebo: 0%).

**Conclusion:** In this study, all treatments were effective in reducing LPS; only eszopiclone 3 mg had a significant impact on PSG measures of sleep maintenance including WASO, WTDS, and NAW. In this study, eszopiclone 3 mg was effective and well-tolerated for the management of chronic insomnia in adults.

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0708

**Information Processing During Sleep In Primary Insomnia: An ERP Study**

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**Introduction:** The neurocognitive model of primary insomnia hypothesized that the sleep difficulties in insomniacs may result from enhanced information processing around sleep onset. The model was supported by the findings of increased high frequency EEG power during sleep in primary insomnia. However, high frequency EEG has been shown to be associated with not only cognitive activities but also somatic arousal. The present study measured event-related potentials (ERPs) as an index of information processing to further explore the neurocognitive activities during sleep in primary insomniacs.

**Methods:** 19 patients with primary insomnias (10F 9M; mean age=36.6) and 19 normal controls (11F 8M; mean age=35.6) participated in the study. Oddball paradigm was conducted to elicit ERPs during sleep. Pure tones, 1500 and 1000 Hz alternating as target and non-target tones across subjects, at 80 db were presented via earphone throughout the night. Subjects were instructed to count the number of target tones and to ignore the non-target tones.

**Results:** P220, N350, and P900 were consistently elicited during NREM sleep for both groups. All the ERP components were larger in responding to target tones than non-target tones, and were larger during the first half than the second half of the night. P220 and P900 were also larger during slow wave sleep (SWS) than other sleep stages. N350, on the other hand, was not different among sleep stages. In comparison to control subjects, insomniacs showed a tendency of smaller P900 during SWS (Fz: F=3.46, p=0.061; Cz: F=3.47, p=0.063; Pz: F=3.40, p=0.061).

**Conclusion:** Since the P900 was larger during the SWS than other stages and became smaller during the second half of the night, it may reflect an inhibition of external stimulus for the maintenance of sleep. The finding that patients with primary insomnia tended to have smaller P900 partially supports the hypothesis that insomniacs may have elevated information processing during sleep. However, the decreased P900 occurred primarily during SWS instead of the sleep onset period that was originally suggested by the neurocognitive models.

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0709

**Sleep Complaints And Diagnoses In The National Ambulatory Medical Care Survey: 2000-2002**

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**Introduction:** Insomnia symptoms have been reported to impact the lives of approximately 83 million people in the United States general population. However, insomnia complaints are often underreported and under-diagnosed. This study describes patient characteristics of those who do and do not present with insomnia complaints in the National Ambulatory Medical Care Survey (NAMCS).

**Methods:** Data was obtained from the 2000, 2001 and 2002 NAMCS. Descriptive analyses were utilized to examine individuals who listed insomnia as one of three possible reasons for their office visit relative to those who did not have an insomnia complaint. Patient level weights were utilized to derive US national population estimates. Given the complex stratified survey design, Rao Scott and Wald Chi-square tests were used to assess statistically significant differences within groups.

**Results:** Patients reported an insomnia complaint as the reason for their visit in only 0.6% of all visits. The majority of these patients (64%) were treated by primary care specialists. Across all age groups, approximately twice as many women as men presented with a complaint of insomnia. However, a greater percentage of males under the age of 18 years presented with an insomnia complaint compared to females in the same age category, 19.4% compared to 10.5%, respectively. While organic diagnoses (59.8%) were the most common, an insomnia diagnosis occurred in 8.2% of patients and a diagnosis of depression occurred in 19.9% of patients who listed insomnia as a reason for their visit.

**Conclusion:** At any point in time insomnia complaints are known to impact a significant portion of the US population, yet, in only 0.6% visits do patients list insomnia as a reason for their visit. This study provides an important descriptive look at those who do and do not present with a complaint of insomnia.

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0710

**Sleep Habits In Healthy Normal Sleepers**

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**Introduction:** Although there has been speculation about the relationships between sleep habits and demographic variables few studies have systematically investigated these associations. We analyzed eight demographic variables in predicting time in bed (TIB), total sleep time (TST), and sleep efficiency (SE), which is derived from TIB and TST.

**Methods:** A random sample of 872 healthy normal sleepers were selected from the Detroit tri-county population (mean age=39±11years;48%Female) and completed a 20 minute phone inter-
view. The following demographic data were analyzed in order to predict TIB, TST, and SE: work status, race, income, number of children, gender, marital status, age, and highest grade of education completed. Participants with sleep disorders, medical disease, depression, substance abuse, and any shift work were excluded.

Results: Multiple regression analysis was used to determine significance in the prediction of each self-reported sleep variable (TIB, TST, and SE). For TIB, higher income was associated with a decrease (p<.05), being male was associated with a decrease (p<.01), and having more children was associated with an increase (p<.01). For TST, higher income was associated with a decrease (p<.05), current employment was associated with a decrease (p<.05), being a male was associated with a decrease (p<.01), lower education was associated with a decrease (p<.05), and being African-American was associated with an increase (p<.05). For SE, having more children was associated with a decrease (p<.01), current employment was associated with a decrease (p<.01), and lower education was associated with a decrease (p<.01).

Conclusion: These data demonstrate that signs associated with success: income, employment and having children are all predictors of decreased TST. This decrease in TST can be attributed to both reduced TIB and disturbed sleep, as evidenced by a decrease in sleep efficiency. These data suggest that successful individuals in our society are either not educated regarding the importance of sleep or do not follow available recommendations regarding appropriate sleep practices.

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0711

Familial Vulnerability To Sleep Disturbance
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Introduction: It is important to determine what underlying factors may predispose an individual to develop insomnia. One way to investigate a potential familial predisposition to sleep disturbance is to examine the relationship between adult siblings on a standard measure of sleep-related vulnerability to stress.

Methods: A random sample of 31 individuals (age= 49 ± 12.88 years, 61.3% F) was drawn from the tri-county Detroit area. Participants and one of their siblings answered questions regarding their sleep habits, psychological status, and current medical conditions by phone. Scores on the Ford Insomnia Response to Stress Test (FIRST), Epworth sleepiness scale (ESS), and the Eysenck 12-item neuroticism questionnaire were also obtained. In addition, participants were assessed for insomnia using the Global Sleep Assessment Questionnaire (GSAQ). FIRST scores, ESS, and Eysenck scores were compared between siblings using Pearsons correlations.

Results: The FIRST scores for sibling pairs were significantly correlated (r = .51, p<.003). No sibling pair correlations were found for the ESS or the Eysenck questionnaires. After excluding the 7 (11.3 %) participants and their siblings who met criteria for insomnia, the correlation of FIRST scores for sibling pairs remained significant (r = .64, p<.001). Individuals with insomnia had higher FIRST scores than those without insomnia (insomnia= 24.9 ± 5.5, no insomnia = 18.2 ± 7.4, t= -2.32, p<.05).

Conclusion: The relationship of stress-related sleep disturbance between siblings provides evidence for a familial relationship to stress. The effect size of the FIRST correlations found in this study is similar to a correlation found in a previous study done on siblings and their IQ. Further research using twins and examining potential candidate genes will be necessary to determine if the familial relationship found in the present study has a genetic component.

Research Supported by MH Grant: K23MH068372

0712

Using Medical Claims Data And Clinical Literature To Forecast The Impact Of Adding A New Drug Onto The Formulary: A Case Study Of Insomnia Treatment

Introduction: Medical claims and clinical trial data may be combined effectively to develop budget impact models that estimate the potential costs of adding new drugs to the formulary. A case study of eszopiclone, an insomnia drug, is presented.

Methods: A 3-step process was used to estimate the costs of treating insomnia patients with eszopiclone and other insomnia agents. First, insomnia drug efficacy was estimated globally from the available literature on marketed drugs and specifically from clinical trial reports of eszopiclone. Adjustments for the different characteristics of each clinical trial (size, location, patient characteristics, etc) were made prior to summarizing the trial data. A multiple regression model was then applied to the MarketScan claims data (database of over 86,000 insomnia patients) and to the clinical trial efficacy data in order to estimate a relationship between medical expenditures and treatment efficacy. Patient-reported total sleep time was the primary efficacy measure, and five other sleep variables (patient-reported latency and awakenings, PSG latency, sleep efficiency, and WASO) were included in the model. Eszopiclone expenditures (premium pricing assumed) were estimated by multiplying eszopiclone efficacy estimates (step 1) by the regression-based estimates of expenditures obtained in step 2. The regression model additionally accounts for the impact of other demographics and clinical characteristics that influence expenditures. A budget impact model was then developed.

Results: For a representative health plan with 100,000 enrollees, the model estimated that using eszopiclone decreased annual insomnia treatment costs by $498,204 using total sleep time. Results were consistent regardless of which efficacy endpoint was used.

Conclusion: This modeling approach showed that the addition of eszopiclone to a representative health plan formulary could decrease annual treatment costs for insomnia. These results were consistent across 6 parameters, and represent an alternative and potentially effective way of estimating the cost of care impact of new treatment for insomnia formulary.

Support for this study provided by Sepracor Inc., Marlborough, MA

0713

Trajectory Analysis Of Treatment Response Across A Twelve-Month Study Of Nightly Eszopiclone In Patients With Chronic Insomnia
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Introduction: A 12-month (6-month double-blind, 6-month open-label) study suggested that eszopiclone was an effective insomnia treatment. Although these data showed no evidence of tolerance, individual patients may have different treatment response patterns. This secondary analysis determined whether distinct treatment outcome trajectories could be identified among study patients.

Methods: Patients included 788 men and women 21-69 years of age who reported insomnia (sleep duration ≤6.5 hours and/or sleep latency >30 minutes). Eszopiclone 3mg (ESZ-ESZ group) or placebo (PBO-ESZ...
group) was taken nightly for 6-months, followed by 6-months of open-label eszopiclone. Subjective sleep data were collected weekly and included sleep latency, wake time after sleep onset, and total sleep time. The SAS TRAJ procedure was used to calculate the probability of each subject belonging to each trajectory across the 12-month study.

**Results:** Linear models were fitted in the ESZ-ESZ group. For each endpoint, trajectories of treatment response subgroups had similar slopes regardless of the number of subgroups included in the analysis. Subgroups differed only in mean symptom levels, not in time course. Descriptively, each subgroup showed a rapid treatment response followed by a stable course or slight improvement across the 12-month trial. Similar models were used to test the PBO-ESZ group. Trajectories for each sleep endpoint had similar slopes regardless of number of groups, and again differed only in mean symptom level. Descriptively, each PBO-ESZ subgroup showed slight improvement during the first 6-month placebo-period, with a rapid treatment response followed by a relatively stable course after initiation of eszopiclone treatment.

**Conclusion:** There were no evidence of tolerance or any other distinct treatment response trajectory in either dose group in this 12-month clinical trial. The results provide further evidence that nightly eszopiclone treatment was associated with rapid and sustained response and showed no evidence of tolerance, even among specific patient subgroups.

Support for this study provided by Sepracor Inc., Marlborough, MA

**0715**

**Acute Administration Of Gaboxadol Improves Sleep Initiation And Maintenance In Patients With Primary Insomnia**

**Deacon S, 1, 2 Stater L, 1 Stater C, 1 Vorstrup S, 1 Lundahl J**

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**Introduction:** Gaboxadol is a selective extrasynaptic GABA agonist in development for the treatment of sleep disorders. This study was designed to evaluate its acute efficacy and safety in the treatment of primary insomnia (PI).

**Methods:** This was a randomised, double-blind, 3-way crossover, polysomnography (PSG) study designed to compare 5mg and 15mg doses of gaboxadol to placebo (PBO) in 26 PI patients aged 18-65 years. Patients met the DSM-IV criteria for PI and the following PSG criteria: latency to persistent sleep (LPS) > 30min, total sleep time (TST) < 420min and wakefulness during sleep (WDS) > 48min or > 10 night awakenings (NAW). Gaboxadol or PBO was administered 30min before bedtime on two nights during 3 periods separated by 7-14 days. The patients own evaluation of their sleep was recorded using the Leeds Sleep Evaluation Questionnaire. Next day residual effects were evaluated using the Cognitive Drug Research test battery.

**Results:** The per protocol efficacy analyses (n=23) were based on pooled data from nights 1 and 2 and are presented as means. Both gaboxadol doses significantly improved TST (5mg: 419.8min, 15mg: 420.3min, PBO: 408.7min) and reduced total time awake (5mg: 58.2min, 15mg: 57.3min, PBO: 68.5min) with no effect on WDS or NAW (although both doses significantly reduced WDS on night 1). Only 15mg significantly reduced LPS (23.6min vs PBO: 30.0min). Slow wave sleep (SWS) was significantly enhanced by 15mg only (113.5min vs PBO: 93.9min). Patient reports of reduced time to sleep and increased sleep quality showed significant improvement. No next day residual effects were observed. All adverse events were mild or moderate.

**Conclusion:** Acute administration of 15mg gaboxadol improved sleep initiation and sleep maintenance as well as enhanced SWS in patients with PI. Objective improvements were complemented by subjectively reported improvements in sleep quality and latency. Gaboxadol was well tolerated with no next day residual effects.

This research was supported by H. Lundbeck A/S, Denmark.
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**Conclusion:** These data suggest that insomnia severity may be mediat-
mediated/moderated by sleep homeostasis and that the homeostat, or input to the
homeostat, may be abnormal in patients with Primary Insomnia. Clinically, the data are
useful in that one may encourage patients to "take heart" in that a good night's sleep is
generally only 1-2 nights away.

0717 Insights From Focus Groups On How To Make Nonpharmacologic
Treatments For Insomnia Available To People With Cancer

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**Introduction:** Insomnia is reported by almost one third of cancer
patients. Nonpharmacologic (cognitive-behavioural) programs can
improve the sleep of cancer patients, yet such interventions are rarely
offered to them. The purpose was to find ways of making nonpharmaco-
logic insomnia treatments easily available.

**Methods:** Five focus groups were held. Participants were 12 women and
8 men with various cancer diagnoses and with sleep difficulty; mean
age=57 yrs (range: 44-76). After explaining the general nature of non-
pharmacologic treatments for insomnia, the moderator posed the follow-
ing key questions: What would be the best way to find out about such a
service for insomnia treatment? Once you found out about the program
what would make it easy to participate? What would make it difficult to
participate? If this program were offered, at what type of location would
you like to attend the sessions? Major themes were identified by the mod-
erator immediately after each focus group, and by two reviewers who
independently examined the transcripts.

**Results:** The convergent themes identified by the moderator and the two
reviewers included the following. Ways to find out about a service: from
the family physician (or his/her staff, brochures, signs); cancer centre
(nurse, social worker, posters, brochures); trusted health-care internet
sites; newspaper; public library (bulletin board); home care nurse; cancer
buddy; Canadian Cancer Society; pharmacy (brochures). Ideas for mak-
ing it easy to participate: no interference with work schedules; explicitly
supported by the medical system; physician referral; easy contact process
(little paperwork); easy transportation; no cost; easy parking; not early in
the day. Location: central non-medical or medical setting; comfortable
room; low lighting. The notion was also expressed that the best approach
was supported by the medical system; physician referral; easy contact process
offered to them. The purpose was to find ways of making nonpharmaco-
logic insomnia treatments easily available.

0718 Sleep State Misperception In A Psychiatric Hospital Outpatient Sleep
Clinic

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**Introduction:** Medical, psychiatric, and sleep disorder patients commonly
report variations in the perception of having slept, "sleep state misper-
ception" (SSM). Previous studies show mainly sleep underestimation.
This study used a sleep clinic sample containing psychiatric patients and
general medical sleep disorders to explore SSM.

**Methods:** A retrospective review was conducted of 263 consecutive
patients. Each had polysomnography, ESS, BDI, and a subjective morn-
ing questionnaire. SSM definitions: SSMonset = subjective SL - measured
SL; SSMtot = measured TST - subjective TST; Subj#Wakes = (subjective
#Wakes) / (measured #Wakes). A MANCOVA on drugs [2 x 4
model with "age" as covariate: +/- benzodiazepines, antipsychotics, anti-
depressants, mood stabilizers] was performed using the 3 SSM measures
as dependent variables. Similarly, a MANCOVA on diagnosis [+/-
mood disorder, anxiety, RLS-PLM, apnea] was performed. VARIMAX factor
analysis on the entire dataset extracted grouping factors, upon which 1-
way ANOVAs were done.

**Results:** Grand means (S.D.): SSMtot = 0.94 (1.80) hr.; SSMonset = 0.39
(0.83) hr.; Subj#Wakes = 4.18 (3.13). The "drug" MANCOVA for
SSMtot was significant (p<0.0002), as was its main effect for AD
(p<0.048), plus the AD*AP (p<0.027), AD*BZD (p<0.002) and
AD*AP*BZD (p<0.008) interactions. SSMtot and Subj#Wakes were not
significant. The "diagnosis" MANCOVA was not significant. Factor
analysis isolated 5 factors (young psychotic depressives, pure OSA,
UARS with depression, EDS, RLS-PLM with depression). One-way
ANOVA of SSMtot on a subset of 90 patients unique to the upper quartile
of a single factor showed that pure OSA patients had the lowest
SSMtot (p<0.04). SSMonset and Subj#Wakes analyses were not signifi-
cant.

**Conclusion:** Psychiatric patients have significantly more SSMtot than
OSA patients, despite OSA patients having a shorter, more fragmented
sleep. Most psychiatric medications serve to reduce SSM. Overall,
these results indicate that SSM is largely a feature of psychiatric illness,
and is reduced with appropriate drug treatment.

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0719 No Link Between Distal Vasodilation And Sleep Onset Latency In
Insomniacs

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**Introduction:** A close association has been established between ther-
moregulatory changes and initiation of sleep. The present study tested the
hypothesis that sleep-onset insomnia may result from an inability to lose
sufficient heat from distal skin regions, thereby preventing the normal
nocturnal core temperature decline.

**Methods:** Ten Sleep Onset Insomniacs (SOI) and eight healthy controls
completed a habituation and three non-consecutive overnight
experimental sessions. Subjects were selected on the basis of no medica-
tion use, normal scores on depression and anxiety scales and absence of
other medical disorders. Polysomnographic sleep recordings were made.
A Novel Brief Behavioral Therapy For Primary Insomnia
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Introduction: Chronic insomnia is a prevalent disorder, often associated with significant daytime deficits. Clinical research has demonstrated that cognitive behavioral therapies for insomnia produce lasting benefits. However, implementing these therapies usually requires considerable time, effort, and commitment that may reduce compliance. In response to these issues we have been investigating a brief, concentrated therapy for insomnia. The therapy involves a 28-hour period of acute sleep deprivation during which 50 sleep onset opportunities and very brief naps (less than 4 minutes sleep) are given. The aim was to use the sleep deprivation to produce numerous short sleep onset latencies (most less than 5 minutes) to reduce the putative psychophysiological conditioned response of primary insomnia. The present study evaluated the efficacy of this novel, brief therapy.

Methods: Seventeen volunteer chronic primary insomniacs (12 females and 5 males) participated in the study (Mean age = 39.12, SD = 12.41 years). Treatment response was determined using sleep diaries, actigraphy, and psychological questionnaires. Assessment involved two-week periods of measurement 1. Prior to treatment, 2. Immediately following treatment, and 3. Six weeks after treatment.

Results: Improvements in subjective sleep latency over time (70 mins. to 39 mins. and 47 mins.), sleep efficiency (62% to 76% and 74%), and total sleep time (317 mins. to 382 mins. and 360 mins.) were all significant as shown by repeated measures ANOVAs (F(15)=9.46, p<0.05), (F(15)=22.66, p<0.001), and (F(15)=16.46, p<0.001) respectively. Improvements in actigraphy measured sleep latency and efficiency were also significant (F(10)=4.15, p<0.05 and F(10)=10.5, p<0.05 respectively). Questionnaires indicated significant improvements in sleep self-efficacy, fatigue, vigour, and cognitive aspects of sleep anticipatory anxiety.

Conclusion: This preliminary data indicates the potential for this brief behavioral therapy to rapidly treat chronic insomnia. To maximize treatment response and enhance long-term improvement, however, a follow-on adjunctive therapy may be a worthwhile addition to this accelerated therapy procedure.

**0721**
Evidence For Greater Night To Night Variability In Standard Sleep Parameters In Primary Insomniacs Versus Controls In The Naturalistic Setting
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Introduction: Documented differences in standard sleep parameters between controls and insomnia patients in the home environment have been equivocal. Recently, additional measures have been used to discriminate between insomnia and controls and include autonomic measures of arousal and night to night variability in sleep parameters. A comfortable, in-home PSG system would enable the assessment of variability and concomitant arousal measures across several nights in a naturalistic setting. We quantified time to persistent sleep latency (TPSL) and sleep efficiency (SE) over five nights in the home in patients with primary insomnia (PI) and controls (CTL) using an ambulatory, PSG system.

Methods: Subjects (n = 5 primary insomnia, age = 29.0±8.8 yrs. n = 5 controls, age 23.4±2.6) wore the LifeShirt® PSG system (VivoMetrics, Inc, USA) while sleeping at home for a total of five nights. EEG data were scored according to R&K for TST and TPSL (lights out to 3 consecutive epochs of stage 2 sleep). Differences between group means were identified by ANOVA. Homogeneity of variances was tested with the Levene statistic.

Results: When compared to controls, mean SE over the five nights was lower (CTL, 0.84±0.142%; PI, 0.948±0.039%; p = 0.002) in the insomnia patients, while TPSL was longer (CTL, 12.2±8.9 min; PI, 31.9±28.8 min; p = 0.004). Intra-subject variance was quantified by the mean standard deviation over the five nights and was greater in the PI group for SE (CTL, 0.023±0.003; PI, 0.078±0.038; p = 0.017) and TPSL (CTL, 7.2±2.3; PI, 12.0±5.4; p < 0.001).

Conclusion: These data suggest that the LifeShirt PSG system is sensitive to differences in time to persistent sleep latency and total sleep time during home assessment. The increased nighttime variability in each of the sleep parameters assessed suggests that this objective metric may be an important reflection of sleep dysregulation in primary insomnia which is not always captured by mean differences in sleep parameters. Effective ambulatory PSG will enable multiple-night, in-home studies for the evaluation of sleep in a way that has not been previously possible. Further investigation of the specific physiological parameters associated with night to night variability in sleep may lead to important insights regarding the underlying pathophysiology of this disorder.

Study was supported by VivoMetrics

**0722**
Feedback Of Sleep/Wake State Improves Subjective And Objective Sleep Of Insomniacs
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Introduction: Insomniacs overestimate wake time compared to good sleepers, and are more likely than good sleepers to report already being in addition to finger, foot and rectal core temperature measurements for 90 minutes prior to and including sleep onset. Digital infrared thermal images of the upper torso were also made to calculate distal-proximal gradient (DPG), as an indicator of heat loss from distal skin (e.g. hands and feet).

Results: Repeated measures ANOVA revealed that core temperature decreased significantly (p<0.0001), while hand and foot temperature and DPG increased significantly (p<0.0001) across time for all subjects. No differences were observed between core temperatures of SOI and Controls. Finger temperatures of SOI (mean±SEM=34.3±0.1°C) were significantly higher than Controls (31.5±0.2°C) in the 90 minutes before sleep onset (p<0.01). DPG was also significantly higher in SOI (0.6±0.1°C) compared with Controls (-1.1±0.2°C) for the same time period (p<0.05). Most important was the observation that a significant negative correlation between the DPG and log-transformed sleep onset latency in Controls (R2=-0.77, p<0.05) was not present at all in the SOI group (R2=-0.01, p=0.75).

Conclusion: We confirm that an index of distal heat loss is a strong predictor of sleep onset latency in healthy sleeping adults. However, any functional link between distal vasodilation and sleep propensity appears to break down in non-anxious and non-depressed SOI subjects. Contrary to our initial hypothesis, there may actually be greater than normal heat loss from distal skin regions in insomniacs. In summary, the current results suggest that normal thermoregulatory processes around sleep onset are dysfunctional in sleep onset insomniacs and could be a target for future insomnia therapies.

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awake when awoken from Stage 2 and REM sleep. This misperception may prolong nocturnal wakefulness. If sleep perception could be improved, insomniacs' sleep may improve as a result. The present study examined the effects on sleep of two forms of feedback intended to correct this misperception.

Methods: The 10 participants (8F, mean age 49.7) met ICSD criteria for Psychophysiological Insomnia, and had participated in a previous experiment involving 6 nights of PSG without feedback on their sleep. In the present study, following two nights of home PSG, participants were given retrospective feedback in a structured interview. This incorporated general information about sleep and specific feedback of their subjective and objective sleep. Two home PSGs were repeated a month later. Participants then attended four weekly laboratory sessions where they were given immediate feedback of their sleep/wake state several times across the night. Prior to each feedback, participants were asked to evaluate whether they had been awake or asleep. The feedback then stated whether they were awake or asleep and how long they had been sleeping since they had last been given feedback. Half of the overnight feedbacks were presented during wake while the sleep feedbacks were given following awakenings from Stage 2 and REM sleep. The combined probability of reporting being awake prior to sleep decreases from 51.7% on night 1 to 14.0% on night 4. A month after completing the laboratory sessions, two further home PSGs were conducted.

Results: PSG measured sleep significantly increased from before retrospective feedback [334.8 (sd54.7)] to after [382.6 (sd51.3)], t = -3.26, p <.01, and increased further following the laboratory immediate feedbacks [422.0 (sd56.0)], t = -3.01, p <.01. Similarly, initial Sleep Efficiency [75.5% (8.58)] increased following retrospective feedback to 81.5% (7.19), t = -2.55, p <.05, and increased to 85.0% (7.31) following immediate feedbacks (t = -2.26, p <.05). Subjective Sleep Efficiency improved from 61.6% (22.3) to 73.1% (11.4) following retrospective feedback (t = -2.70, p <.05), and improved further following immediate feedback [81.6% (15.2), t = -3.29, p <.01].

Conclusion: Both retrospective and immediate feedback improves the objective and subjective sleep of insomniacs.

National Health and Medical Research Council of Australia

0723
Personality In The Interpretation Of Late-Life Insomnia: Introducing The Sleep Discrepancy Index
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Introduction: Previous research has identified a role for personality in the development and maintenance of insomnia, most notably through high levels of neuroticism and perfectionism. However, the mechanism by which personality influences insomnia, through lowered problem-identification or actual poor sleep parameters, is poorly understood. The present study investigated whether personality dimensions were more influential in the self-diagnosis of insomnia, reported sleep parameters, dysfunctional beliefs about sleep or a combination of the latter two. It was proposed that an evaluation process, between the perceived quantity of a sleep episode and the associated beliefs about the costs and consequences of a poor sleep episode (Sleep Discrepancy Index), occurs and it is this evaluation that is largely moderated by neuroticism and perfectionism, resulting in insomnia self-identification.

Methods: One hundred and sixty seven participants were recruited through a poster campaign in two counties within the U.K. (32 insomniacs and 135 normal sleepers). Participants were administered the PSQI, Sleep Catastrophizing Scale, a measure of the Big Five, with the additional dimension of perfectionism, and the Dysfunctional Beliefs and Attitudes about Sleep scale.

Results: As predicted, insomniacs scored higher on perfectionism, neuroticism, engaged in more sleep catastrophizing and scored higher on the DBAS than normal sleepers. Additionally, the biggest predictors of sleep catastrophizing were high scoring on the sleep discrepancy index and higher levels of neuroticism. Together these factors explained 48% of the variance in sleep catastrophizing. Using the PSQI, a subgroup analysis was undertaken between subjective insomniacs and objective insomniacs. The findings showed no differences between the groups on any personality dimension but subjective insomniacs reported a higher sleep discrepancy index and higher levels of sleep catastrophizing.

Conclusion: The present study sought to examine whether neuroticism and perfectionism were related to reporting insomnia or whether it is related to reporting poor sleep. The results suggest that independently, personality has a limited influence on problem identification and poor sleep efficiency but is most influential on the daily evaluation between these two factors and subsequent catastrophic interpretations.
**Zolpidem Modified-Release Objectively And Subjectively Improves Sleep Maintenance And Retains The Characteristics Of Standard Zolpidem On Sleep Initiation And Duration In Elderly Patients With Primary Insomnia**

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**Introduction:** A modified-release (MR) formulation of zolpidem has been developed with the aim of providing optimal treatment of several symptoms of insomnia, including difficulty maintaining sleep. The present study was carried out to investigate the efficacy and safety of a dose of 6.25 mg of zolpidem MR in a population of 205 elderly insomnia patients.

**Methods:** A polysomnography (PSG) study comparing nightly zolpidem MR 6.25 mg versus placebo was conducted in elderly patients (mean age 70.2 +/- 4.5 years) with primary insomnia (DSM-IV criteria) and sleep maintenance difficulties. The hypnotic efficacy was assessed on mean PSG sleep parameters from Nights 1, 2, 15, and 16 of double-blind treatment and using subjective estimates from sleep questionnaires throughout the 3-week period.

**Results:** Zolpidem MR 6.25 mg improved sleep maintenance by significantly reducing PSW Wake time After Sleep Onset (WASO) during the first 6 hours of the night on the first 2 nights of treatment and after 2 weeks of nightly administration. The results also confirmed the known hypnotic properties of zolpidem on sleep induction (decrease of PSG Latency to Persistent Sleep) and on sleep duration (increase in PSG Sleep Efficiency). The daily subjective evaluation of sleep parameters provided a clinical confirmation of the positive effect of zolpidem MR 6.25 mg on the patients sleep as shown by the PSG analysis. The safety evaluation demonstrated a good tolerability of zolpidem MR 6.25 mg with a comparable percentage of patients experiencing adverse events between zolpidem MR and placebo and no evidence of clinically relevant next-day residual effects.

**Conclusion:** The 6.25-mg dose of zolpidem MR (Ambien CR) was found to be safe and effective in the treatment of elderly patients with primary insomnia and sleep maintenance difficulties.

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**Zolpidem Modified-Release Improves Sleep Induction, Sleep Maintenance, Sleep Duration, And Quality Of Sleep Without Next-Day Residual Effects In Adults With Primary Insomnia**

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**Introduction:** The effect of tiagabine, a selective gamma-aminobutyric acid reuptake inhibitor, on objective measures of sleep in adult and elderly patients with primary insomnia was evaluated.

**Methods:** In this exploratory study, adults (n=15, 18-64 years) and elderly (n=16, 65-85 years) patients with primary insomnia received nightly tiagabine 8 mg (8 adults), tiagabine 4 mg (10 elderly), or placebo (7 adults and 6 elderly). Assessments included polysomnography at baseline (2 screening nights) and on nights 1-2, 15-16, and 29-30. This study was designed to gain preliminary 30-day efficacy and safety information; no inferential statistics were performed.

**Results:** In adult patients, median increase from baseline in slow-wave sleep (SWS) at nights 1-2, 15-16, and 29-30 was 25.0 min, 24.0 min, and 32.0 min, respectively, for tiagabine and 14.5 min, 23.0 min, and 6.3 min, respectively, for placebo. In elderly patients, median change from baseline in SWS at nights 1-2, 15-16, and 29-30 was +3.3 min, +15.0 min, and +6.8 min, respectively, for tiagabine and -4.0, +5.3, and +2.8 min, respectively, for placebo. In adults, median reduction from baseline in WASO at nights 1-2, 15-16, and 29-30 was 51.8 min, 34.8 min, and 46.0 min, respectively, for tiagabine and 23.5 min, 23.5 min, and 28.8 min for placebo. In elderly patients, median reduction from baseline in WASO at nights 1-2, 15-16, and 29-30 was 15.5 min, 12.8 min, and 16.8 min, respectively, for tiagabine and 15.0 min, 20.0 min, and 10.3 min for placebo. No differences between tiagabine and placebo were observed in latency to persistent sleep or total sleep time. Tiagabine was generally well tolerated. Only one patient (adult) withdrew from the study because of an adverse event (restlessness).

**Conclusion:** Tiagabine may have a positive effect on SWS and WASO in adult and elderly patients with primary insomnia. The clinical correlates of these effects warrant further investigation.

**Sponsored by Cephalon, Inc.**

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**Zolpidem Modified-Release Improves Sleep Induction, Sleep Maintenance, Sleep Duration, And Quality Of Sleep Without Next-Day Residual Effects In Adults With Primary Insomnia**

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**Introduction:** Epidemiologic surveys confirm that insomnia is characterized by multiple symptoms, including difficulty initiating sleep, problems maintaining sleep, early-morning awakening, and nonrestorative sleep.
Zolpidem, a hypnotic, shows clear effects on sleep onset latency and sleep efficiency. Zolpidem modified-release (MR), a new formulation of zolpidem, has been developed to also improve sleep maintenance without inducing next-day residual effects.

Methods: A polysomnography (PSG) study comparing nightly zolpidem 12.5 mg versus placebo was conducted in adult patients (n=212, 123 female, mean age 44.3 +/- 13 years) with primary insomnia (DSM-IV criteria) and sleep maintenance difficulties. Hypnotic efficacy was assessed on mean PSG sleep parameters from Nights 1, 2, 15, and 16 of double-blind treatment and using daily subjective estimates from sleep questionnaires throughout the 3-week treatment period.

Results: Zolpidem MR improved sleep maintenance by significantly reducing PSG Wake time After Sleep Onset (WASO) during the first 6 hours of the night on the first 2 nights of treatment and after 2 weeks of nightly administration. The effect on WASO, which was decreased up to 6 hours postdosing but not in the final part of the night (H7,8), appears optimal in terms of benefit/risk, allowing refreshed awakening with no clinically relevant next-day residual effects. Objective results also confirmed the hypnotic properties of zolpidem MR on sleep induction (decreased PSG Latency to Persistent Sleep) and sleep duration (increased PSG Sleep Efficiency). Subjective measures of hypnotic effects showed that the actions of zolpidem MR 12.5 mg on sleep induction, sleep maintenance, sleep duration, and quality of sleep were maintained during 3 weeks of treatment. Safety characteristics of zolpidem were retained with zolpidem MR: there was no evidence of clinically relevant residual effects.

Conclusion: Zolpidem MR (Ambien CR) was found to be safe and effective in the treatment of patients with primary insomnia and sleep maintenance difficulties.

0729 Zolpidem Modified-Release 6.25 Mg And Double Dose 12.5 Mg Have No Residual Effects On Central Nervous System Integrative Capacity, Sensorimotor Performance, And Immediate And Delayed Memory Recall In Healthy Elderly Subjects Legangneux E,1 Hindmarch I,2 Zobouyan I3
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Introduction: Short-acting hypnotic drugs for treating insomnia have minimal residual effects but may not provide optimal efficacy throughout the night. A modified-release (MR) formulation of zolpidem has been developed to overcome this limitation. This study assesses the residual psychomotor, cognitive effects, and safety of a new zolpidem MR formulation 8 hours after a single nocturnal dose in healthy elderly subjects.

Methods: A randomized, double-blind, placebo- and reference-controlled, 4-way crossover study in 24 subjects (65-78 years old, 10 male) compared zolpidem MR 6.25 mg and 12.5 mg (double the recommended elderly dose) or flurazepam 30 mg to placebo. Tests included Critical Flicker Fusion (CFF), Choice Reaction Time (CRT), Compensatory Tracking Task (CTT), Immediate and Delayed Word Recall (WRi, WRd), and Digit Symbol Substitution Test (DSST) and the Leeds Sleep Evaluation Questionnaire (LSEQ). Hematology, biochemistry, vital sign monitoring, and adverse-event recording evaluated safety.

Results: Neither zolpidem MR doses demonstrated a significant difference in performance vs placebo for CFF, CRT, total reaction time, CTT, WRi, WRd, and DSST, 8 hours postdose. Flurazepam significantly impaired performance with respect to placebo on all tests. LSEQ assessment showed no negative effects.

Conclusion: In contrast to flurazepam, a single dose of zolpidem MR (Ambien CR) 6.25 mg or 12.5 mg produces no residual effects on CNS integrative capacity, sensorimotor or psychomotor performance, or immediate and delayed memory recall compared to placebo in healthy elderly subjects. Zolpidem MR was well tolerated with no serious adverse events observed.

0730 Zolpidem Modified-Release Demonstrates Sustained And Greater Pharmacodynamic Effects From 3 To 6 Hours Postdose As Compared With Standard Zolpidem In Healthy Adult Subjects Greenblatt DJ,1 Zammit G,2 Harmatz J,1 Legangneux E3
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Introduction: A zolpidem modified-release (MR) formulation has been developed to provide sustained plasma zolpidem concentrations in the middle portion of the night (3-6 hours postdose) and so improve sleep maintenance, while possessing the same elimination half-life as standard zolpidem. The purpose of this study is to demonstrate prolonged sedative activity of a zolpidem MR formulation (12.5 mg) using relative electroencephalogram (EEG) beta frequency band (EBFB) and to establish the relationship of activity to plasma drug concentrations.

Methods: Double-blind, placebo-controlled, 3-way crossover study of 81 subjects (aged 29.5 +/- 7 years, 46 male) comparing zolpidem MR to standard zolpidem (10 mg) and placebo (minimum washout periods: 7 days). After a single, morning dose, EEG recordings and blood samples were obtained at 1-hour intervals for 10 hours except for the period 3 to 6 hours postdose (20-minute intervals). Digit Symbol Substitution Test and visual analogue scales (VAS) for sedation were also performed concomitantly.

Results: 72 subjects completed the study. Zolpidem MR, compared to standard zolpidem, demonstrated a longer duration of action through the duration of relative EBFB power change in 3 parameters: quarter-value duration, half-value duration, and three-quarter-value duration of the expected maximum effect of EBFB. Effect was significantly greater at 3 to 6 hours postdose. As expected, zolpidem MR administration was associated with sustained plasma concentration as compared with the standard zolpidem formulation.

Conclusion: Zolpidem MR (Ambien CR) demonstrates longer duration of action compared to standard zolpidem, with a significantly greater effect 3 to 6 hours postdose. VAS for sedation also differentiates the 2 formulations.

0731 Zolpidem Modified-Release Significantly Reduces Latency To Persistent Sleep 4 And 5 Hours Postdose Compared With Standard Zolpidem In A Model Assessing The Return To Sleep Following Nocturnal Awakening Hindmarch I,1 Stanley N,1 Legangneux E,2 Emegbo S3
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Introduction: Zolpidem rapidly induces sleep and increases sleep duration with a low incidence of next-day residual effects. A zolpidem modified-release (MR) formulation incorporating both immediate- and prolonged-release preparations has been developed to provide sustained plasma zolpidem concentrations in the middle portion of the night (3-6 hours postdose) and so improve sleep maintenance, while possessing the same elimination half-life as standard zolpidem. This study uses a model of middle-of-the-night insomnia to assess persistence of efficacy of zolpidem MR formulation (12.5 mg) to induce sleep after awakening subjects 3, 4, and 5 hours after a single nocturnal dose.
**Category L—Sleep Disorders-Insomnia**

**Methods:** A double-blind, placebo-controlled, 9-way crossover study of 54 healthy subjects (aged 27.9 ± 7 years, 28 male) comparing zolpidem MR to standard zolpidem and placebo. Polysomnography (PSG) recordings were performed for 8 hours postdose. Subjects were awakened 3, 4, and 5 hours postdose and exposed to a noise model that prolongs latency to persistent sleep (LPS). Primary endpoint was LPS following awakening at 3, 4, or 5 hours postdose. Digit Symbol Substitution Test (DSST) and Leeds Analog Rating Scales (LARS) were performed 3, 4, and 5 hours postdose.

**Results:** Zolpidem MR demonstrated a significant reduction in LPS vs standard zolpidem at 3 and 4 hours postdose. Both formulations significantly reduced LPS compared to placebo at all time points. DSST and the drowsy LARS item followed a similar pattern. Total sleep time, wake time after sleep onset, and shift of sleep stages indicated that zolpidem treatment groups slept better.

**Conclusion:** Zolpidem MR (Ambien CR) exhibits significantly greater hypnotic activity at Hours 4 and 5 postdose compared to standard zolpidem and placebo without compromising psychomotor performance or sleep architecture.

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**0732**

Sleep Problems And Usual Alcohol Consumption: A Population-Based Study Of Men And Women

**Introduction:** We investigated the relationship of usual alcohol consumption with self-reported sleep problems and habits in 527 women and 599 men in the Wisconsin Sleep Cohort Study.

**Methods:** Participants reported sleep problems (difficulty falling asleep, difficulty sleeping, difficulty wakening after sleep, or difficulty getting back to sleep). Sleep problems occurring ≥ 5 times/month were considered "frequent." Weekly consumption of alcoholic beverages, as well as smoking status and medication use were assessed by health questionnaire. Drinks per week were categorized as: 0, 1-6, 7-13, or 14+. Sleep problems were modeled using logistic regression/GEF. Time to fall asleep was modeled using linear mixed models. All models were adjusted for age, BMI, smoking status, and medications. Separate models were fit for men and women.

**Results:** Men and women differed in alcohol consumption and sleep problems, with 9% of women vs. 26% of men consuming 7 or more drinks/week, but more women reporting frequent sleep problems. Men who drank 7-13 drinks/week vs. 0 had fewer odds of difficulty falling asleep (OR = 0.34, 95% CI: 0.15 - 0.74); there was no relationship in women (OR = 0.98, 95% CI = 0.41 - 2.37). Men who drank 14+ drinks/week had increased odds of difficulty getting back to sleep (OR = 2.14, 95% CI: 1.04 - 4.42); women had increased, but non-significant odds (OR = 1.54, 95% CI: 0.58 - 4.08). There were no significant relationships between these two sleep problems and other levels of alcohol consumption or between alcohol consumption and waking repeatedly or time to fall asleep.

**Conclusion:** For men, 7-13 drinks/week was associated with reduced difficulty initiating sleep, but 14+ drinks/week was associated with increased sleep disturbance later in the night. For women, alcohol was not significantly related to sleep problems, though few women reported higher levels of alcohol use.

**Grant A246**

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**0733**

Zolpidem Modified-Release 12.5 Mg Has No Residual Effects On Psychomotor Performance And Cognitive Function In Healthy Adult Subjects

**Introduction:** Short-acting hypnotic drugs for treating insomnia have minimal residual effects but may not provide optimal efficacy throughout the night. A modified-release (MR) formulation of zolpidem has been developed to overcome this limitation. This study assesses the residual psychomotor and cognitive effects and safety of a new zolpidem MR formulation 8 hours after a single dose.

**Methods:** A randomized, double-blind, placebo- and reference-controlled, 3-period crossover study in 18 healthy subjects (22-38 years old, 10 male) comparing zolpidem MR 12.5 mg or flurazepam 30 mg to placebo. Cognitive and psychomotor tests were performed 8 hours postdose: Critical Flicker Fusion (CFF), Choice Reaction Time (CRT), Compensatory Tracking Task (CTT), Immediate and Delayed Word Recall (WRI, WRd), and Digit Symbol Substitution Test (DSST). Subjective sleep quality was evaluated using the Leeds Sleep Evaluation Questionnaire. Clinical laboratory parameters, vital signs, and adverse event recording evaluated safety.

**Results:** Pairwise comparisons between zolpidem MR and placebo demonstrated no significant difference in performance in CFF, CRT, WRI, WRd, and DSST, 8 hours postdose. Flurazepam significantly impaired performance in all tests except DSST compared to placebo.

**Conclusion:** This study demonstrates that unlike flurazepam (positive control), zolpidem MR (Ambien CR) 12.5 mg has no residual effects on CNS integrative capacity, sensorimotor or psychomotor performance, or immediate and delayed memory recall except for CTT time reaction compared to placebo. Zolpidem MR is well tolerated and exhibits a comparable safety profile to placebo.

**Grant A246**

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**0734**

Do The Effects Of CBT-I Vary With Insomnia Subtype?

**Introduction:** The present analysis examines whether treatment outcome with CBT-I varies with insomnia subtype (i.e. initial, middle, or mixed). The data used to address this issue were from two case series data sets drawn from a Behavioral Sleep Medicine Service located at our local sleep disorders center. Services were provided by two experienced CBT-I therapists, both of whom were clinical psychologists.

**Methods:** 74 patients were classified as having Initial, Middle, or Mixed Insomnia. The criteria for Initial, Middle and Mixed Insomnia were as follows: Initial Insomnia = sleep latency (SL) >30 minutes and wake after sleep onset (WASO) <30 minutes; Middle Insomnia = SL <30 minutes and WASO >30 minutes; Mixed Insomnia = SL >30 minutes and WASO >30 minutes. All patients completed baseline sleep diaries for 1-2 weeks and then underwent CBT-I. Post Treatment effects were estimated based on the sleep diaries for last treatment week. Effect sizes estimates were calculated for each insomnia subtype for SL and WASO.

**Results:** The mean age of the group was 43.9 yrs +/- 16 and 59% were women. The groups did not differ with respect to age or gender. The average effect size without respect to group was SL = 1.22 and WASO = 1.39. The Initial Insomnia group exhibited a 2.24 effect of 1.17 and 0.55 for WASO. The Middle Insomnia group exhibited a reverse trend where the
SL effect was 0.66 and the WASO effect was 1.95. The Mixed Insomnia group exhibited a 1.83 for SL and 1.66 for WASO. Overall, the Mixed Insomnia exhibited - predictably - the largest average effect size (1.75), followed by the Middle Insomnia group (1.30) and then the Initial Insomnia group (0.86).

**Conclusion:** These results suggest that CBT-I 1) overall, produces comparable effects for SL and WASO, 2) produces its largest clinical effects in association with the presenting subtype of insomnia, and 3) produces significant improvement in sleep continuity within areas which are not related to the presenting subtype of insomnia. In addition, it would appear that CBT-I, while in general is very effective, is most effective for patients with Mixed Insomnia and least effective for patients with Initial Insomnia. This last finding suggests that it may be useful to develop and evaluate strategies which may be used to augment SL effects.

### 0735

**The Impact Of Insomnia On Absenteeism, Productivity, And Accident Rates**

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**Introduction:** Insomnia is a prevalent condition which has been linked with significant psychosocial and occupational impairments, all of which are costly to individuals and society. This study aims to document the impact of insomnia on absenteeism, productivity, and accident rates.

**Methods:** A subset of measures from a larger epidemiological investigation was used for this study. A random sample of 930 adults from the province of Quebec completed questionnaires regarding sleep, absences from work, reduced productivity and recently experienced accidents. Questions included a subjective rating, on a scale of 1(low) to 10 (high) regarding the extent to which insomnia and/or its consequences was deemed to be a contributing factor in these circumstances. Three sleep/insomnia subgroups were compared: good sleepers, presence of insomnia symptoms, insomnia syndrome.

**Results:** Twenty-nine percent of the insomnia syndrome group reported at least one absence from work in the previous three months, compared to 21% of the symptoms group and 15% of good sleepers. Participants in the good sleepers, symptoms and syndrome groups rated the link between insomnia and absences from work at, on average, 1.6, 3 and 4, respectively. The proportion of missed work attributable to insomnia was significantly higher in the insomnia syndrome group than in the symptoms or good sleepers groups. Regarding productivity, 35% of the insomnia syndrome group reported reduced productivity compared to 19.6% of participants in the symptoms group, and 9.8% in the good sleepers group. Subjective evaluations of the degree to which insomnia contributed to this lost productivity was positively associated with insomnia symptomatology. Finally, while accident rates were not significantly different across groups, 23.5% of all drivers reporting having experienced an accident in the previous 6 months felt that insomnia played an important role in the event. A full 39.5% of participants saw a link between their sleep difficulties and other types of accidents (p < .001 for all comparisons).

Preliminary analyses suggest that costs associated with absenteeism, lost productivity and accidents increase as a function of insomnia severity.

**Conclusion:** These results suggest a link between insomnia and decreased functional capacity, notably in the realm of work absenteeism and productivity, and a significant contribution of insomnia to accidents. These findings further document the indirect costs of insomnia.

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### 0736

**The Association Of Insomnia With Anxiety Disorders: Exploration Of The Direction Of Risk Among Adolescents**

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**Introduction:** The association of insomnia with anxiety disorders has received relatively little attention in community-based studies. Suggesting relationships between insomnia and anxiety disorders may differ from that between insomnia and depression, Ohayon and Roth (2003) found that, among adults with both conditions, anxiety symptoms most often preceded insomnia, while insomnia symptoms most often preceded depressive symptoms. To examine the degree to which insomnia is predominantly a risk factor for, or a consequence of anxiety disorders, we estimated the increased risk of anxiety disorders associated with prior onset of insomnia and the increased risk of insomnia associated with prior onset of anxiety disorders.

**Methods:** Data come from 1014 youth randomly selected from all eligible households in a 400,000 member HMO in metropolitan Detroit. Insomnia was defined by DSM-IV criteria. DSM-IV anxiety disorders were assessed using the Diagnostic Interview Schedule for Children. Retrospectively reported ages of onset were used in Cox proportional hazards models to estimate increased risk of one disorder associated with prior onset of the other.

**Results:** 10.7% of adolescents had a lifetime history of insomnia and 11.3% had a history of one or more anxiety disorders. Insomnia was cross-sectionally associated with each anxiety disorder (odds ratios from 3.7, for panic disorder, to 8.7 for OCD). Prior insomnia increased the risk of subsequent onset of any anxiety disorder over four-fold (hazard ratio = 4.6, 95% CI 2.3, 9.2). A similar association was found from any prior anxiety disorder to subsequent onset of insomnia (HR = 4.6, 95% CI 3.0, 7.2). This bidirectional association was reduced by half, but remained significant, after adjusting for depression and neuroticism.

**Conclusion:** The moderate associations of insomnia with anxiety disorders appear to be bidirectional among adolescents; suggesting that ‘third’ factors common to both, such as comorbid depression and neuroticism, may account for their relationship.

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### 0737

**The Self-Help Behavior And The Attitude About Sleep In Insomniacs**

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**Introduction:** There is little research about the coping strategies of insomniacs to alleviate insomnia symptoms. The purpose of this study was to assess the attributing factors, self-help behaviors, and the beliefs and attitudes about sleep at psychiatric sleep clinic in Taiwan.

**Methods:** Participants were 138 consecutive patients with the complaint of insomnia. Subjects with unstable physical conditions or substance-related disorders were excluded. All subjects completed the sleep disturbance questionnaire and the Dysfunctional Beliefs and Attitudes about Sleep (DBAS) Scale. The DSM-IV criteria were used to confirm the diagnoses of insomniacs. According to the diagnoses, subjects were divided into four diagnostic categories, the primary insomnia group, the depres-
Subtyping Self-Reported Insomnia In Older Adults

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Introduction: The complaint of insomnia in older adults is thought to be the result of a number of factors. Initial analyses of a case-control study of insomnia in older adults found relatively few differences on objective variables, despite substantial differences on specific self-report measures. Cases may have represented a heterogeneous sample of insomnia subtypes such that averaging across subjects obscured differences. The current analyses sought to determine if there is support for the existence of insomnia subtypes due to heterogeneity of causes for the insomnia complaint.

Methods: 100 older adults (mean [SD] age=71.4 [4.6]) with self-reported insomnia participated. Subjects spent 2 days in a sleep lab and underwent a comprehensive assessment including polysomnography, psychometric evaluation, and neurobehavioral functioning. Variables from these various measures were chosen to reflect factors thought to produce insomnia including sleep measures, number of medical diagnoses, and ratings of pain, alcohol use, depression and anxiety. These variables were subjected to K-means cluster analyses and the clusters were compared on means for each variable.

Results: A four cluster solution was determined to be optimal for the data (F(3,96)=9.46). The clusters were interpreted to represent insomnia associated with: depression and/or anxiety (n=7), chronic pain (n=28), medical problems (n=40), and objectively poor sleep (n=25). The last cluster was the only subgroup with PSG-defined sleep disturbance that was substantially worse than that of controls.

Conclusion: These results provide support for the likelihood that different etiologies underlie insomnia in older adults who otherwise appear to present with the same symptom complaint. The categories identified using cluster analyses have a relative good correspondence with specific ICSD-2 insomnia diagnoses. Further examination of the available data and targeted treatment studies will be helpful for validating the importance of differential diagnosis within the category of insomnia.

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0739

Behavioral Management Of Hypnotic Dependent Insomnia In Older Adults

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Introduction: Chronic prescription hypnotic use can lead to hypnotic dependent insomnia (HDI); drug dependence, insomnia return, and daytime health risks. Adverse effects of hypnotic dependence in older adults may be more severe than in other age groups due to sluggish drug elimination, heightened site sensitivity, and polypharmacy effects. This paper presents final pre-post self-report data from a 5-year randomized clinical trial on the management of HDI.

Methods: Volunteers were recruited with media announcements. Qualifying participants were over age 50, free of medical/psychiatric contributors to insomnia, chronic users of prescription hypnotics, insomnia symptomatic, and free of clinically significant apnea/PLMD as per PSG screening. Participants were randomized to 8 sessions of behavioral treatment (primary treatment group comprising stimulus control, relaxation, sleep hygiene) followed by hypnotic weaning, placebo biofeedback followed by hypnotic weaning, or weaning only.

Results: We have complete data on 64 participants; 19 men and 45 women; mean age of 63 years (SD = 8); mean duration of medication use of 4.3 years (SD = 4.8); mean insomnia duration of 9.1 years (SD = 9.2). Groups ? time ANOVA on medication consumption found only a main effect for time. Combining groups, there was an 86% medication reduction. We tested sleep change with a covariance model equating for baseline levels across groups. While medication use was nearly eliminated, significant differential sleep improvement occurred in the behavioral treatment group on sleep diaries with two of four primary sleep measures. Our primary treatment group was therapeutically superior to the other two groups on sleep onset latency and sleep efficiency percent, but not on wake time after sleep onset or sleep quality rating.

Conclusion: People with HDI who wish to discontinue their medication achieve substantial success with gradual weaning. If this is supplemented by behavioral treatment, sleep improvement is also likely to occur.

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0740

Sleep Perceptions Among Alcohol Dependent Patients With Insomnia

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Introduction: Insomnia patients are more likely to overestimate sleep onset latency (SOL), total sleep time (TST), and wake after sleep onset (WASO) as compared to polysomnography (PSG). Evidence has shown that alcohol-dependent patients have disrupted sleep architecture and sleep continuity. No study, to our knowledge, has compared the subjective impression of sleep to objective PSG measures in this population.

Methods: Eighteen individuals (9 males and 9 females, mean age 44.6 years (+/-13.2) met DSM-IV criteria for alcohol dependence and study criteria for insomnia that was not due to an etiology other than alcoholism. Pre-study sleep diaries confirmed persistent insomnia that was
Cyclic Alternating Pattern (CAP) and Primary Insomnia

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Introduction: Cyclic Alternating Pattern (CAP) is a periodic EEG phenomenon organized in sequences that occupy wide stretches of NREM sleep. It involves two phases, (1) a burst of activity (usually a high amplitude and slow frequency- sometimes mixed with alpha) followed by a quiet phase of low voltage mixed frequency activity. CAP is thought to indicate CNS arousal and elevated CAP (time and/or rate) is associated with both endogenously and exogenously generated sleep disturbances. The purpose of the present study was to determine if CAP scoring can provide a more sensitive measure of sleep instability than traditional sleep macroarchitectural indices used to evaluate patients suffering from insomnia.

Methods: EEG recordings were collected from patients clinically diagnosed with primary insomnia according to DSM-IV criteria. Some of these patients qualified, while others did not qualify, for inclusion in an investigational new drug trial based on subsequent PSG screening criteria (sleep efficiency index and sleep latency). Recordings from control subjects were also collected. EEG recordings from three groups were analyzed for NREM sleep CAP time and CAP rate using i-way ANOVA and Tukey multiple comparison testing.

Results: NREM CAP rate for controls (CNTRL) was 13.0; for insomnia patients who qualified by PSG criteria (I-PSG) was 16.5; and for patients with insomnia who did not qualify by PSG criteria (I-DNQ) was 26.4. Mean CAP times were 48.7, 56.6, and 84.8 for CNTRL, I-PSG, and I-DNQ groups, respectively. Total CAP time for I-DNQ was significantly elevated relative to both the PSG qualified insomnia and control groups (p=0.0011). CAP rate over all non-REM sleep was also found to be significantly elevated in PSG screen failures when compared to both insomnia and control groups.

Conclusion: Elevations in CAP among primary insomnia PSG screen failure subjects reflects increased CNS arousals relative to subjects with PSG verified primary insomnia and control subjects. This elevation may reflect greater sleep instability in patients with insomnia regardless of whether they manifest macroarchitectural polysomnographic disturbance. As such, CAP may provide sensitive measures for identifying patients with insomnia based on objective sleep measures.

0742

Mood Effects Of Pre-Sleep Ethanol In Insomniacs

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Introduction: Previous studies indicated that pre-sleep ethanol improved sleep in insomniacs, but tolerance developed within 6 nights. This study assessed the pre-sleep mood effects associated with pre-sleep ethanol and the change in those effects across 6 nights.

Methods: Forty-two (51% female-male), 21-55 yrs old, healthy insomniacs with no history of alcoholism or drug abuse participated. All had chronic insomnia and sleep efficiencies <85% on a 8-hr NPSG and showed no primary sleep disorders. They were randomized to placebo (n=23) or 0.45-0.6 g/kg (n=19) ethanol before sleep for 6 nights. Beverages were consumed over 30 min and drinking was completed 30 min prior to bedtime. The Profile of Mood States (POMS) was completed before and after beverage. Between group pre-post consumption changes in mood on night 1 were compared to those on night 6 by MANOVAs.

Results: Two patterns of mood effects were observed. First, the pre-post beverage increases in Fatigue seen with ethanol on night 1 were lost by night 6 (2.75 Nt1 vs 0.80 Nt 6), whereas Fatigue increased (0.43 Nt1 vs 1.43 Nt6) from night 1 to 6 with placebo (p<0.03 Grp x Nt interaction). Similarly, the reductions in Vigor with ethanol on night 1 were lost by night 6 (3.25 Nt1 vs 0.95 Nt6), while Vigor reduction (2.65 Nt1 vs 3.83 Nt6) improved from night 1 to 6 with placebo (p<0.05 Grp x Nt interaction). Secondy, overall (pre + post) Tension improved from night 1 to 6 with placebo (4.33 Nt1 vs 2.63 Nt6), but not with ethanol (2.98 Nt1 vs 2.98 Nt6) (p<0.02, Grp x Nt interaction).

Conclusion: These results suggest that tolerance develops to the sedating mood effects of ethanol, and positive mood effects (i.e. in the placebo group) across the 6 nights were reversed by ethanol.

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0743

What Can Yawning Reveal About Insomnia?

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Introduction: The function of yawning remains unknown. It appears to modify cortical arousal, is a universal, paralinguisitc signal of drowsiness and is contagious. How yawning relates to sleep and insomnia is unknown; contemporary models of insomnia are based on arousal modulation, with insomniacs hyperaroused relative to good sleepers. We are investigating how yawning relates to normal sleep and Insomnia, and what effect a yawning stimulus will have on arousal levels of both.

Methods: Actigraphy and sleep diaries were used to obtain sleep efficiency, circadian rhythm measures, and yawn timing and frequency. We then identified a robust stimulus to evoke yawning during physiological mon-
Results: A combination of EMG and respiration can discriminate a yawn from a cough, sigh or laugh. Primary Insomniacs yawn on average 14.3 times/day (n = 6), while good sleepers yawn 8.4 times/day (n = 11). The difference was not significant (t = -1.357, df = 15, p = 0.195). Both Good sleepers and insomniacs have a similar distribution of yawns that follows the circadian rhythm, but insomniacs yawn proportionately more between 8 and 14 hours before sleep intention (45.1% of total yawns compared to 28.12%). Viewing ten video clips of people yawning interspersed with periods of blank screen will evoke an average of 8.5 yawns in 66.7% of subjects (3 males, 6 females, mean age 26.8 years) within 5 minutes of observing the tape.

Conclusion: Insomniacs yawn less at times of day traditionally associated with yawning (mornings/nights). If yawning is related to arousal, and arousal to insomnia then modifying the yawning pattern may alter arousal levels.

0744
Assessment Of The First Night Effect Among Insomnia Sufferers And Good Sleepers
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Introduction: Clinical experience suggests the presence of a first night effect (FNE) in laboratory polysomnographic (PSG) recordings of good sleepers and insomniacs. As a result, researchers often discard the first night among insomniacs with a low and high accuracy in their sleep perception. The aim of this study is to determine whether insomniacs experience a greater FNE than good sleepers according to objective and subjective measures of sleep.

Methods: The participants were 12 individuals suffering from insomnia (mean age=42 years) and 12 good sleepers (mean age=38 years). Following a multi-step clinical evaluation (sleep, medical and psychological), participants underwent three consecutive nights of PSG recordings (N1 to N3) and completed subjective sleep estimates upon arising after each night.

Results: Repeated measures ANOVAs were computed for sleep measures on each night. Significant statistical differences were found in both groups from N1 to N3 for objective number of awakenings (NA) and Stage 1 (min and %) and subjective NA and WASO. These measures differed significantly from N1 to N3 and N2 to N3. There were no significant differences from N1 to N2. There were also no between groups differences. In both groups, the subjective morning item sleep soundness negatively correlated with subjective NA on N3. No other significant correlations were found on other nights between objective and subjective sleep measures and morning items.

Conclusion: Results suggest a slight similar first night effect for both groups. Surprisingly, the first effect was also observed on the second night of sleep. A reverse first night effect may thus be observed in both groups of sleepers. Since home recordings may be more representative of usual sleep patterns than the laboratory environment, between groups first night effect might be more observable in at home recordings.

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0745
The Effects Of Tiagabine In Elderly Patients With Primary Insomnia: A Double-Blind, Placebo-Controlled Study
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Introduction: Tiagabine (Gabitril®) is a selective gamma-aminobutyric acid (GABA) reuptake inhibitor (SGRI) that increases synaptic GABA availability via inhibition of the GAT-1 GABA transporter. Since GABA plays a central role in promoting sleep, increased availability of GABA may have therapeutic use in insomnia. Tiagabine has been reported to have sleep-consolidating effects in healthy elderly subjects and adult patients with primary insomnia. In this study, the effect of tiagabine on sleep in elderly patients with primary insomnia was investigated.

Methods: Patients aged 65-85 years who met DSM-IV-TR criteria for primary insomnia were studied. After two baseline nights of polysomnography, patients were randomized to receive two nights of treatment with tiagabine 2, 4, 6, 8 mg, or placebo.

Results: Efficacy data were obtained from 204 patients. Tiagabine 2-mg had no statistically significant effect on slow-wave sleep (SWS) (+11.7 min) or stage 1 sleep (-6.6 min). With all other doses, mean change from baseline in minutes of SWS was significantly greater with tiagabine than with placebo (4-mg, +19.9 min; 6-mg, +38.0 min; 8-mg, +46.9 min; placebo, +4.5 min; P<0.05 for each). Mean change from baseline in minutes of stage 1 of sleep was significantly greater with tiagabine than with placebo (4-mg, -10.9 min; 6-mg, -10.6 min; 8-mg, -17.5 min; placebo, -2.1 min; P<0.01 for each). No significant differences (P>0.05) between tiagabine and placebo were observed in total sleep time. Tiagabine was generally well tolerated. The only adverse event that occurred with an incidence of ≥5% in the 2-mg, 4-mg, and 6-mg dose groups was dizziness (7%; 6-mg). The most commonly reported adverse events associated with tiagabine 8-mg were dizziness (23%) and nausea (16%).

Conclusion: Tiagabine increased SWS and reduced stage 1 sleep in elderly patients with primary insomnia. Further research on the clinical relevance of this effect is needed.

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0746
Nocturnal Heart Rate Pattern In Insomniacs With Different Degree Of Sleep Duration Perception
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Introduction: Patients with primary insomnia, are known to often present a discrepancy between subjective and objective measures of sleep quality (so-called ‘misperception’). The aim of this study was to assess demographic characteristics, sleep measures and cardiac pattern through the night among insomniacs with a low and high accuracy in their sleep perception.

Methods: Fourteen subjects with primary insomnia (7 women, age 48 ± 9 years) without any medical or psychiatric disorder, underwent standard sleep study. Sleep perception was considered as the ratio between subjective estimation of the duration of sleep and objective results from polysomnography *100. We considered a 80% cut-off of the ratio subjec-
Results: Subjects with lowA have a lower sleep efficiency (72 ± 13%) compared to subjects with highA (87 ± 11%) (p = 0.05). The 2 groups had a similar HR during wakefulness (p = 0.9). However, the physiological sleep related nocturnal HR reduction was observed only in subjects with highA (time effect p<0.05), while the HR remained stable from wakefulness throughout sleep in subjects with lowA (p=0.66). The HR changes throughout the night did not correlate with sleep efficiency (p=0.8).

Conclusion: A low accuracy in the perception of sleep quality is accompanied, in insomnia, by the lack of the physiological HR reduction throughout sleep.

0747 Valerian-Hops Combination And Diphenhydramine For Treating Insomnia: A Randomized Placebo-Controlled Clinical Trial Morin CM, Koetter U, Bastien C, Ware J, Woolten V
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Introduction: Insomnia is a prevalent health complaint that is often treated with herbal/dietary supplements or with over-the-counter sleep aids. There is still little evidence on the risks and benefits of those products. The objective of this study was to evaluate the efficacy and safety of a valerian-hops combination and diphenhydramine for the treatment of insomnia.

Methods: This was a multi-center, randomized, placebo-controlled, parallel study. The sample included 184 adults (110 women, 74 men; mean age of 44.3 years old) with mild insomnia. Treatments involved two nightly tablets of native extracts of valerian roots (187 mg) and hop cones (41.9 mg) combination for 28 days (n = 59), placebo for 28 days (n = 65), or 2 ly tablets of native extracts of valerian roots (187 mg) and hop cones (41.9 mg) combination for 28 days (n = 60). The main outcome variables were derived from daily sleep diaries and polysomnography, clinical outcome ratings were compared between the 2 groups by t-test; HR changes were compared by one-way ANOVA with repeated measures (time) in each group.

Results: Subjects with lowA have a lower sleep efficiency (72 ± 13%) compared to subjects with highA (87 ± 11%) (p = 0.05). The 2 groups had a similar HR during wakefulness (p = 0.9). However, the physiological sleep related nocturnal HR reduction was observed only in subjects with highA (time effect p<0.05), while the HR remained stable from wakefulness throughout sleep in subjects with lowA (p=0.66). The HR changes throughout the night did not correlate with sleep efficiency (p=0.8).

Conclusion: A low accuracy in the perception of sleep quality is accompanied, in insomnia, by the lack of the physiological HR reduction throughout sleep.

0748 Psychometric Properties Of The Restorative Sleep Questionnaire And Daytime Consequences Of Sleep Questionnaire Hays RD, Morlock RJ, Spritzer K, Drake C, Roth T
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Introduction: The Restorative Sleep Questionnaire (RSQ) and Daytime Consequences of Sleep Questionnaire (DCSQ) were developed to assess perceptions of the restorative aspects of sleep and the consequences of non-restorative sleep. To evaluate their psychometric properties, we administered the RSQ and DCSQ to 774 individuals in a telephone survey of sleep habits.

Methods: The 774 person sample assessed by telephone survey were healthy individuals and individuals pre-identified with specific conditions (ie.,sleep deprived, arthritis, and insomnia). Included were the 9-item RSQ; the 10-item DCSQ; the 12-item Medical Outcomes Study (MOS) Sleep Scale, a 13-item daytime sleepiness scale, the 8-item Epworth Sleepiness Scale (ESS), and the SF-36. The average age of the sample was 45 (range: 18-65); 56% were female; 69% were employed. Thirty-five percent scored 10 or higher on the ESS. The average SF-36 PCS and MCS scores were 49 and 47, respectively.

Results: Item-total correlations (corrected for overlap) for the RSQ Ranged from 0.40 to 0.84 and from 0.46 to 0.73 for the DCSQ. Coefficient alphas were 0.91 and 0.88 for the RSQ and DCSQ, respectively, and the two scales were significantly positively correlated (r = 0.62). More restorative sleep (RSQ and DCSQ) was associated with lower ESS scores (r's = -0.28, -0.34), MOS sleep problem scores (r's = -0.64, -0.69), and better SF-36 PCS (r's = 0.28, 0.49) and MCS (r's = 0.42, 0.52) scores.

Conclusion: These results provide preliminary support for the reliability and construct validity of the RSQ and DCSQ. Future studies are needed to assess responsiveness of the scales to change over time or in response to an intervention.

Pfizer

0749 Evening/Morning Preference As A Predictor Of Insomnia And Sleepiness Younger E, Young T, Finn L
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Introduction: The Horne-Osberg morningness-eveningness questionnaire (MEQ) is widely used as an indicator of circadian typology. However, there has been little research in how morning or evening tendencies may predispose individuals to sleep problems, particularly insomnia or daytime sleepiness.

Methods: The sample for this study comprised 1141 middle-aged adults in the longitudinal Wisconsin Sleep Cohort Study. Participants completed the MEQ, and reported on frequency (never, rarely, sometimes, often, always) of the occurrence of 4 insomnia symptoms and 2 indicators of daytime sleepiness as part of an overnight study protocol. A composite score was calculated from the MEQ and standard cut points were used to
create four strata on preference, (early morning, morning, no preference and evening). Logistic regression was used to estimate odds ratios and 95% confidence intervals for frequent (often or always) insomnia and sleepiness problems and MEQ strata, adjusted for age and sex.

**Results:** Eveningness was associated with more difficulty falling asleep (OR = 4.2, CI 1.7-10.8), excessive daytime sleepiness (OR=4.1 , CI 1.7-10.0) and not feeling rested (OR=2.69, CI 1.22-5.95). Eveningness did not correlate with other insomnia symptoms: trouble falling back asleep (OR=1.0, CI 0.4-2.6), waking repeatedly (OR=0.56, CI .2-1.4), or waking too early (OR=.6 CI 0.2-1.8).

**Conclusion:** Our findings suggest that persons with eveningness, relative to morningness tendencies have more difficulties in adapting to the sleep and wake schedules that typify middle-aged men and women. It is possible that sleep onset insomnia in eveningness types compromises sleep length among those who must adhere to a typical early morning wake time, and leads to daytime sleepiness.

0750 Relation Between Sleep Misperception And The Predisposition

**Arousal Scale On Consecutive Nights**

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**Introduction:** Insomniacs often misperceive their sleep difficulties. This misperception has been linked to an inability to de-arouse or a maintained state of arousal. Little is known about the stability of this misperception and its link to a predisposed pre-sleep arousal state. The aim of the present study was twofold: 1) document the relation between scores on the Predisposition Arousal Scale (PAS) and objective and subjective measures of sleep and 2) compare the stability of this relation on consecutive nights.

**Methods:** Thirteen psychophysiological insomniacs (mean age 41 years) and 15 good sleepers (mean age 39 years) were invited to spend three consecutive nights in the sleep laboratory. Participants completed the PAS before going to bed each night and a questionnaire targeting subjective measures of state and sleep upon awakening. Difference scores were computed between objective and subjective measures of sleep.

**Results:** Good sleepers overestimated their total sleep time (TST) on all three nights, t(14) = 35.76, whereas insomniacs underestimated theirs, t(12) = 14.83. Both good sleepers and insomniacs overestimated their sleep onset latency (SOL) on the first night, F(1,27) = 1.2, p<0.05. Insomniacs also overestimated SOL on both the second and third night (F(1,27) = 4.46, and F(1,27) = 5.79 respectively). A significant correlation was found between insomniacs PAS scores and the perception of decreased TST during the first night, r(13) = 0.69. Insomniacs PAS scores were also correlated with a decrease in SOL on the second night, r(13) = -0.69. Significant level was set at pc0.05.0.

**Conclusion:** Results on SOL measure suggest a first night effect in good sleepers and insomniacs. Supporting other studies, results showed that insomniacs overestimate SOL and underestimate TST. Furthermore, pre-arousal state appears to be linked to the misperception of some sleep measures in insomnia sufferers.

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0751 Treatment Outcomes And Sex Differences For Insomnia

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**Introduction:** The present report examines the relationship between sex differences and outcome measures for various sleep indices from a random assignment treatment design. This is part of a larger ongoing study.

**Methods:** Baseline and post-test measures were assessed for 45 participants, 29 females (age M = 50.17, range = 23 - 78) and 16 males (age M = 54.06, range = 33 - 76) who met criteria for insomnia. The participants were randomly assigned to one of two treatment groups, a therapy classes group or a self-guided booklet group. Stimulus control therapy, sleep restriction therapy and sleep hygiene were the main components of both treatments. Findings reported here are from daily sleep diaries.

**Results:** A 2 X 2 (Treatment X Sex) MANOVA analysis indicated that over all of the measured sleep variables, the classes treatment showed more improvement than the booklet treatment (F (1, 34) = 4.35, p < .001). There was neither an overall main effect for Sex differences nor an overall interaction. However, examining separate dependent variables showed a marginally significant effect of sex differences on Awakenings (p = .057) in which women tended to have a decrease in the number of Awakenings regardless of the treatment assignment. A Treatment X Sex difference interaction on Time in Bed was shown in which only women in the classes group significantly reduced their time in bed after treatment, (p = .05).

**Conclusion:** The results reveal that the classes treatment produces substantially improved sleep outcomes compared to the self-guided booklet treatment. In addition, women may improve more than men for specific sleep variables across both treatments. The interaction on Time in Bed raises the possibility that women in the classes group were more conscientious than men in following homework assignments.

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0752 Young Women Compared To Men Are More Resilient To The Sleep Disturbing Effects Of External Stressors

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**Introduction:** Women’s sleep is of a better quality and quantity compared to men and pre-menopausal women appear to be more resilient to the effects of sleep loss. The goal of this study was to assess whether there is a differential response between genders to the sleep disturbing effects of blood drawing.

**Methods:** Sixty-six, young, healthy, normal sleepers (32 men and 34 women) of similar age (mean age ± SD, 23.7±3.7 for men; 24.5±3.3 for women) and BMI (mean BMI ± SD 24.4±2.3 for men; 23.1±2.6 for women) participated in a 4 consecutive-night sleep laboratory protocol (adaptation night, nights 2&3 (baseline), and a fourth night associated with serial 24-h blood sampling). We compared differences of night 4 with serial 24-h blood sampling). We compared differences of night 4 minus the average of nights 2 and 3 between men and women by using a two sample t-test.

**Results:** At baseline women compared to men tended to have higher percentage of slow wave sleep (SWS) (P=0.054). Blood draw in men compared to women was associated with significantly longer sleep latency, decreased percentage of total sleep time, and increased percentage of wake time after sleep onset (all P<0.05). Also, men compared to women experienced higher percentage stage 1 sleep (P<0.05). Percentages of SWS and REM sleep, and REM latency were not affected differentially by the blood draw procedure.

**Conclusion:** Healthy, young women compared to men are more resilient to the sleep disturbing effects of blood draw techniques. These results suggest that pre-menopausal women not only sleep better but also can cope better with external stressors. Whether this strength is present for emotional stressors and whether it is lost after menopause remains unknown. This marked sexual dimorphism in sleep regulation may have...
been to protect women from the profound demands of infant and childcare for the most of mankind's history.

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0753
Insomnia And Sleep Perception: Effects Of The Cognitive Behavioral Therapy And Relation To Sleep Microstructure
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Introduction: Insomnia is associated with an inaccurate perception of sleep that is thought to contribute to the overestimation of sleep difficulties. While the cognitive behavioral treatment (CBT) for insomnia has been proven to produce significant sleep improvements, it is not known whether this intervention normalizes sleep perception. The aims of the current study were: (1) to examine the impact of the CBT for insomnia on sleep perception, as measured by the ratio of perceived total sleep time to objective total sleep time (TST ratio), and (2) to relate the observed effects on sleep perception to changes in sleep microstructure.

Methods: Participants were 13 individuals with insomnia (INS; 6 women, 7 men; mean age = 46.23 years, SD = 6.13) and 12 normal sleepers (GS; 6 women, 6 men; mean age = 47.17 years, SD = 8.03) matched for age and gender. INS were offered CBT in a 6-week group format. Polysomnographic recordings were conducted before and after CBT. Sleep diaries were completed for each night of polysomnography. In addition, power spectral analysis of the EEG was computed for the NREM sleep of the first four sleep cycles.

Results: At baseline, INS have a lower TST ratio, suggesting a greater sleep underestimation. Lower TST ratios are associated with greater insomnia severity. Compared to baseline, the TST ratio is increased at post-treatment, suggesting improved sleep perception. Increased TST ratio is also associated with an increase in delta (1-4 Hz), theta (4-7 Hz), alpha (7-11 Hz) and sigma (11-14 Hz) spectral power after CBT.

Conclusion: CBT appears to improve the estimation of total sleep time in insomnia sufferers. This greater accuracy of sleep perception is associated with increased activity in the lower and intermediate frequency bands of the sleep EEG.

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0754
Sleep Spindle And Spontaneous K-Complex: A Preliminary Comparison Between Insomnia Sufferers And Good Sleeper Controls
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Introduction: Sleep spindles and spontaneous k-complexes are EEG features that are unique to sleep. Evidence suggests that both have sleep-protective functions. Recent PSG studies found that the objective sleep of insomnia sufferers is unstable and lighter compared to good sleepers. This suggests that the sleep-protection mechanism might be deficient in insomnia sufferers. The objective of the present study is to examine an aspect of this mechanism by compiling the occurrence of sleep spindles and spontaneous k-complexes.

Methods: The sample included 6 participants suffering from insomnia (INS; mean age = 42.8 years) and 10 good sleepers (GS; mean age = 35.4 years). Participants underwent sleep, psychological and medical evaluations. INS participants met diagnostic criteria for primary insomnia (mean duration = 11 years). Participants underwent four consecutive nights of PSG recordings. Sleep spindles and spontaneous k-complexes were scored during stage 2 sleep on the second night of the protocol.

Results: Average time spent in stage 2 sleep was 228 minutes for INS (SE = 79.17%) and 266 minutes for GS (SE = 91.60%). The total number of sleep spindles and spontaneous k-complexes was compiled according to the total time spent in stage 2 sleep (sleep spindles/minutes, spontaneous k-complexes/minute). Between groups ANOVAs showed no significant differences in the sleep spindles or spontaneous k-complexes frequency between INS (0.31 and 4.55) and GS (0.49 and 4.76) respectively.

Conclusion: These preliminary results suggest that there is no deficiency in the sleep-protection mechanism of insomnia sufferers in comparison to good sleeper controls, as measured by sleep spindles and spontaneous k-complexes frequencies. However, some caution in the interpretation of data is advised since the sample is small. Nonetheless, the use of power spectral analysis for measuring EEG activity surrounding the occurrence of sleep spindles and spontaneous k-complexes could reveal additional information about the sleep-protection mechanism in insomnia sufferers.

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0755
Hot Flushes And Chronic Insomnia In Pre, Peri And Post Menopausal Women
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Introduction: Hot flushes, especially when occurring during night, may cause sleep disturbances in menopausal women. However, several other factors such as sleep apnea, psychiatric disorders, obesity and drug use can be responsible for the sleep disturbances.

Methods: The study was performed in 2003 and 2004. The target population was the adults (18 years and older) living in the State of California, USA. This represents 24 million of inhabitants. A total of 2,865 subjects participated in the survey (participation rate 82.5%). The sample included 1,056 women aged 40 years or older. The participants were interviewed by telephone using the Sleep-EVAL system. The interviews covered several topics including sleeping habits, sleep quality, sleep disturbances, physical symptoms related to menopause. Chronic insomnia was defined as difficulty initiating or maintaining sleep or non-restorative sleep lasting for at least 6 months.

Results: Among the 1,056 women aged 40 years or older, 34.4% were in pre-menopause, 16.4% were in menopause and 49.2% were in post-menopause. A total of 35.7% of women reported mild to severe hot flushes. Chronic insomnia was more frequent in peri-menopausal women (43.7%) than in post (29.5%) and pre-menopausal women (31%; p<0.01) and more frequent in women who reported hot flushes (40.8% vs. 27.9%; p<0.001). A logistic regression was performed to identify factors positively related to chronic insomnia. Factors significantly associated with chronic insomnia were: smoking (<= 20 cig/day: OR: 2.2; > 20 cig./day: OR: 4.6); having hot flushes during the night (OR: 1.9); being obese (BMI between 27 and 30kg/m2; OR: 2.4) or with morbidity obesity (BMI>= 30kg/m2; OR: 2.0); having a poor health (OR: 1.6); having a heart disease (OR:4.3); having breathing pauses during sleep (OR: 3.4).

Conclusion: Hot flushes during the night are one of the many factors that can contribute to chronicity of insomnia in women aged 40 years or older. Menopausal status (pre, peri, post) appeared unrelated to chronic insomnia.

Unrestricted educational grant from Organon
**0756**  
Effects Of Induced Sympathetic Arousal On Sleep Of Normal Subjects  
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**Introduction:** Patients with primary insomnia (PI) show evidence of physiological arousal on multiple measures, but the role of this arousal in the pathogenesis of the objective and subjective sleep disruption characteristic of that disorder remains unclear. We have previously shown that acute dietary salt restriction (ADSR) can induce SNS activation in normal subjects. We repeated this study to determine whether ADSR could produce sleep disruption consistent with PI in normal subjects.

**Methods:** Thirty healthy, normal sleepers (mean age=25.3±70) were studied in the laboratory for five consecutive nights and four days. All participants were restricted to a low sodium diet (≤17mEqNa/day) during their visit. Using a double-blind procedure, participants were randomized to receive capsules containing either 10g of salt (n=6; 3f) or a placebo (n=7; 4f) each day. While in the lab, participants underwent nocturnal PSGs, MSLTs, performance measures, and subjective assessments. In addition, urine was collected throughout the study in 8-hour aliquots for assessment of sodium, cortisol and catecholamines.

**Results:** As expected, daily urine sodium excretion differed significantly between the two groups (p<0.01). Urine norepinephrine and cortisol increased in the salt-restricted group, although not significantly (p=.10). Relative to baseline, there was a significantly greater decrease in sleep efficiency (p<0.04) and increase in sleep latency (p<0.04) in the salt-restricted subjects. Despite greater deterioration in sleep, MSLT values differentially increased in salt-restricted subjects (p=.04). Subjective sleep measures showed consistent trends, but were not statistically significant.

**Conclusion:** Using a double-blind, placebo-controlled design, we were able to replicate our previous finding that ADSR induces SNS activation in normal subjects, and this activation results in deterioration in objective nocturnal sleep measures and increased daytime alertness that together are suggestive of PI. These data are consistent with a model in which centrally mediated sympathetic activation is involved in the pathogenesis of PI.

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**0757**  
Stress-Induced Insomnia: Effects Of Pharmacological Treatments On Activation Of Neuronal Circuits  
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**Introduction:** Primary insomnia, the most prevalent sleep disorder, is generally caused by stress. We have developed a rodent model of stress-induced insomnia by exposing rats to a mild psychological stressor (cage exchange), which causes an interval insomnia characterized by decreased nREM and REM sleep and increased wake and transitions. The pattern of Fos, a marker of neuronal activation, in the brain of rats killed 90 min after the onset of insomnia is decreased in the ventrolateral preoptic area (VLPO), the main sleep-promoting region, and increased in wake-promoting regions such as the tuberomammillary nucleus (TMN) and locus coeruleus (LC). Fos is also increased in VLPO inhibitory afferents (lateral septum (LS), lateral hypothalamus, and dorsomedial hypothalamus) and in stress-sensitive areas (central amygdala/bed nucleus of stria terminalis, infralimbic cortex (ILC), cingulate cortex, and hippocampus). In previous lesion studies, we determined that different components of this circuitry produce different aspects of stress-induced insomnia.

**Methods:** In the present study we inhibited specific brain areas that are activated during insomnia by injecting several drugs i.p., simultaneously with cage exchange, and analyzing the pattern of sleep disturbances and Fos expression in the brain. The drugs injected were: Immepip, an H3 agonist that activates TMN inhibitory autoreceptors; Dexametomidine, an alpha-2A agonist used as a sedative/mild anesthetic, that binds to inhibitory noradrenergic receptors; and SB-334867, an orexin non-peptide antagonist that binds to both orexin receptors with more affinity for the type 1 receptor.

**Results:** Immepip completely inhibits TMN and decreases Fos in LC and ILC. It reverses the changes in wake, nREM sleep and number of wake bouts, but has no effect on REM sleep. Dexametomidine suppresses Fos expression in LC, TMN, and ILC but produces a strong activation of orexin neurons. Rats seem to be deeply asleep or sedated but they can be easily awakened with gentle touch; REM sleep is completely suppressed. SB-334867 abolishes Fos in TMN and strongly decreases Fos in LC, ILC, and LS. It has moderate effects on sleep but produces normalization of the number of state transitions.

**Conclusion:** Our results suggest that this rat model is useful to test drugs that can cross the blood-brain-barrier and target specific components of the brain circuitry activated during stress-induced insomnia.

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**0758**  
Heart Rate Variability During Sleep In Women With Insomnia  
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**Introduction:** Physiological arousal is a component of chronic insomnia, likely indicated by sympathetic autonomic nervous system (ANS) dominance. Patterns of heart rate variability (HRV), a measure of ANS balance/imbalance, were compared in women with insomnia (I) (n=12, mean age 46.0±2.7 years) and controls (C) (n=12, mean age 45.4±5.6 years).

**Methods:** Comparative analyses were performed on data obtained from three sleep studies, (insomnia laboratory (n=10), insomnia home (n=2); controls as PSG laboratory confirmed good sleepers)). Insomnia subjects had PSG sleep efficiencies of <85% and were matched to controls for age and body mass index. Time and frequency domain HRV measures for total sleep time (TST), non-rapid-eye-movement (NREM), and REM sleep states were compared, based on second night PSG heart signal and sleep data.

**Results:** Women with insomnia exhibited significant sleep disturbance compared to controls (t Test, SINDX: I=0.78±0.04, C=0.91±0.03, p=.001; TST(min): I=352±61, C=417±37, p=.004; NREM Sleep Stages 1,2,3,4 Combined(%): I=63.0±5.7, C=73.2±4.3, p=.001; and NREM Sleep Stage 4(%): I =2.1±4.3, C=8.0±7.6, p=.032); REM Sleep, I=19.6±4.3, C=20.6±5.0, N.S. However, with GLM analyses, only one HRV variable tended to be significantly different for TST (SDANN (I=65.0±24.3, C=42.8±14.2, p=.046)). Other variables for TST did not differ by group nor were any differences by group seen for NREM or REM sleep.

**Conclusion:** Despite significant PSG sleep disturbance, these women with insomnia show only marginal evidence of ANS physiological arousal during sleep as measured by HRV.

Kappa Kappa FDN, MARN, Hester Mc Laws (UW), NINR-NR01118/NR04001.
0759
Role Of Actigraphy In Patients With Insomnia
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Introduction: Actigraphy has been utilized in patients with insomnia and in a variety of circadian rhythm disorders. Few studies have compared the utility of actigraphy verses that of a sleep log in a large series of patients of this type.

Methods: We evaluated 20 patients complaining of sleep onset and maintenance insomnia associated with anxiety and depression for several years. All these patients were on antidepressant medications but despite improvement of the depression the sleeping problems persisted. They also had a history of hypnagogic-dreams over the years. After clinical evaluation the patients were given a sleep log and an actigraph to be worn on the wrist or the ankle for 1-2 weeks.

Results: We studied 14 women and 6 men with the age range of 39-69 years. In addition to the nighttime complaints of sleep, these patients also had daytime symptoms of inattention, impairment of work and quality of life as well as daytime sleepiness. Actigraphy recording clearly showed a pattern of highly irregular sleep-wake schedule, with erratic bedtime and wake-up time in all, and evidence of excessive body movements during sleep at night and short naps in several patients. On strict enforcement of regular sleep-wake schedule and attention to sleep hygiene measures, sleep disturbance improved in many of these patients. The patients did not always fill the sleep log correctly and therefore the log data was not reliable.

Conclusion: Irregular sleep-wake schedule and inadequate sleep hygiene can be major contributory factors in patients with insomnia with anxiety and depression. Actigraphy appears to be a more objective measure of demonstrating the schedule as compared to the sleep log. Regularizing sleep wake schedule and improving sleep hygiene can improve insomnia in these patients.

0760
Subjective And Objective Sleep Patterns, Daytime Functioning, Psychological Adjustment, And Health In Community-Dwelling Older Adults
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Introduction: Insomnia is diagnosed based on individuals subjective estimates of their sleep quality (complaints) and quantity (SOL, WASO). Behavioral interventions focus on improving quantitative sleep. Although sleep complaints are rarely targeted, we believe they hold great potential for treating late-life insomnia. Before interventions can be developed, however, greater understanding of risk factors for sleep complaints is needed. This study investigates several biological and psychological risk factors. It also examines the relationship between sleep complaints and subjective and objective estimates of quantitative sleep variables.

Methods: A sample of 104 adults aged 60+ (M=72.81 years; SD=7.12) were recruited from North Central Florida. Inclusion criteria: absence of sleep disorders other than insomnia, absence of severe psychiatric disorders, no cognitive impairment; and no sleep altering medications. Participants completed measures of daytime functioning, psychological adjustment, and health as well as 14 days of sleep diaries and actigraphy. Four groups were created based on subjective sleep quantity (good vs. poor) and subjective sleep quality (complaints vs. no complaints).

Results: Forty eight percent of the sample were classified as noncomplaining good sleepers, 11% as complaining good sleepers, 23% as noncomplaining poor sleepers, and 18% as complaining poor sleepers. Only health distinguished complainers from noncomplainers. Complainers reported 1-2 more health conditions on average than noncomplainers. Actigraphy did not distinguish complainers from noncomplainers. Subjective and objective quantitative sleep variables were correlated for noncomplainers only. Gender influenced these correlations. For TST, correlations were strong for noncomplaining men and women. For SOL, correlations were weak for noncomplaining men and strong for noncomplaining women.

Conclusion: Sleep complaints are related to poorer health in older adults. Noncomplainers appear to alter their perceptions of their sleep. These perceptions and their relationship to sleep complaints warrant further study. Actigraphy appears useful for estimating SOL (women only) and TST (women and men) in individuals unable to complete sleep diaries.

0761
A Pilot Study Of The Sleep EEG Power Spectral Effects Of Relaxation Training In Primary Insomniacs
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Introduction: Relaxation training (progressive muscle relaxation) is known to be a viable treatment for primary insomnia. Yet, the underlying neurophysiological changes associated with the positive effect of progressive muscle relaxation on sleep in insomniacs remain unknown. Frequency spectral analysis of the sleep EEG has been employed to study the neurophysiology of sleep alterations and treatments in more depth than can be achieved with standard polysomnographic analysis (Armitage, 1995), and spectral analysis of the sleep EEG has shown alterations in spectral amplitude in primary insomniacs treated with cognitive behavioral therapy (Krystal et al., 2001), however a spectral analysis of the sleep EEG has not been carried out in primary insomniacs treated with relaxation training. As a result, we carried out this pilot study in which we assessed the changes in sleep EEG spectral analysis associated with relaxation training in primary insomniacs.

Methods: The subjects were 14 primary insomniacs who received relaxation training and who were part of a larger study comparing cognitive behavioral sleep therapy (CBT), progressive muscle relaxation (Relaxation training), and placebo control (Edinger et al., 1992). The subjects underwent standard polysomnography prior to and after progressive muscle relaxation including 2 EEG channels (C3-M2 and Oz) which were used for spectral analysis. The polysomnographic data was scored manually and muscle artifacts and arousals were eliminated. The data underwent FFT in 2 second epochs. Six frequency bands were employed: Delta (0.5-3.5 Hz), Theta (4.0-8.0), Alpha (8.5 - 12 Hz), Sigma (12.5 - 15 Hz), Beta (16.5 - 30 Hz), and Gamma (30.5 - 60 Hz). Exploratory Spearman correlation coefficients between the changes in power spectral amplitude from pre-treatment to post-treatment were carried out.

Results: There was a decrease in alpha power from pre-treatment to post-treatment in the relaxation training group compared to the control group and CBT group. No other measures of spectral analysis were different in the relaxation training group compared to the other treatment groups.

Conclusion: The preliminary finding suggests relaxation training may have a particular effect on decreasing alpha power in the spectral analysis of Non-REM-Sleep-EEG. The clinical significance of this remains unknown and should be subject to future study.
The Role Of Fear Of Sleep In Trauma-Related Insomnia

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Introduction: Most researchers would agree that insomnia sufferers would like more sleep, and yet, some insomniacs fear sleep. Fear of sleep may be particularly relevant for trauma survivors who may fear the loss of vigilance that accompanies sleep, feel unsafe in darkness, or dread nightmares. We hypothesized that a) fear of sleep would be higher among trauma survivors than individuals with no trauma, and highest among those with PTSD b) fear of sleep would be associated with insomnia c) individuals traumatized in a sleep-related context (bed, bedroom, or darkness) would report greater fear of sleep and worse insomnia.

Methods: We constructed a measure of fear of sleep that includes items assessing vigilant behaviors, fear of loss of vigilance, and dread of nightmares. This study examined psychometric properties of the fear of sleep measure and test hypotheses about the role of fear of sleep in trauma-related insomnia among 543 respondents to an Internet-based survey that included Trauma Assessment for Adults, PTSD Checklist, Pittsburgh Sleep Quality Index, and Insomnia Severity Index.

Results: Fear of sleep showed high internal consistency (alpha=.97) and 1-week retest reliability (r=.89, p<.01). PTSD showed highest fear of sleep relative to trauma only, which was greater than no-trauma (p<.01). Fear of sleep correlated moderately with sleep quality and impairment, (15% and 12% of the variance, respectively, p<.001). Participants traumatized in a sleep context reported worse sleep quality (but not impairment) and higher fear of sleep relative to other trauma contexts and no trauma.

Conclusion: These data suggest that fear of sleep can be reliably assessed and is relevant to the sleep of trauma survivors, particularly those traumatized in a sleep-related context. Future research should investigate the factor structure of the fear of sleep measure and determine whether the effect of sleep context on sleep is mediated by fear of sleep.

Dex-CRH Test In Primary Insomnia

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Introduction: Several recent studies have established that there is an important link between chronic insomnia and major depressive disorder (MDD). While the nature of this link remains unclear, one element that may be common to both disorders is dysfunction of the hypothalamic-pituitary-adrenal (HPA) axis. Hyperactivity of this axis, particularly as assessed with the dexamethasone-CRH (dex-CRH) test, is among the most robust biological abnormalities of MDD. While some data suggest HPA hyperactivity in PI, there has been little effort to formally evaluate HPA function in PI.

Methods: Ten patients with PI lasting at least one year (mean age=31.3; 5f) and fifteen normal sleepers (mean age=31.3; 6f) were recruited from subjects participating in other research protocols. After self-administration of the previous evening of 1.5mg dexamethasone, subjects were admitted to the laboratory, a forearm catheter placed, and baseline venous samples for ACTH, cortisol binding globulin (CBG), and dex level were drawn. 100 mcg ovine corticotropin was administered at 3PM, and q15min samples were drawn until 6PM. Standard questionnaire assessments, sleep recordings, and urine measurements of catecholamines and cortisol were performed as part of other protocols.

Results: PI patients showed significantly greater peak (p<0.05) and cumulative (p<0.03) ACTH response than did normal sleepers. Despite a 72% greater ACTH response, however, there was no significant difference in the cortisol response (AUC; p=.28). Hamilton sleep scores were similarly related to ACTH response, but total HDS was not correlated with either ACTH measure. There was no relationship between ACTH response and baseline objective sleep measures.

Conclusion: Dex-CRH results are unambiguously abnormal in patients with primary insomnia (PI). The normal cortisol response despite the exaggerated ACTH suggests that the HPA axis abnormality in PI may be distinct from that of MDD. In particular, this pattern suggests intact adrenal compensation to pituitary hyperactivity. The HPA abnormalities of PI may represent an intermediate step in the evolution of HPA dysregulation in MDD.

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The Kingston Insomnia Program (KIP): 6-Month Follow-Up Data On An Effective 30-Minute Sleep Restriction Program On 138 Consecutively Treated Patients

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Introduction: Non-drug insomnia treatment programs have proven to be effective. However, they are usually time-intensive, and require a psychologist. The KIP utilizes only graduated sleep restriction. Training requires a 30-minute session.

Methods: A prospective 6-month follow-up study was conducted of 138 consecutively seen insomnia patients treated with KIP. The diagnosis of a psychophysiological insomnia was made during a medical consultation and a behavior therapist with a 2-year college diploma, conducted the training session.

Results: One hundred and thirty eight consecutively seen patients were followed-up at least 6 months after the KIP training session. All patients were at least diagnosed with psychophysiological insomnia. Other insomnias were also present in some patients. Patients were followed up by telephone calls and then with mail-outs. Success was defined as not reporting any further difficulty with their sleeping. The results are as follows: Data on the contacted patients: 90 (65% of 138) Patients who completed the program: 58 (64%) Patients who completed the program with success: 48 (83%) Patients who completed the program without success: 10 (17%) These patients reported that they did follow the program instructions and yet still had persistent insomnia. Patients who did not perform the program after being trained: 32 (36%) Conclusion: Patients who follow the program have an 83% chance of setting their insomnia. The program is simple to use. It does not need to be delivered by a trained professional. Ways need to be found to increase the utilization of the program. It was only completed by 63% of the patients. The high percentage of patients who could not be contacted for follow-up is problematic for the statistical validity of the results. However, the initial results in 65% of the patients indicates KIP is an effective, quick, non-drug solution to the insomnia problems of many patients.
0765
Topographical Differences In NREM Sleep EEG In Male REM Sleep Behavior Disorders Patients: A Preliminary Report
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Introduction: A quantitative EEG study performed during NREM sleep showed that RBD patients have more delta power in the central region than controls (Massicotte-Marquez et al., in press). The aim of the present study was to further document this increase in delta power by analyzing various cortical regions during the NREM sleep of male RBD patients.

Methods: Ten men (51-72 y; mean age: 64.6 y) meeting the ASDA criteria for idiopathic RBD and ten healthy men matched for age (52-73 y; mean age: 64.2 y) underwent one night of polysomnographic recording. A Student t-test was used to assess between-group differences for the percentage of slow-wave sleep (SWS). ANOVAs were performed to assess between-group differences in delta (0.75-4 Hz) spectral power from frontal, central, parietal, occipital and temporal regions during the entire NREM sleep episode and for the first three NREM cycles.

Results: When compared to controls, RBD patients had more SWS (p ≤ 0.05). There was a clear Group effect for the EEG spectral analysis showing, for all regions, that RBD patients had a higher power in delta band (p ≤ 0.02). When results were analyzed by cycles, RBD patients had more delta power than controls in each cycle, for all regions.

Conclusion: The present results show that the NREM sleep of male RBD patients has more SWS and higher power in the low EEG frequency range without topographical differences. However, it is still unclear whether the increase of SWS and delta power results from activation of normal neurophysiological processes responsible for slow waves or reflects an abnormal EEG pattern due to neurodegenerative processes. Further studies are required to elucidate these possibilities.

Canadian Institutes of Health Research (CIHR), Canada

0766
25 Hours Of Sleep Deprivation Increases The Frequency And Complexity Of Somnambulistic Episodes In Adult Sleepwalkers
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Introduction: Adult sleepwalking can result in injury to the sleeper or to others. A polysomnographically-based diagnosis is often difficult to establish as somnambulism rarely occurs in the sleep laboratory. We recently showed that 40 hours of sleep deprivation significantly increases the number and complexity of somnambulistic events. This protocol, however, is overly demanding for patients and most clinical settings. The goal of the present study was to evaluate the effects of 25 hours of sleep deprivation on the frequency and complexity of sleepwalking episodes.

Methods: Participants were 15 sleepwalkers (7 males, 8 females; mean age: 29.1±5.5 years) referred to our Sleep Disorders Clinic. They were investigated in the laboratory for one baseline night and during recovery sleep following 25 hours of sleep deprivation. All patients were screened for other sleep disorders during both sleep periods. The complexity of somnambulistic episodes was scored according to a 3-point scale (see Joncas et al. 2002).

Results: Fourteen somnambulistic episodes were recorded at baseline and 29 during recovery sleep. Sleep deprivation resulted in a significant increase in the mean frequency (0.9±1.0 vs 1.9±1.2, p=0.001) and complexity (1.1±1.2 vs 2.3±1.5, p=0.003) of the episodes. Whereas only 9 of the 15 patients (60%) experienced one episode at baseline, all 15 had one or more episodes during recovery sleep (p=0.02). No other sleep disorder was found in any of the patients.

Conclusion: Our data show that 25 hours of sleep deprivation increases the frequency and complexity of sleepwalking episodes recorded in the laboratory and suggest 100% sensitivity for adult sleepwalkers. The results thus provide further evidence that sleep deprivation can facilitate the occurrence of a polysomnographically-based diagnosis for this parasomnia. The data also indicate that many adult sleepwalkers do not suffer from other sleep disorders.

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0767
REM Sleep Behavior Disorder In Probable Alzheimer’s Disease
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Introduction: REM sleep behavior disorder (RBD) is a parasomnia characterized by the occurrence of complex motor activity with a concomitant loss of muscle atonia during REM sleep. It has been hypothesized that RBD is strongly associated with neurodegenerative diseases called synucleinopathies [ex: dementia with Lewy bodies (DLB)], but is rare and only sporadically reported in non-synucleinopathy disorders [ex: Alzheimer’s disease (AD)]. The aim of the present study was to determine the frequency of RBD and to quantify the time spent with muscle activity during REM sleep in patients with probable AD.

Methods: Fourteen patients meeting the NINCDS-ADRDA criteria of probable AD (6 men; mean age, 70.7 ± 5.5 years) and 18 healthy controls (14 men; mean age, 66.7 ± 5.8 years) were studied in a sleep laboratory for one night. Polysomnographic recordings included EEG, EOG, chin EMG and infrared video monitoring. REM sleep was scored using the method of Lapierre and Montplaisir (1992). Time spent with muscle activity during REM sleep corresponds to the duration of all periods of EMG activity during REM sleep with an amplitude at least twice that of the background or greater than 10μV, divided by the total REM sleep duration.

Results: No between-group difference was observed for the time spent with muscle activity during REM sleep (24.8 ± 28.4% for probable AD group versus 13.4 ± 10.5% for control group). Four of the 14 patients (29%) with probable AD showed excessive muscle activity during REM sleep (two standard deviations below the mean of controls) and one (woman) manifested complex movements consistent with the diagnosis of RBD. None of the control subjects had behavioral manifestations during REM sleep.

Conclusion: These results suggest that RBD and excessive muscle activity during REM sleep could be observed in probable AD. However, their incidence is less likely than that observed in DLB.

Fonds de la Recherche en Santé du Québec and Instituts de la Recherche en Santé du Canada.
Introduction: Sleep bruxism (SB), reported by approximately 8% of the adult population, has been studied in our laboratory for over 15 years. This is a report on the comparison of various experimental treatments of SB using the analysis of the “number needed to treat” (NNT) method. With most effective treatments, the NNT should range between 2 – 4, or less.

Methods: Raw data was retrieved from 5 experimental randomized and controlled SB studies done in our laboratory over 8 years: with bromocriptine, propranolol, clonidine, and 2 dental splint studies. A total of 38 healthy SB subjects were recruited (21W; 17M; 19 to 39 yrs). Subjects were selected according to tooth-grinding history (>3 nights/week) and confirmed by a polysomnographic recording of habituation (#1) and diagnosis (#2) nights. Experimental nights were nights #3 and #4. Sleep and SB variables were recorded with the Harmonic software (Stellate Systems, Canada). Sleep variables (Rechtschaffen and Kales, 1968), oromotor/SB activity (Lavigne, 1996) and NNT (Altman, 1998; Walter, 2001) were analyzed. The studies in the NNT comparison are homogenous since experimental designs, outcomes and selection criteria were similar.

Results: Overall, a NNT of 1.5 was observed with the dental splint, with a reduction of 41.1% in the SB index compared to night #2. Clonidine has a NNT of 4, with a reduction of 46.2% in the SB index. The NNT observed with propranolol was infinite, with a very low reduction of 1.8% of the SB index. A negative NNT (~7) was observed for bromocriptine, which reflects an increase in the SB index of 21%.

Conclusion: The dental splint seems to be the most effective short-term treatment to reduce SB followed by clonidine. However, clonidine was associated with morning hypotension in 25% of subjects.

0769
Effect Of Double Arch Device And Occlusal Splint In Sleep Bruxism Patients
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Introduction: Occlusal splints are frequently recommended by dentists to manage sleep bruxism. The aim of the present study was to compare the efficacy of a double arch device (DAD) vs. a standard single upper occlusal splint (OS).

Methods: A group of 13 patients with a sleep diagnosis of SB participated in this randomized controlled crossover study. Subjects were recruited in the sleep laboratory for 6 nights. The DAD (Silencer Custom II, BC, Canada), designed to manage sleep apnea, was used in 3 configurations: without pin between arches (freedom of movement) and in slightly (<40%) and pronounced (>75%) lower arch advancement positions. Masticatory muscle activity was evaluated in SB episodes per hour and SB bursts per hour. Pain reports were scored on a 1-5 scale. Statistics included repeated measures ANOVA and Friedman two-way ANOVA.

Results: The total sleep time was reduced during the night with the DAD in the most advanced position compared to other nights (all p’s<0.02). Interestingly, the time (in minutes and %) spent in slow wave sleep was increased with the OS and DAD nights in comparison to baseline night. A statistically significant reduction in the number of SB episodes per hour (decrease of 42%, p=0.002) and SB bursts per hour (decrease of 51%, p=0.0001) was observed between baseline night and night with OS. Further reduction was observed between nights with OS and with DAD (all p’s<0.05). In comparison to baseline night, in the night with DAD in the most advanced position, 8 patients over 13 reported an increase in oro-dental pain (p=0.02).

Conclusion: The reduction of SB with DAD may be explained by one of the following factors: thickness of device, presence of pain, reduction of freedom in mandibular movement or alteration in airway patency.

Canadian CIHR and Québec FRSQ. DAD were provided free.

0770
Clinical And Neurological Findings In Sleep Bruxism (SB) Compared To Others Sleep Disorders
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Introduction: SB is a common parasomnia characterized by periodic movements with stereotyped grinding or clenching of the teeth, affecting sleep in many ways. Several clinical and polysomnographic (PSG) abnormalities are described in these patients. Our aim was to evaluate SB subjects and a sample of other sleep disorder subjects from our Sleep Disorders Center (SDC).

Methods: We compared SB and non-SB patients considering age, medication, caffeine, nicotine and alcohol intake, stress, anxiety, prior brain injuries, gastroesophageal complaints, mental concentration and other coexisting parasomnias. Twelve subjects with SB recruited by ads, and 6 control subjects picked from our SDC, excluding those with SB, were analyzed. All subjects were assessed by clinical examinations and questionnaires. All patients were submitted to at least one PSG. We applied Mann-Whitney test to our data.

Results: The mean age of the patients was 57.16 yrs (SD±6.73) in the control group and 37.41yrs (SD=17.12) in the SB group. The average time of teeth grinding in SB group was 12.75 yrs. There were significant differences between the groups considering stress (U=15,000; p=0.020); apnea index (U=4,500; p=0.047); hypopnea index (U=4,500; p=0.049); and fluoxetine use (U=15,000; p=0.078), favoring SB group. No statistical differences were found in caffeine, nicotine and alcohol intake, prior brain injuries, gastroesophageal complaints, mental concentration and other coexisting parasomnias. Familial history of SB was found similar in both groups.

Conclusion: Our data indicates a tendency to breathing disorders during sleep in SB patients. There was also a slight linkage between fluoxetine and SB. Stress may play an important role in SB by our data. Other clinical and PSG abnormalities were found not different between the groups.

No support

0771
Experimentally-Induced Somnambulistic Episodes In Adult Sleepwalkers: Effects Of Forced Arousal And Sleep Deprivation
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Introduction: Sleepwalkers: Effects Of Forced Arousal And Sleep Deprivation
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Conclusion: Our data indicates a tendency to breathing disorders during sleep in SB patients. There was also a slight linkage between fluoxetine and SB. Stress may play an important role in SB by our data. Other clinical and PSG abnormalities were found not different between the groups.

No support
**Introduction:** Early studies reported that forced arousals during slow-wave sleep (SWS) could induce somnambulistic episodes in predisposed children. However, the efficiency of forced awakening as a trigger for sleepwalking in adults has not been systematically evaluated. We previously found that sleep deprivation increased the frequency of somnambulistic events recorded in the laboratory. The goal of the present study was to use auditory stimulations to assess the effects of forced arousals during normal sleep and following sleep deprivation.

**Methods:** Eight sleepwalkers (3 males, 5 females; mean age: 28.5±6.7) were investigated. All underwent at least one polysomnographic screening night prior to the study. Patients were presented with auditory stimulations at four fixed periods either during normal sleep or recovery sleep following 25 hours of sleep deprivation. One week later, these conditions were reversed. In the targeted sleep stage, 3 second auditory stimulations were presented at 1 minute intervals in ascending intensities (40dB to 90dB) after at least 1 minute of stable EEG and EMG until an arousal, a somnambulistic episode, or a maximum of 6 stimulations was reached.

**Results:** Twenty-seven auditory stimulations were presented during SWS at baseline resulting in 5 induced somnambulistic episodes and 37 were presented during recovery SWS resulting in 16 episodes. One episode was also induced during stage 2 sleep at baseline and 3 during recovery stage 2 sleep. Sleep deprivation significantly increased the mean frequency of experimentally induced episodes (0.8±1.2 vs 2.3±1.2, p=0.03), the percentage of success in inducing an episode during SWS (19% vs 43%, p=0.04), and the number of subjects experiencing at least one induced episode (3/8 vs 8/8, p=0.03).

**Conclusion:** The data indicate that a) auditory stimulations can be used to experimentally induce somnambulistic episodes during adult sleepwalkers’ SWS and stage 2 sleep, and b) 25 hours of sleep deprivation significantly increases the efficacy of these forced arousals.

Research supported by the Canadian Institutes of Health Research and the Natural Sciences and Engineering Research Council of Canada.

**0772**

**The Relation Of Coping, Attributional Style, Stress/Trauma And Daily Mood On Nightmares And Bad Dreams: A Prospective Study**

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**Introduction:** Frequent distressing nightmares are a highly underreported parasomnia that affects anywhere from 4-10% of the general population, with significantly higher rates for clinical populations. While nightmare prevalence and frequency are consistently associated with poorer psychological well-being, the pathogenesis of these disturbed dreams is poorly understood. The present study investigated pertinent psychosocial characteristics of individuals who prospectively reported frequent nightmares over a three-week period.

**Methods:** 305 undergraduates (185 women, 120 men, mean age 20 years) at a large state university were recruited for course credit. They completed a packet of self-report measures including measures of coping, attributional style, life events, history of child abuse, psychopathology, and sensitivity to somatic complaints. Participants also completed daily ratings of mood, hassles and uplifts and completed a detailed dream and nightmare measure each morning.

**Results:** Both bad dreams (disturbing dreams without awakening) and nightmares were associated with histories of impactful life events, particularly negative events. These individuals also reported more early childhood adverse experiences. Disturbed dreams were also associated with higher levels of somatic amplification, dysfunctional cognitive attributional styles and emotion-focused coping. Significantly, nightmares were also associated with more weekly hassles and greater levels of negative affect the previous day. Significantly, these results were stronger for individuals who had higher psychopathology scores.

**Conclusion:** Prospective disturbed dreams are associated with a number of sociocognitive factors including emotion-focused coping, dysfunctional attributional cognitive styles and greater somatic amplification. They are also associated with higher daily stress levels and negative mood. The results are discussed within an emerging model of nightmare production.

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**0773**

**Zolpidem-Induced Amnestic Sleep-Related Eating Disorder (SRED) In 19 Patients**

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**Introduction:** Amnestic SRED induced by zolpidem was reported by Morgenthaler & Silber (2002) in 5 cases with RLS & other sleep disorders. We now report on zolpidem-induced amnestic SRED unassociated with RLS (apart from one case).

**Methods:** Over a 2-year period, 19 cases of zolpidem-induced SRED were identified at our hospital’s psychiatry clinic (n=11) and sleep clinic (n=8) by 7 treating physicians. (During this time period 4 cases of zolpidem-induced non-eating amnestic parasomnias were identified along with one other case of drug-induced SRED involving triazolam). All 19 cases were prescribed zolpidem because of persistent insomnia. The first author conducted a chart review & the first two authors further questioned the psychiatry clinic pts.

**Results:** Females, 84% (16/19); mean age, 47.4±13.4 yrs (range, 17-78); 84% (16/19) had recent &/or current major depression. N=1 had winter depression; n=1 had anorexia/bulimia nervosa. N=6 (31.6%) had chemical dependency, 5 in remission. 89.5% (17/19) were taking antidepressant drugs when zolpidem induced SRED, and many were taking other drugs for various psychiatric & medical disorders. The high-caloric foods consumed & sloppy manner of eating were typical for SRED. During episodes of SRED, pts became injured, 4 pts engaged in cooking (2 started small fires), 2 pts engaged in sleep-related driving with buying food & returning home. All pts had multiple episodes—including nightly—of SRED while taking zolpidem, mostly 10-20 mg. All pts before &/or after zolpidem had used other sedative-hypnotic & other psychotropic drugs (often many others) without SRED. The mother of one pt also had episodes of zolpidem-induced SRED (each was taking 20 mg). One pt with "Nocturnal Eating Syndrome" (abnormal eating while fully awake) developed amnestic SRED with zolpidem. All pts had persistent insomnia & 42.1% (8/19) had > 1 other sleep disorder (OSA, n=3; narcolepsy, n=2; RLS, RBD, SW, DSPS, n=1), but no prior SRED. Cessation of zolpidem promptly stopped the SRED.

**Conclusion:** Zolpidem appears to be the most common drug that can induce (amnestic) SRED, with potential hazards. Nevertheless, only a small % of pts treated with zolpidem will develop SRED. Females with insomnia who are receiving drugs for major depression (& other psychiatric, sleep or medical disorder), and who are taking 10-20 mg zolpidem appear to be most vulnerable for SRED. Physicians should alert pts about this possible side effect when prescribing zolpidem.
Sleep-Laughing (Somnorismus)

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Introduction: Scarce and anecdotal evidence sometimes describes laughing in sleep as part of the sleep-talking clinical spectrum, and rarely of a seizure disorder. The aim of the study was to better define this parasomnic behaviour.

Methods: A prospective study of patients who underwent sleep assessment for a variety of reasons during a 10-month period included screening for sleep-laughing. All of the patients had a PSG.

Results: Nine patients (age range 27-72, 5 males) who exhibited sleep-laughing were identified. Four patients also exhibited sleep-talking. Three patients have had a history of sleepwalking emerging in childhood, but none was present at the time of assessment. The frequency of occurrence ranged from once or twice every week, to once every few months. Typically, patients describe episodes of sleep-laughing associated with dream mentation, occurring in the last half of the night and often resulting in awakening. Awareness about the events is much stronger when compared to sleep talking - patients are aware of the content of a preceding dream, often describing it as bizarre but usually not disturbing. The general consensus is that the same content would not incite much laughing if they were awake. The PSG assessment recorded sleep-laughing episodes in three patients. On two occasions the episodes arose from the last REM episode. In one patient (male, age 72) the episodes occurred during two separate REM periods, associated with loss of atonia and suggestive of REM sleep Behaviour Disorder.

Conclusion: Sleep-laughing is a sleep-wake transition parasomnia with distinctive features. It is typically seen in transition from REM sleep to partial or complete awakening. Sleep-laughing may be an exclusive parasomnic occurrence or sometimes associated with other parasomnias (most often sleep-talking). While not indicative of any significant sleep pathology, in some cases it may be associated with REM sleep Behaviour Disorder or seizure disorder.

Lack Of Effect Of Pramipexol On REM Sleep Behavior Disorder (RBD) In Subjects With Parkinson Disease

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Introduction: The pathogenesis of REM sleep behavior disorder (RBD) is unknown although reduced midbrain dopaminergic activity is suspected since RBD is frequent in Parkinson disease (PD). We prospectively studied the effect of pramipexol on RBD in subjects with PD.

Methods: Eleven consecutive patients (age 62.2 +/- 8.0 years, PD duration 7.2 +/- 4.9 years) with RBD (duration 3.9 +/- 2.8 years) that did not receive dopamine agonists were evaluated at baseline and 3 months after stable pramipexol treatment (dose 2.2 +/- 0.3 mg/day). Videopolysomnography analyses were done during the second night of two consecutive studies. During REM-sleep we measured tonic and phasic EMG activity, percentage of time with movement (9.8 +/- 8.6 vs 7.6 +/- 6.1, p=0.04) and REM density (15.12 +/- 5.3 vs 13.7 +/- 6.5, p=0.5). Before treatment, movement severity on videotapes was mild in 5, moderate in 4 and severe in 2. After pramipexol, severity did not change in 9 and increased in 2. After treatment, subjects experienced reduction in the frequency of unpleasant dreams recall, but difference was no significant (p=0.05). Before pramipexol, 5 patients reported fearful dreams once or several times per week and 6 less than once a week. After treatment, this changed to 1 and 10, respectively.

Conclusion: Pramipexol does not improve RBD in PD suggesting that dopamine impairment does not play a major role in the pathogenesis of RBD.

REM Sleep EEG Activity Induced By Repeated Sleep Interruptions

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Introduction: Isolated sleep paralysis (ISP) without narcoleptic symptoms is considered as a state dissociation between wakefulness and REM state. A previous study demonstrated the close link between ISP and sleep-onset REM (SOREM) episodes with multi-phasic sleep-wake (MPSW) schedule using exclusively ISP subjects (Takeuchi et al. 2002, Sleep). The current study aimed at finding specific physiological markers during REM state in ISP subjects that reflect their vulnerability to state dissociation under MPSW schedule in comparison to control (CTL) subjects.

Methods: Eleven subjects (age 23.27±2.98 yrs, 6 CTL, 5 ISP) slept 3 consecutive nights. On night 3, subjects were repeatedly awakened every 5 min of REM sleep and kept awake for 60 min for mentation reports, questionnaires, and a vigilance task. REM episodes appearing within 25 minutes of sleep-onset were regarded as SOREM and those longer than 25 min were regarded as typical REM (TREM) episodes. On average, 3 TREM and 2.8 SOREM episodes were obtained in ISP and 2.2 TREM and 2.8 SOREM episodes for CTL per subject. For each 5-min REM episode, FFTs were performed every 2 sec on Central and Occipital EEGs, EOG potential (0.3-2.5 Hz) and total EMG power. Power was log-transformed, averaged for each REM episode and within subjects separately for SOREM and TREM episodes in order to test interactions and group effects with mixed ANOVAs (SOREM/TREM x ISP/CTL).

Results: The interaction indicated increased delta-theta (0.5-8.5 Hz) and alpha-beta (12.5-20.5 Hz) activities in Central and Occipital during TREM episode exclusively in the ISP group. Main group effects indicated increased beta (24.5-32.5 Hz) activity for Occipital and increased EMG activity in the ISP group.

Conclusion: Under a MPSW schedule, TREM episode in ISP subjects showed EEG activity suggestive of wakefulness (alpha-beta, less EMG inhibition) compared to CTL subjects. These physiological measures can serve as physiological markers to predict individual vulnerability to state dissociation under altered sleep schedule.

Fonds de la recherche en santé au Québec

Validation Of A Polysomnographic Score For REM Sleep Behavior Disorder (RBD)

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Introduction: Rapid eye movement (REM) sleep behavior disorder (RBD) was described more than two decades ago, but only one report on 5 patients and 5 normal subjects describes a method by which relevant polysomnographic findings can be quantified. We sought to validate this method in a larger sample of patients and control subjects.

Methods: A clinician interviewed 17 patients at risk for RBD secondary to neurodegenerative disorders and 6 age-matched controls to assess whether RBD was present by history. Bed partners completed a questionnaire that quantified RBD symptom severity. From two consecutive nocturnal studies in each patient, two different polysomnographic RBD scores were generated: the percentage of 30-second REM epochs with at least 15 seconds of tonically-maintained EMG activity, and the percentage of 3-second REM mini-epochs that contained phasic EMG bursts.

Results: The tonic and phasic measures, combined together, were higher in patients with clinical determinations of probable or possible RBD (n = 9) than in patients judged unlikely to have RBD (n = 14, p = 0.023). The overall polysomnographic measure correlated with the symptom scores (rho = 0.42, p = 0.048). Specific polysomnographic RBD measures on night 1 correlated highly with those on night 2 (rho > 0.70, p < 0.0001). Using this method, the cutoff point of 10% (average of EMG-active tonic REM percent and phasic REM percent) appeared optimal, in our data, to suggest RBD.

Conclusion: This quantitative method to assess the severity of RBD polysomnographic features appears to be both valid and reliable in patients at risk for RBD because of neurodegenerative disorders.

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0778

Sexual Behavior While Asleep -- Medicolegal Consequences

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Introduction: Parasomnia involving sexual behavior is more frequent than previously thought, consisting of several distinct features that distinguish it from sleep-walking. State-dependent, sleep related sexual acts are an important concern of forensic sleep medicine, yet have been rarely reported and clearly not systematically addressed. Determining the state-dependent nature of a sexual act is predicated upon comprehensive multidisciplinary sleep evaluation that utilizes specific protocols. This presentation will review the protocols and the available electrophysiological monitoring means that must be included in such an evaluation.

Methods: Using three selected cases, a) alleged nighttime rape of a spouse in the couple’s bedroom; b) alleged sexual assault of a teenager by another teen sleeping in the immediate vicinity; and 3) alleged sexual fondling of a child by an adult while napping in bed, the author will present his findings on sleep related phenomena such as sleepwalking, night terrors, confusional arousal, REM behavioral disorder, nocturnal seizures, and dissociative states originating in sleep that can be potentially associated with violence. Specific references to the comprehensive protocols used to answer the question of sleep related sex, both medically and legally, and how they pertain to these cases, will be discussed.

Results: The legal outcomes of these cases differed significantly and demonstrate that the question of a sexual act/assault carried out allegedly in the sleep state requires a careful, thorough and systematic work-up. Clinicians must follow clearly defined scientific methods to limit the risk of opening a Pandora’s box of unsubstantiated precedence or wrongly convicting a legitimate case of an action that might not have been carried out with the individual’s conscious awareness.

Conclusion: Utilizing sleep related science and guidelines, sleep experts can assist the medico-legal system in assessing for the possibility of sleep related sexual behavior. The forensic implications of this question, including directions for future research will be discussed.

0779

Olfactory Function In REM Sleep Behavior Disorder

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Introduction: REM sleep behavior disorder (RBD) is a parasomnia characterized by complex motor activity during REM sleep. Several evidences indicate that idiopathic RBD (iRBD) may be the harbinger of Lewy Body disease, including Parkinson’s disease (PD) and dementia with Lewy bodies (DLB). Olfactory impairment involving odour identification, detection and differentiation is a frequent and very early feature of PD and DLB. The aim of the study was to assess olfactory function in idiopathic and symptomatic RBD, compared to control subjects.

Methods: Thirty-three consecutive polysomnographic-confirmed iRBD patients (28M:5F; mean age:70.9 7.2 yrs), 8 patients with RBD+PD (6M:2F; mean age:71.7 7.8 yrs, mean Hoen Yahr:1.7) and 16 healthy subjects (12M:4F; mean age:70.7 6.3 yrs) entered the study. Subjects underwent to a Brief Smell Identification Test (B-SIT), a smaller and cross-cultural 12-items version of the University of Pennsylvania Smell Identification Test (UPSIT). All subjects, except four patients with PD-RBD, were free of psychotropic medication that may influence dopamine transporter binding and/or olfactory function and none had conditions known to influence olfactory function. Between-group differences on B-SIT score were assessed by a one-way ANOVA and post-hoc analysis were done using the Tukey HSD test.

Results: Mean B-SIT Score was significantly lower (F(2,54)=11.2; p=0.00008) in both patients with iRBD (6.6 2.4; p=0.0016; range:2-11) and patients with RBD+PD (5.0 2.0; p=0.003; range:2-8) compared to control subjects (9.1 1.6; range:6-12). No difference was observed in the mean B-SIT score between iRBD and PD-RBD patients (p=0.14). However, iRBD patients showed a greater heterogeneity


0780

Multiple Confusional Arousals Mimicking Nocturnal Seizures In A Single Night

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Introduction: Confusional arousal (CA) is a partial arousal disorder, which generally occurs during slow wave sleep as a single episode. Multiple episodes of CA in a single night are extremely rare and may be mistaken for nocturnal seizures.

Methods: Four patients (Pt 1 An 11 yr old boy; Pt 2: a 13 yr old brother of pt 1; Pt 3: A six year old boy; Pt 4: A 4 year old girl) presented with history of multiple episodes of nocturnal spells. During the spells the subjects would sit up in bed, look confused and unresponsive without fearful appearance and after several minutes would go back to sleep. On
some occasions when the mother forced patient 1 to lie down, he started struggling and sleep walking. None of them had clonic movement, tongue biting or urinary incontinence. These spells occurred both in the early and late part of the night.

**Results:** Video polysomnography study including 16 channel EEG recording showed 3-4 episodes of arousals with behavioral confusion but without choreoathetoid, ballistic or clonic movements, epileptiform discharges or sleep apnea. Patient 3 was treated by several neurologists with anticonvulsant without benefit for a mistaken diagnosis of nocturnal seizure and in patient 4 a diagnosis of partial complex seizure was strongly considered.

**Conclusion:** It is important to be aware of these unusual manifestations of CA from which the youngster will generally outgrow. The clues are the occurrence of EEG arousals usually from slow wave sleep without epileptiform discharges and the behavioral confusion without abnormal movements or response to anticonvulsants. A correct diagnosis will eliminate unnecessary costs and adverse effects of anticonvulsants.
0781 Improvement In PLMD-Associated Daytime Sleepiness With Modafinil In A Randomized, Double-Blinded, Placebo-Controlled Trial
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Introduction: The aim of this study was to assess the efficacy of modafinil (Provigil®) in treating the excessive daytime sleepiness (EDS) associated with Periodic Limb Movement Disorder (PLMD). We conducted a randomized, double-blinded, placebo-controlled trial to explore the effects of treatment with modafinil on objective and subjective measures of PLMD-associated daytime sleepiness.

Methods: Subjects 18-65 years old recruited from our sleep disorders clinic were consented to participate in the study. Subjects were included if they had EDS, PLMD diagnosed by clinical evaluation and polysomnography, no serious medical/sleep disorders, and no stimulant or sedating medication use. They had 2 consecutive baseline polysomnograms (PSGs), and a Multiple Sleep Latency Test (MSLT) following the second PSG to objectively measure their level of daytime sleepiness. Ten subjects were categorized as on dopaminergic medications, 10 were untreated for their PLMD. The 10 subjects in each group were then randomized to either a modafinil or placebo group for 21 consecutive days. Those in the modafinil group took 100 mg for the first 3 days, and then 200 mg for the remaining 18 days. Subjects returned to the laboratory for an additional 2 consecutive PSGs on the 19th and 20th nights and an MSLT on day 21. The MSLT was the primary outcome measure, the Epworth Sleepiness Scales (ESS) and Stanford Sleepiness Scales (SSS) were secondary outcome measures.

Results: Of the 10 subjects taking dopaminergic agents, there were 4 men and 1 woman (47.4 ± 6.91 years) in the modafinil group and 2 men and 3 women (40.8 ± 4.92 years) in the placebo group. Of the remaining 10 subjects who were untreated for their PLMD, there were 3 men and 2 women (42.6 ± 7.83 years) in the modafinil group and 3 men and 2 women (37.2 ± 3.70 years) in the placebo group. MSLT results were significantly improved in the modafinil vs. placebo group; the ESS and SSS results revealed trends toward EDS reduction in the modafinil vs. placebo group. When differences from baseline for each measure were compared for the modafinil vs. placebo group, the largest improvement was observed for the SSS in those subjects on dopaminergic medications.

Conclusion: Modafinil has been approved to treat EDS associated with narcolepsy, sleep apnea, and shift work. The results from this first systematic study to test modafinil on patients with PLMD revealed that this medication has potential as treatment for the EDS that is frequently associated with this condition.

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0782 Restless Legs Syndrome In Treated Depressed Outpatients: Prevalence And Clinical Correlates
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Introduction: Both population and clinic-based studies have consistently demonstrated high rates of depressive symptoms in individuals with RLS. However, little is known about rates of RLS in depressed outpatients, either before or during treatment.

Methods: One hundred and thirteen unselected patients being treated in two outpatient depression clinics completed a questionnaire investigating mood and somatic aspects of depression. Standardized inventories for depressive symptoms (the HANDS), for daytime sleepiness (the Epworth Sleepiness Scale), and for fatigue (the Brief Fatigue Inventory) were employed. The four standard screening questions for RLS, with an additional frequency question, were used to assess RLS. Informed consent was obtained from all patients, and the study was approved by the Partners IRB. Two-thirds of the sample were women, average age was 42.1 (12.6) years, most described themselves as minimally depressed, and had been on their current antidepressant for a median of 9 months. Nearly 50% were on at least two psychiatric medications, but none were treated for RLS.

Results: Twelve of 113 (10.6%) subjects with treated depression endorsed all four cardinal RLS symptoms. Ten of these had symptoms at least once per week, and 7 had symptoms at least twice per week. The ten subjects with at least weekly RLS were older than those without RLS symptoms (p=0.02), had more difficulty falling asleep (p=0.04), and trended towards higher levels of daytime fatigue (p=0.06). There were no differences in gender distribution, severity of depression, or level of daytime sleepiness between those with, and those without, RLS.

Conclusion: We found a rate of RLS in depressed patients taking antidepressants that approximates the prevalence in the general population, but is much lower than what has been previously reported in the one other published study on this subject. Consistent with RLS patients in the general population, both increased difficulty falling asleep, and excess daytime fatigue were observed in our treated depressed patients with RLS.
symptoms. Furthermore, a history of cardiovascular disease was more common in individuals in the High RLS group (OR=2.44, 1.26-4.72) than those without RLS symptoms.

**Conclusion:** Our overall prevalence rates for RLS are comparable to other U.S. epidemiologic studies. Similar to others, we found that RLS was associated with poor general health. Our sample of individuals with RLS also had a complaint of EDS as well as abnormal Epworth scores. These associations were all more pronounced in individuals with more frequent RLS. Our finding of an association between RLS and cardiovascular disease (but not with hypertension) merits further investigation.

### 0784

**Alternating Leg Muscle Activation (ALMA) During Sleep And Arousals Can Produce Limb Movement**

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**Introduction:** The phenomenon of ALMA was described recently as a polysomnographic pattern of anterior tibialis electromyographic bursts that occur bilaterally in reciprocating fashion. The ALMA commonly occur in association with arousals but sometimes during sleep without arousals. However, no published evidence shows whether any limb movement occurs during ALMA, and if so, in what pattern. In this series of 7 patients, the same electromyographic features are present along with video evidence of coordinated leg movement.

**Methods:** Cases were identified from over 300 polysomnograms reviewed in the course of standard clinical care at a large academic sleep disorders laboratory. Five men and two women (mean age 55, range 31-91) comprised this series. Anterior tibialis surface electromyography (EMG) was used to identify activity consisting of brief activation of these muscles bilaterally in an alternating fashion. Digital video obtained with polysomnograms was reviewed and only cases with clear lower extremity movement were included in this series.

**Results:** The frequency was approximately 1-2Hz, each lasting 0.1 to 0.5 seconds. Sequence duration was typically 2-20 seconds. This phenomenon mainly occurred in stage 1, 2 and REM sleep. Two of the seven patients were taking antidepressant medication. Three of the seven patients also experienced periodic leg movements of sleep. Video recordings show lower extremity movement in coordination with the electrographic pattern of ALMA. Although blankets or the camera angle sometimes obscured detailed observation, two cases clearly showed alternating movement of the legs with flexion at the hip and knee on one side followed by the same movements in the other leg.

**Conclusion:** This report documents for the first time that ALMA can be seen in association with arousals but sometimes during sleep without arousals. Indeed, these results suggest that it is essential to administer the test after 21:20 since symptoms of RLS are then more severe and more sensitive to immobility.

This research program has been supported by the Canadian Institutes of Health Research.

### 0786

**Severity Of Restless Legs Syndrome And Sensory Nerve Dysfunction**

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**Introduction:** RLS is an urge to move the legs often associated with uncomfortable sensations. As RLS severity increases, sensory disturbances often become more prominent which suggests alteration of peripheral sensory processing. The correlation between RLS symptoms and sensory dysfunction has not been clearly established.

**Methods:** Twenty-four RLS subjects were separated into high and low severity groups (HSG & LSG) based on the International RLS Study Group questionnaire. Each subject had bilateral ulnar and sural sensory nerve conduction (SNC), sympathetic skin response (SSR), Heart Rate Variability (R-R interval), and examination of 5 sensory modalities. Laboratory testing consisted of HbA1c, TSH, T4, SPEP, B12, folate, BUN, creatinine, copper, iron, ferritin. All variables were analyzed separately for significant differences (two-tailed t-test; p value of < 0.05) of computed means and standard errors between the total RLS group versus normative data, and HSG versus LSG.

**Results:** The presence of RLS symptoms was significantly correlated with abnormal R-R intervals (p < 0.01), leg SSR (p < 0.01) arm SSR in arms (p < 0.01), sural SNC (p < 0.01) and ulnar SNC (p < 0.01). The leg SSR and SNC were more abnormal than the arms (p < 0.01). As compared to LSG, the HSG had significantly more abnormal R-R intervals (p = 0.04) and leg versus arm SNC (p < 0.01).
Conclusion: The presence of RLS symptoms was significantly correlated with both small and large sensory fiber dysfunction as reflected in R-R intervals, SSR, and SNC (legs >arms). Further, increased RLS severity correlated with worsening of autonomic function and large sensory fiber function in the legs. These findings are the first to specifically correlate RLS symptoms with electrophysiological abnormalities. The early identification of autonomic and sensory (small and large fiber) dysfunction in RLS subjects may point to underlying etiology and/or specific symptomatic treatment.

0787
Periodic Limb Movements During Nocturnal Wakefulness In Restless Legs Syndrome
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Introduction: Polysomnographic findings in RLS have been described, including increased periodic limb movements in sleep and increased wake after sleep onset; however, these measures are neither sensitive nor specific. Recently, periodic limb movements during nocturnal wakefulness (PLMW) have been evaluated in RLS patients, but a normal range for this measure has not been well established and the measure is not used by many laboratories. Also, the appropriate duration of PLMW is debated. A previous study found that a PLMW-index greater than 15 was sensitive and specific for a clinical diagnosis of RLS; however, the application of this data is limited because the control subjects were free of sleep complaints and therefore not representative of typical patients undergoing polysomnography in the sleep laboratory. The aim of this study is to evaluate the frequency of PLMW in RLS and non-RLS patients evaluated in our sleep laboratory.

Methods: A database search was performed for a one year period to identify adult patients evaluated in the outpatient clinic who were diagnosed with RLS and who underwent polysomnography. Control subjects were randomly selected from the same database. All control subjects had documented denial of RLS symptoms. The polysomnograms were reviewed. PLMW were scored separately based on the Coleman criteria and based on the Michaud criteria for the Suggested Immobilization Test (SIT).

Results: 100 RLS patients were identified, 88 of whom had complete records available. 90 control patients were selected. The groups did not differ significantly in age, total sleep time, sleep efficiency, sleep latency, wake after sleep onset, or arousal index. The mean periodic limb movements in sleep (PLMS) and PLMS-arousal indices were significantly higher in the RLS group. The mean PLMW index was significantly higher in the RLS group (29.1 vs. 19.7, p=0.038) when the Coleman criteria were used. When the Coleman criteria were applied, a PLMW index of 15 or greater yielded a sensitivity of 62.5% and a specificity of 58.9% for the diagnosis of RLS. When the SIT criteria were applied, a PLMW index of 15 or greater yielded a sensitivity of 64.8% and a specificity of 55.6%.

Conclusion: The PLMW index is significantly higher in RLS patients compared with control subjects; however, a value of 15 or greater is not sensitive or specific for a diagnosis of RLS in our study group. Further analyses will be performed to look for a PLMW-index value with higher sensitivity and specificity in our group.

0788
Beneficial Effect Of PPX In RLS Patients After 6 Months Treatment-Results From A Prospective Open Label Study
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Introduction: Several papers were published about the longterm effect of pramipexole in the treatment of RLS from retrospective studies. We report about the 30 weeks data from a prospectively planned open label study which followed a three week double-blind, placebo controlled study and a one week washout period. The results of the placebo controlled double-blind part of the study were presented by the authors at the APSS meeting in 2004.

Methods: All patients had to undergo a one week washout period after finishing the three week double blind period. Afterwards all patients started their treatment with 0.125mg PPX. The dose could be up titrated weekly depending on the PGI assessment up to the highest dose of 0.75mg. After a total treatment period of 30 weeks RLSRS and CGI-I were compared to the baseline value at the beginning of the double-blind placebo controlled period.

Results: 97 patients had 30 week treatment values. The mean overall RLSRS score was reduced by 16.9 points to an average of 6.0 points compared to baseline. The 95% confidence intervals for the mean change from baseline did not include zero for any dose group indicating significance at the 5% level. The CGI-Improvement showed a dramatic advance in patient condition: 94.8% of all patients were regarded as having either much or very much improved compared to baseline. Likewise, a marked therapeutic effect (CGI-Therapeutic effect) was seen by the investigator in 75% of all patients at week 30.

Conclusion: The results of this open label extension study demonstrate that pramipexole is highly effective in achieving and maintaining a very substantial reduction in the severity of RLS symptoms over 30 weeks of treatment over the entire dose range tested. This goes along with a sustained improvement of the clinical global impression. This study supports the published evidence that pramipexole shows continuous efficacy over a longer period of time in the treatment of RLS symptoms.

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0789
Skeletal Muscle Function And Morphology In Persons With Restless Legs Syndrome (RLS)
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Introduction: Sleep deprivation significantly decrease aerobic and anaerobic exercise capacity. In patient with obstructive sleep apnoea syndrome (OSAS) structural and bioenergetic changes have been demonstrated in skeletal muscle, may be due to sleep loss and/or intermittent hypoxia. Skeletal muscle consists of mainly three different fibre types typ I, type IIA and type IIX based on type of myosin. The size of the capillary bed indicates endurance capacity. The aim of this study was to investigate skeletal muscle morphology and function in patients with restless legs syndrome (RLS).

Methods: Twenty patients with RLS and 16 healthy age matched controls participated. A submaximal ergometer test was performed including oxygen uptake. Muscle biopsies were obtained from m. tibialis anterior using the semi-open biopsy technique. Muscle fibre classification was based on myosin heavy chain expression using monoclonal antibodies and classified as type I, Iha, Ila, Ix, and IIX and fibre area and perimeter were calculated. Capillaries were visualised using an antibody labelling endothelial cells.
Results: Daily physical activity and VO2 in l/min did not differ between the groups. However VO2 in ml/min/kg bw was different due to higher BMI in the RLS group (33.7 ± 8.1 ml/min/kg bw for RLS and 40.4 ± 2.7 ml/min/kg bw for the controls, p = 0.011). There were no significant differences in fibre composition (67.5 ± 8.93 vs 72.1 ± 8.93 % of type 1 fibres) in area of type 1 (5288 ± 1222 vs 4830 ± 684) and type 2 fibres (6389 ± 2273 vs 6948 ± 1239), as well as in micro vessels indices.

Conclusion: Patients with RLS will result in deteriorated physical fitness according to VO2 in ml/min/kg bw. However skeletal muscle morphology based on fibre type distribution, fiber area and capillary supply was unaffected. Further investigations will include sleep deprivation with severe intermittent hypoxia.

0790
Pramipexole Reduces The Impact Of RLS Symptoms On Daily Functioning

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Introduction: Patients with restless legs syndrome (RLS) suffer from some limitations in activities of daily living (ADL) compared to healthy people; i.e. they are rarely able to sit still during an opera performance, a long flight, or suffer from day-time sleepiness due to sleep disturbances during the night.

Methods: In a 6-week, double-blind, placebo-controlled study, patients with idiopathic RLS where randomised to treatment with pramipexole or placebo (2:1). Patients underwent a flexible dose titration phase during weeks 1 to 4 (dose range: 0.125-0.75 mg/ per day). Patients were on stable dosages for at least 2 weeks until week 6. The RLS rating scale consists of 10 different subitems; item 9 asks the patient about the impact of RLS on their ability to carry out daily affairs. The patient can rate 0= no, 1=mild, 2=moderate, 3=severe, 4=very severe. We analysed the shift of the impact of RLS on their ability to carry out daily affairs. Moreover we put this result in perspective to the results of the quality of life scale SF-36, which was filled-in by all patients in parallel.

Results: A total of 345 patients (out of 37 centres from 5 European countries) were included in this study. 217 patients receiving pramipexole and 107 patients receiving placebo had completed baseline and final visit values (2:1 randomisation ratio) and were included in the analysis. 22 patients on placebo (20.6%) and 36 on pramipexole (16.6%) reported a severe or a very severe impact of the RLS on their ability to carry out daily affairs at baseline. After 6 weeks of treatment significantly more patients treated with pramipexole 21/36 (58.3%) had only a mild or none impact of their RLS symptoms anymore on their ability to carry out daily affairs as compared to 6/22 (27.2%) treated with placebo (p=0.0305, Fishers Exact Test, 2-sided). Moreover the score for the subdomain “social functioning” of the SF-36 was significantly higher in the pramipexole group as compared to the placebo group (adjusted mean change from baseline + 6.0 [SE =1.3] vs. placebo +0.8 [SE =1.8], p=0.016).

Conclusion: Pramipexole reduces the impact of RLS symptoms on daily functioning in a statistically significant way as compared to placebo treatment after a 6-week treatment period. These findings are in line with the outcome of the quality of life assessment (SF-36) in the same study (submitted elsewhere) in which, beside others, the subdomain “social functioning” was significantly improved in pramipexole treated patients as compared to the placebo group.

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0791
Increase Of Symptom Free Days For RLS Patients By Treatment With Pramipexole

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Introduction: Pramipexole was shown to significantly decrease the score of the restless legs syndrome (RLS) rating scale (RLSRS) over a 6-weeks treatment period (Oertel et al, MDS 2004, abstract). Considering the unpredictability of the occurrence of symptoms it is an important feature of a valuable treatment option if the number of symptom free days could be increased.

Methods: In a 6-week, double-blind, placebo-controlled study, idiopathic RLS patients were randomised to treatment with pramipexole or placebo (2:1). Patients underwent a flexible dose titration phase during weeks 1 to 4 (dose range 0.125-0.75 mg/day). Patients were on stable dosages for at least 2 weeks until week 6. RLSRS item 7 asks about the frequency of RLS symptoms in the week before the assessment. Patients can rate 0= never, 1=occasionally, 2=sometimes, 3 =often, 4=very often. We analysed the frequency shift of days with RLS symptoms from baseline to week 6 by determine the rates of patients that were symptom-free for one week at the last assessment.

Results: A total of 345 patients (out of 37 centres from 5 European countries) were included in this study. 217 patients receiving pramipexole and 107 patients receiving placebo had completed baseline and final visit values (2:1 randomisation ratio) and were analysed. 64 patients on placebo (59.8%) and 123 on pramipexole (56.7%) suffered very often from RLS symptoms the week before baseline. After 6 weeks of treatment significantly more patients treated with pramipexole were symptom-free during the last week of treatment as compared to the patient group treated with placebo (29/123; 23.6% vs 4/64; 6.3%, p=0.0019, Fishers Exact Test 2-sided).

Conclusion: There is increasing and robust evidence that pramipexole is efficacious in treating overall RLS symptoms. Pramipexole leads to remission, defined as absence of symptoms during the last week, in one fifth of the patients after a 6-week treatment period. This is an additional beneficial feature of pramipexole in the treatment of RLS.

The study was supported by Boehringer Ingelheim International

0792
Prevalence, Severity And Predictors Of Restless Legs Syndrome In Norway And Denmark

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Introduction: Restless legs syndrome is a common, but often misdiagnosed or undiagnosed neurological movement disorder. To date, there are few population-based epidemiological studies, especially investigating risk factors. Thus, we conducted an epidemiological study to estimate prevalence and severity (using International Restless Legs Syndrome
0793 Dopamine D3 Receptor Polymorphism In Patients Undergoing Treatment With Dopamine Receptor Agonists For Restless Leg Syndrome

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Introduction: Dopamine receptor agonists are currently the drugs of choice for the treatment of restless leg syndrome (RLS). Exploring the efficacy of individual agents, as well as their relationship with dopamine receptors is a potential means for better characterizing the underlying neuro-biochemical dysfunction in RLS. Dopamine D3 membrane receptor plays an essential role in the pharmacology of dopaminergic neurotransmission. This study was undertaken to determine whether dopamine D3 receptor polymorphism has any influence on the efficacy of pramipexole therapy in idiopathic RLS.

Methods: Only patients diagnosed with idiopathic RLS were enrolled. Following screening, subjects received pramipexole with binding affinity to D2/D3 receptors in an average daily dose of 0.75 to 1 mg. Genomic DNA was extracted from peripheral blood. The PCR reaction was carried out in the presence of appropriate primers. The PCR product was digested with MscI. The electrophoresis was carried out on 5% acrylamide/bis acrylamide gel. The therapeutic effect of pramipexole was monitored using a questionnaire and actigraphy, both performed at baseline as well as after 2 months of pramipexole treatment.

Results: The distribution of dopamine D3 receptor genotypes involved in dopaminergic neurotransmission was explored in 46 patients with idiopathic RLS and in 51 control subjects. Ser/Ser polymorphism was ascertained in 17 patients, whereas 26 had Ser/Gly and 3 had Gly/Gly genotype. In the control group, the distribution of these variants was the following: Ser/Ser 23, Ser/Gly 26 and Gly/Gly 2 subjects. Khi square test did not reveal a statistically significant difference between the two groups as regards allele distribution (p=0.301, df: 2). Therapeutic efficacy in relation to D3 receptor polymorphism was analyzed with paired, two-tailed t-testing. Assuming a p<0.05 limit of significance, the scores obtained using the questionnaire reflected significant improvement in patients with Ser/Ser (p=0.0006, df: 15) or Ser/Gly genotype (p=0.098, df: 24) and non-significant in patients with the Gly/Gly genotype (p=0.109, df: 1). Actigraphic work-up, by contrast, showed significant improvement in all three subsets: Ser/Ser p=0.018, df: 15; Ser/Gly p=0.027, df: 24; Gly/Gly p=0.039 df: 1.

Conclusion: The distribution of dopamine D3 receptor genotypes was not significantly different in patients with idiopathic RLS and in controls. Pramipexole was equally effective in all three subsets with different genotypes.

0794 Clinical And Polysomnographic Characteristics Of High Frequency Leg Movements

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Introduction: The anterior tibialis EMG is primarily used in standard polysomnography (PSG) to record periodic leg movements of sleep (PLMS). In addition, periodic leg movements with a much shorter intermovement interval than observed with PLMS have also been reported. The aim of this study was to describe the clinical and polysomnographic characteristics of patients who showed high frequency leg movements (HFLM) on polysomnographic recording.

Methods: Among 486 patients (male 232, female 254) referred for overnight diagnostic PSG over a nine-month period, 37 patients demonstrated HFLM:19 males (8.2% of PSGs) and 18 females (7.1% of PSGs). An equal number of age- and sex-matched consecutive controls who did not show HFLM were selected. HFLM was defined as more than four discrete leg movements occurring at a frequency of 0.5-3 Hz.

Results: Two-thirds (64.3%) of all HFLMs occurred during waking and 35.7% occurred during sleep. Of those HFLM episodes occurring during sleep, 44.8% occurred during stage 1, 45.0% during stage 2, 0.5% during stages 3 and 4, and 9.5% during REM stage. The movements usually tended to appear unilaterally, but sometimes they showed a bilateral alternating pattern. The mean frequency was 1.6 ± 0.6 Hz (range 0.4 - 3.7), the mean number of episodes of HFLM per subject per night was 25.6 ± 30.5 (range 2 - 111), and the mean duration was 17.6 ± 35.4 sec (range 1.5 sec - 6.1 minutes). The mean HFLM index (total number of HFLM divided by the time in bed, in hours) was 107.7 ± 254.5 (range 2.0 - 1078.3). Patients with HFLM complained of RLS symptoms significantly more often than the control group (p<0.05).

Conclusion: Further studies are needed to establish criteria for scoring HFLM. Examination of other patient cohorts with HFLM will be needed to determine whether HFLM are in fact associated with RLS.

0795 Altered Renal Excretion Patterns In Idiopathic Restless Legs Syndrome

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Introduction: Aim of this exploratory study was to elucidate preliminary observations of excessive nighttime urine excretion in idiopathic restless legs syndrome (iRLS).

Methods: Eighteen patients with iRLS and with normal serum creatinine, blood urea nitrogen, and urate and eleven healthy controls were examined. Typical parameters of excretory renal function (urine volume, osmolality, sodium, chloride, potassium, calcium, phosphate, microalbumin, aldosterone, creatinine, creatinine clearance, and fractional sodium excretion) were measured during daytime (07:00-22:00) and nighttime (22:00-07:00).

Results: During nighttime, urine volume (87.6±33.8ml/h vs. 48.3±32.5ml/h; p=0.006), sodium excretion (8.09±4.06mmol/h vs.
Category N—Sleep Disorders-Movement Disorders

4.61±2.58mmol/h; p=0.008), and chloride excretion (10.12±5.11mmol/h vs. 4.05±2.42mmol/h; p=0.001) were significantly higher, urine osmolarity (454.9±245.7mosmol/l vs. 665.6±227.7mosmol/l; p=0.02) was significantly lower in iRLS patients as compared to healthy controls. As compared daytime to nighttime excretion, controls showed the physiological reduced nocturnal excretion values of urine volume (91.8±40.2ml/h vs.48.3±32.5ml/h; p=0.009) and chloride (6.49±3.05mmol/h vs. 4.05±2.42mmol/h; p=0.023) and a nocturnal increase in urine osmolarity (429.3±232.4mosmol/l vs. 665.6±227.7mosmol/l; p=0.026). But patients showed similar excretion rates of urine volume (89.3±41.0ml/h vs. 87.6±33.8ml/h; n.s.), chloride (8.27±4.43mmol/l vs. 10.12±5.11mmol/l; n.s.), and osmolarity (454.1±232.5mosmol/l vs. 454.9±245.7mosmol/l; n.s.) during daytime as well as nighttime.

Conclusion: These data indicate a loss of some rhythms of renal excretion in our group of iRLS patients. The elevated nighttime excretion found, with values similar to daytime, hint on a possible elevated fluid, sodium, and chloride intake during daytime.

0796 Spectral Analysis Of Sleep EEG In Patients With Restless Legs Syndrome

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Introduction: Conventional analyses of sleep EEG according to standard criteria indicate severe sleep disturbances in patients with restless legs syndrome (RLS). Spectral analysis of sleep EEG may be a sensitive tool to detect functional alterations of sleep mechanisms beyond the visual scoring of polysomnographic records. We analysed sleep EEG spectral power differences between RLS patients and healthy subjects and studied the relationship of sleep EEG spectral power to the occurrence of periodic leg movements in sleep (PLMS) and arousal events.

Methods: Sleep EEGs from 20 patients with idiopathic RLS and of 20 age and sex matched healthy subjects were investigated. The spectral analysis was carried out on the same 30 second epochs for which sleep stages had been determined. As a first step, whole-night spectral power excluding epochs with an arousal or with a PLMS was compared separately for REM and NREM sleep between RLS and healthy subjects. In a second step, we evaluated the spectral effects of PLMS, PLMS with associated arousals and isolated arousals relative to epochs of sleep without such events in both groups. In this part of the analysis we only included the epochs of sleep stage 2 (the main and most stable non-REM sleep stage) and of REM sleep.

Results: Spectral power of all sleep epochs (excluding arousals and PLMS) did not differ between patients with RLS and healthy subjects. As expected, arousals and PLMS-associated arousals resulted in a significant increase in higher-frequency activity (alpha, beta1, beta2 and gamma bands) in both groups. Spectral power in epochs with PLMS alone did not significantly differ from spectral power in epochs without PLMS and arousal in any of the groups.

Conclusion: Our data suggest that RLS related symptoms may intermittently disrupt sleep but do not appear to involve a persistent disturbance of the basic sleep generating patterns.

0797 Cardiovascular Variability During Periodic Leg Movements: A Spectral Analysis Study

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Introduction: Changes in cardiovascular measures have been advocated as sensitive markers of phasic events arising from sleep such as apneas, arousals and periodic leg movements (PLMS) inducing abrupt changes in heart rate variability (HRV). In this study we analyze whether time and frequency domain analyses of HRV can provide a simple tool to evaluate the sympatho-vagal balance changes occurring during PLMS.

Methods: The study group consisted of 14 patients having Restless Legs Syndrome. In all patients HRV was analyzed in 10-min periods with (PLMS+) and without (PLMS-) PLMS in NREM sleep. Only PLMS associated with EEG arousal were considered. For each 10-min period, the absolute and normalized high and low frequency peaks from spectral analysis of R-R intervals, the HRV changes using wavelet transform, the geometric and time domain HRV were measured.

Results: The HRV triangular index, the TINN, the average SDNN and SDNN index significantly rose in PLMS+ periods. The LF power increased of 789.5±41 (p<0.0001) and the LF/HF ratio rose in PLMS+ periods by 6.6±0.8. In contrast, HF power showed a small and not significant decrease. The rise in sympathetic activity was also demonstrated by wavelet analysis. Comparison of PLMS+ period in stage 2 and SWS showed a tendency toward reduced sympathetic hypertonus in SWS (p<0.01). The number of PLMS occurring in the 10-min periods was related to LFnu, LF/HF ratio, LF nuwavelet and LF/HF ratiowavelet (p<0.0001).

Conclusion: The primary cardiac effect of PLMS consists in a strong increase in sympathetic activity associated with a weak reduction in parasympathetic tonus. FFT and wavelet HRV analysis appears to be a sensitive tool to detect not only the HRV related to PLMS but also the influence of sleep stage. The magnitude of increased sympathetic activity was related to PLMS frequency suggesting that frequency-domain HRV analysis could be an easy method to evaluate PLMS and the related sleep fragmentation.

0798 Night-To-Night Variability In Periodic Leg Movements In Patients With Restless Legs Syndrome

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Introduction: Although a night-to-night variability in periodic leg movement during sleep (PLMS) has been described in patients with primary PLM disorder and sleep apnea, no study has considered the inter-night effect in Restless Legs Syndrome (RLS). In the current study we investigated the night-to-night variability of PLMS and PLM occurring during wakefulness (PLMW) in a group of RLS patients examined during two consecutive nights.

Methods: 28 RLS patients, having a mean IRLSSG severity score of 20.2±1.6 were examined. PLMS and PLMW were scored according to standard criteria and their index, duration and interval were computed for wakefulness, total sleep, as well as for each sleep stage and each sleep cycle. To quantify the PLM temporal occurrence over the course of the night, PLM analyses were performed for the first four sleep cycles.

Results: No differences in all sleep measures including PLMS arousal index were found between nights. The index, the duration and the interval of PLMW and PLMS did not show significant differences between nights. The PLMW index (PLMWI) and the PLMS index (PLMSI) were highly reproducible with a correlation coefficient between nights, respectively, of 0.60 and 0.54. However, there was considerable intra-individual variability in the density, respectively, of 0.79±1.1 for PLMW (range: minus 111 to plus 53) and 0.59±0.9 (range: minus 37.4 to plus 70.1) for PLMS. No relation between the changes in the PLMWI and PLMSI between nights and the changes in sleep parameters, age, RLS severity score and duration of the disease were found. Comparison of
PLMS index in the different sleep stages and sleep cycles in the two consecutive nights revealed no significant differences.

**Conclusion:** Despite the PLMW and PLMS index, duration, interval and the over-time PLM evolution showed a good night-to-night reproducibility, an intra-individual difference was noted independent of RLS severity score, age, duration of the sleep and sleep parameters. These results may be considered in the evaluation of efficacy of therapy.

### 0799

**Prevalence Of Restless Legs Syndrome (RLS) In Liver Disease An Interim Analysis**

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**Introduction:** RLS is a clinical syndrome that affects approximately 10% of the general population. RLS is more prevalent in certain disease states such as iron deficiency, neuropathy, and renal insufficiency. Identification of these populations has lead to increased awareness and treatment for these patients. No such prevalence data exists for liver disease and RLS.

**Methods:** The present project was limited to prospective survey and chart review. Previously validated RLS survey tools were used to measure the presence of RLS. Those with clinical encephalopathy were excluded. A one-page survey featuring the core symptoms of RLS was administered to patients in a university-based hepatology clinic. RLS herald symptoms as agreed upon by the International RLS Study Group were incorporated as 5 key questions addressing RLS.

**Results:** 121 hepatology clinic patients were surveyed to date. This survey was considered positive for RLS if 3 of 5 core symptoms were present. 76 of 121 completed surveys were positive and in follow up interview, only 2 false positives were detected. This yields a prevalence estimate of 61% (p<0.00001). Further, of the 74 positive surveys, 58% reported 4 key symptoms and 33% reported all 5 core symptoms. Of the positive surveyed only 32% had self reported risk factors including kidney disease(3), iron deficiency (12), and/or neuropathy (14).

**Conclusion:** RLS occurs with a surprisingly high prevalence in patients with liver disease. Some of this prevalence is explained by conditions known to cause RLS, yet a substantial number of respondents had no self-reported risk factor. Analyses using chart review are underway. Additional study of the severity and impact on quality of life are also underway.

### 0801

**Are Respiratory Related Limb Movements (RRLM) A Marker Of Arousal?**

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**Introduction:** Cortical arousal associated with periodic limb movements in sleep (PLMS) is well known and pulse rate has been shown to rise around the time of PLMS. Our previous work and that of others has documented a rise in blood pressure at the time of PLMS. However no one has specifically looked to see if comparable rises in blood pressure and pulse rate occur with Respiratory Related Limb Movements (RRLM). Nor has anyone determined the degree to which RRLM occur with cortical arousal. The aim of this study is to determine the degree to which RRLM serve as a marker of arousal of either the autonomic or cortical type.

**Methods:** We studied four patients with mild sleep apnea and RLS/PLMD. We analyzed 33 hypopnea related RRLMS. RRLMS were recorded during sleep by electromyography, EEG arousals were recorded with RRLMS. Pulse rate and blood pressure were monitored continuously during sleep with a Portapres machine.

**Results:** 93% of RRLM were associated with EEG arousals. 90.9% of RRLM were associated with a rise in pulse rate. The average rise in pulse rate was 6.06 beats per min. 96.9% of RRLM were associated with an increase in systolic and diastolic blood pressure. The average rise in systolic blood pressure was 18.6 mm Hg and the average rise in diastolic blood pressure was 9.27 mm Hg. Our results are comparable to our previous observations with PLMS.

**Conclusion:** Our preliminary data suggest that a) cortical arousals and autonomic arousals (an increase in pulse rate, systolic and diastolic blood pressure) are highly associated with RRLMS. Therefore, we suggest that RRLMS may be used as a surrogate marker of an autonomic or cortical Health Study Sleep Habits Questionnaire, the Center for Epidemiological Studies Depression (CES-D) measure, height, weight, and blood pressure. A subset of veterans (n=55) had fasting morning serum blood draws for leptin levels. Leptin ELISA assays were done in triplicate. Backward logistic regression was used with RLS as the dependent variable and age, ethnicity, BMI, smoking status, diabetes history, leptin levels, and CES-D scores as independent variables.

**Results:** Of the 229 veterans (44% Hispanic; mean age 68 years), 23.6% reported RLS. Veterans with RLS were significantly more likely to have elevated CES-D scores (16.4 vs. 9.0, p<0.0001) and be overweight (BMI 29.3 vs. 27.5, p<0.05). Of the 55 leptin sub-study participants, 30% reported RLS. The RLS sub-study participants also showed higher CES-D scores (20.8 vs. 9.2, p<0.0001), as well as elevated leptin levels (mean pg/ml: 10,447 vs. 4,446, p<0.05); however, BMI did not significantly differ in the sub-groups. There were no significant differences within or between groups for age, ethnicity, smoking, or diabetes. Backward logistic regression indicated that depression (p<0.01) and elevated leptin (p<0.05) were independently associated with RLS.

**Conclusion:** The finding for an association between depression and RLS replicates prior studies in civilians. Altered (elevated) leptin secretion was noted to be correlated with depression, but not BMI, in another study. Results of this study warrant further research into neurobiological links between depression, the pleiotropic nature of leptin, and RLS.

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**Prevalence Of Restless Legs Syndrome (RLS) In Liver Disease An Interim Analysis**

**Franco RA, Deshpande A, Franco J, Saenon K, Braden B, Daniel J, Knox F**

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**Introduction:** Restless legs syndrome (RLS) is an understudied sensorimotor disorder, the pathogenesis of which remains uncertain. Recent studies have reported impaired psychiatric well-being in persons with RLS, as well as dopaminergic system malfunction as an underlying mechanism for the disorder.

**Methods:** Male veterans 54 to 84 years old were recruited from the Southern Arizona VA Health Care System outpatient clinics in Tucson, AZ. Data collection included demographic information, the Sleep Heart
**SLEEP, Volume 28, Abstract Supplement, 2005**

A270

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**0802**

**Ropinirole Decreases Bedtime Periodic Leg Movements In Patients With RLS: Results Of A 12-Week Us Study**

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**Introduction:** RLS (Ekbom syndrome) is a neurological disorder characterized by distressing sensations in the legs and an irresistible urge to move. The primary morbidity of RLS, chronic insomnia, occurs along with periodic leg movements (PLM) when lying down during the sleep period that represents a motor sign of the disorder. This study assessed the efficacy of ropinirole treatment in the reduction of PLM in patients with RLS.

**Methods:** TREAT RLS US was a multicenter, double-blind, placebo-controlled, phase-III study of ropinirole in the treatment of moderate-to-severe idiopathic RLS (protocol: 101468/249). Patients were randomized (1:1) to receive ropinirole, 0.25-4.0 mg/day once daily 1-3 hours before bedtime, dose titrated to subjective efficacy and tolerability, or placebo for 12 weeks. PLM were measured in all patients for 3 consecutive nights prior to baseline and 6-week assessments; an ambulatory actigraphic device (PAM-RL) was placed on each ankle at least 10 mins before bedtime and removed the next morning. Endpoints included: mean change from baseline in International Restless Legs Scale (IRLS) score at week 12 last observation carried forward (LOCF), and change from baseline in PLM Index (PLMI; number of PLM per hour throughout the night while lying down) and total PLM between baseline and week 6. Only patients with a mean PLMI ≥ 10 at baseline and complete 3 nights' data at baseline and week 6 in at least one leg were included in this analysis.

**Results:** Of the 380 patients included in the intention-to-treat analysis, 187 patients (18-79 years) received ropinirole, mean (SD) dose 2.15±1.18 mg/day. At week 12 LOCF, the IRLS scores were significantly improved in the ropinirole group compared with placebo [-13.5 versus -9.8; adjusted mean treatment difference [AMTD] -3.7; 95% CI -5.4, -2.0; p<0.0001]. The actigraphic analysis included 110 patients receiving ropinirole and 113 receiving placebo. At 6 weeks from study entry, PLMI was significantly reduced with ropinirole compared with placebo (-23.8 versus -9.2; AMTD: -14.5; 95% CI, -20.3, -8.7; p<0.0001), as was total PLM (-199.3 versus -77.6; AMTD: -121.7; 95% CI, 168.0, -75.4; p<0.0001).

**Conclusion:** Ropinirole in doses of 0.25-4.0 mg/day effectively reduces the primary nocturnal motor manifestations of idiopathic RLS (PLMI and total PLM, which have been shown to reflect the severity of the symptoms) in parallel with improvements in the subjective restlessness that accompanies the disorder.

GlaxoSmithKline Research & Development.

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**0803**

**Improvement Of Sleep In Patients With RLS During Treatment With Ropinirole: Results Of A Us Study**

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**Introduction:** RLS (Ekbom syndrome) is a chronic neurological disorder, characterized by sensorimotor symptoms that occur primarily at rest in the evening or at night, and is a major cause of chronic sleep disturbance. Although treatment with ropinirole has been shown to improve RLS symptoms in several controlled trials, this study investigated the effect of ropinirole on the subjective sleep problems and daytime functioning associated with this condition.

**Methods:** Patients with moderate-to-severe idiopathic RLS were randomized (1:1) to ropinirole or placebo for 12 weeks in a multicenter, double-blind, parallel-group US study (TREAT RLS US; protocol 101468/249). Ropinirole was titrated from 0.25 mg/day up to a maximum of 4.0 mg/day until optimal efficacy and tolerability was reached. Changes from baseline to week 12 (last observation carried forward) were analyzed for the International Restless Legs Scale (IRLS) total score, the 12-item Medical Outcomes Study (MOS) Sleep Scale domains of sleep disturbance, sleep quantity, sleep adequacy and daytime somnolence, and the Sleep Problems Index II (a summary score for all sleep domains assessed except sleep quantity).

**Results:** Baseline characteristics of the ropinirole (n=187) and placebo (n=193) groups were similar. At week 12, the mean (±SD) dose of ropinirole was 2.15±1.18 mg/day. Ropinirole treatment significantly improved IRLS score compared with placebo [-13.5 versus -9.8; adjusted mean treatment difference [AMTD] -3.7; 95% CI -5.4, -2.0; p<0.0001]. Ropinirole group showed significant improvements in subjective sleep disturbance [-31.1 vs -20.8; AMTD -10.3, 95% CI -15.0, -5.7; p<0.0001], sleep quantity [36 versus 18 min; AMTD 18 min; 95% CI 6, 30; p=0.0047] and sleep adequacy [20.7 vs 9.3; AMTD 11.4; 95% CI 6, 2.1; 11.7; p=0.0001] compared with placebo. Subjective daytime somnolence was reduced [-15.2 vs -12.1; AMTD -3.1; 95% CI -6.8, 0.6; p=0.0961] with ropinirole treatment. Patients receiving ropinirole showed significant improvements in overall sleep problems on the Sleep Problem Index II [-22.8 vs -14.6; AMTD -8.2; 95% CI -11.9, -4.5; p<0.0001] compared with the placebo group.

**Conclusion:** In this US study, patients with RLS treated with ropinirole had significantly reduced RLS symptoms and significantly improved subjective sleep quantity and quality, including improved subjective daytime functioning.

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**0804**

**Sleep And Sleepiness In Patients With Parkinson Disease Before And After Dopaminergic Treatment**

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**Introduction:** Daytime sleepiness was attributed to nocturnal sleep fragmentation in earlier reports while current debate focuses on the association with dopaminergic therapy.

**Methods:** Fifteen previously untreated PD patients (8 women, 7 men) underwent clinical evaluation, subjective sleep evaluation and polysomnographic evaluation (PSG) before and after a treatment period of mean 8±3.1 months with dopaminergic drugs. Comparisons before and after treatment period for clinical, subjective/ objective sleep variables were done by paired t-test, Wilcoxon signed rank test and McNemar chi-square test. Spearman correlation coefficients were used to measure correlations before and after treatment. Multiple regression analysis were run to evaluate the independent contribution of variables on MSLT and ESS scores in case of differences between 2 time periods.

**Results:** Both mean total score and mean subset III score of the Unified Parkinson Disease Rating Scale (UPDRS) were significantly improved with dopaminergic treatment. PSG revealed that administration of
dopaminergic drugs resulted in significant increase in mean percentage of stages 1 and 2. There were no statistically significant differences in the prevalence of sleep disorders between treatment naive and treatment conditions. No correlations were found between objective/subjective sleep variables and clinical variables before and after treatment. The mean Epworth Sleepiness Scale (ESS) score was significantly increased, and mean Multiple Sleep Latency Test (MSLT) score was significantly decreased after dopaminergic treatment indicating the subjective and objective daytime sleepiness. The variable which attained the best explanation for the MSLT score variability was the L-Dopa dose, whereas other variables such as disease duration, treatment duration, Hoehn and Yahr stage, sleep efficiency index or dopamin agonists did not increase the significance. Any of the variables appeared to explain ESS score variability.

**Conclusion:** This study demonstrates that daytime sleepiness is not present in untreated patients but emerges later during dopaminergic treatment. Total daily L-dopa dose is predictive of objective daytime sleepiness.

### 0805

**Treatment Of RLS/PLMS And RBD With Cabergoline As A Single-Drug Night Treatment**


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**Introduction:** Cabergoline is a synthetic ergoline derivative acting as a selective D2-receptor agonist that proved effective in the treatment of idiopathic RLS. A single evening dose (0.5-2 mg) may be efficacious because of its elimination half-life of about 65 hour, the longest half life of all registered dopamine agonists. It has been so far more controversial whether and how to treat PLMs alone or in the context of other movement disorders such as Parkinson or RBD

**Methods:** Following all night polygraphic recording, we decided to treat 12 patients (4 F and 8 M, mean age 56,08, range 41-77) with PLMS (mean index 66, range 17-163). 3 patients had associated RLS, 4 had clinical/polygraphically confirmed idiopathic RBD, 2 had moderate OSAS. Sleep was discontinuous in all patients with low sleep efficiency (mean 75%, range 45-90%). 7 patients complained of EDS that was severe only in the patients with associated OSAS. Patients received a baseline evaluation with chest X-Ray and echocardiography prior to treatment initiation. They all were instructed to take 0.5 mg of Cabergoline 2 hours before bedtime, with an upwards titration of 0.5 mg at a time until the desired effect was reached, to a maximum of 2 mg. After 1 month and at 3 months the clinical global impression was assessed, including the RLS study group rating scale during an office check-up. Instrumental re-evaluation by means of actigraphy at 6 months is being currently achieved.

**Results:** 9 of 12 patients showed consistent improvement (>70%) on clinical global impression, also reporting improvement of sleep continuity, SL, EDS and quality of life. Cessation of violent behaviour during the night was reported by bed partners for all RBD patients. 3 patients (2 with associated OSAS and 1 hypothyroid lady with substitute therapy, with PLMs only) were mildly improved or almost unaffected. No side effects, including augmentation, were reported with the exception of mild asthenia in one subject. At 6 months, baseline XRs and echocardiograms were unmodified. Maximum dosing reached by all patients was 1 mg. Mean follow-up is so far 8,7 months (range 6-13) and complete data from actigraphic reevaluation at 6 months will soon be available.

**Conclusion:** A single night dose of Cabergoline (0.5-1 mg) proves beneficial and safe in the treatment of RLS but also PLMs and idiopathic RBD. PLMS with associated OSAS did not seem to benefit from the treatment although actigraphic re-evaluation might prove a decreased nocturnal activity.

### 0806

**Successful Use Of Botulinum Toxin A For The Treatment Of Restless Legs Syndrome: A Case Series**

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**Introduction:** Injected Botulinum Toxin A (BTXA) has been used to treat movement disorders associated with discomfort, such as tics and dystonia. We report the effective use of injected botulinum toxin A to treat restless legs syndrome(RLS). In a series of three patients, BTXA alleviated symptoms, reduced medication use and/or reduced daytime sleepiness with minimal, if any, untoward effects.

**Methods:** Observational. We identified three, otherwise healthy, adult patients in our clinics with RLS who were refractory to or refused oral medication. Informed consent was acquired for this novel, off-label application of FDA-approved BTXA. Areas of maximal discomfort were identified and injected with BTXA as described below.

**Results:** Patient #1, a 58 year-old male with refractory RLS, was injected into each tibialis anterior muscle in 2 injections. His Epworth Sleepiness Scale dropped from 10 to 6. The effect persisted for twelve weeks after injections. He stopped neurontin and the height of effect. He experienced a mild decrement in his timed run. Patient #2, a 38 year-old male with RLS on multiple medications this disorder, received bilateral intramuscular BTXA injections in his lumbar paraspinal muscles, gastrocnenmii, and quadratus femoris. Three days after injection, he reported great improvement. Within one month, his Epworth Sleepiness Scale dropped from 19 to 5. He stopped oral therapy during the period of maximal effect. There were no untoward effects, and the response was repeated after 12 weeks. Patient #3 was a 38 year-old woman who reported nightly uncomfortable sensations in her calves causing restless and a subjective sleep latency of 90 minutes. She refused oral treatment. BTXA was administered in the gastrocnemii. In 2 days, her discomfort reduced from a 10/10 to a 3/10 and her subjective sleep latency was 15 minutes. Her urge to move and nocturnal restless resolved. Both her RLS symptoms and nocturnal restless recurrence 10 weeks later. There were no untoward effects and the response was repeated with successive injections.

**Conclusion:** Intramuscular BTXA injections caused a significant improvement in RLS symptoms and/or a reduction in medication usage. BTXA was well tolerated. The course of response corresponded with its typical course of efficacy in other disorders. BTXA should be further investigated in controlled studies as a potential treatment of RLS.

The opinions are those of the authors and do not express those of the Army, Air Force of the Department of Defence.

### 0807

**Nonlinear Dynamics In Periodic Leg Movements In Sleep**

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**Introduction:** Periodic Leg Movements (PLM) are defined as stereotyped periodic dorsiflexions of the ankle with distinct strength and pattern. However, recent studies demonstrated that PLM occur with variable and often unpredictable amplitude and periodicity in patients of all age groups, with or without antidepressant therapy and upper airway obstruction. Complex behaviors of PLM permit assumption that pertinent data may represent strange attractor or other chaotic system. The goal of this study was to test this assumption.

**Methods:** 54 polysomnograms of the patients with PLM index >50/hr
and RDI<10/hr were analyzed. ASCII files of 140 to 500 data points were created using 20 to 125 minutes of PLM tracing in all sleep stages with sufficient stationarity of EEG. The intervals (in sec.) between bursts of tibialis EMG activity were processed using professional version of Chaos Data Analyzer (J. Sprott and G. Rowland, 1995).

Results: Time-series analysis revealed broad power spectra with few dominant frequencies and fixed points. Integrated data produced Hurst exponents with persistence (H =0.71 - 0.98). Most positive Lyapunov exponents reached value of 0.3 to 1. When embedding dimension was increased, the capacity dimension (CD) and correlation dimension (D2) also increased but saturated with plateau at correct value (CD = 1.2 ± 0.15 - 2.05 ± 0.31 and D2 = 2.4 ± 0.65 - 4.8 ± 0.95). The phase-space plots, stereoscopic views and return maps demonstrated discernible pattern characteristic of chaotic and sometimes quasi-periodic dynamics. Comparison with surrogate data confirmed statistical significance of the above-mentioned findings.

Conclusion: Time-series analysis of PLM was performed for the first time and demonstrated nonlinear dynamics in behavior of PLM in sleep. The bifurcations with transitions from isolated bursting to doublets and quartets are consistent with deterministic chaos. Methods from non-linear system theory may improve upon analysis and definition of PLM based on traditional linear approach.

Augmentation During Long-Term Treatment With L-DOPA In Restless Legs Syndrome: Results Of A Multicentric Study In Europe

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Introduction: L-DOPA has been extensively used for the treatment of Restless Legs Syndrome (RLS) over many years and remains as the only approved drug in some countries. Although several controlled studies have shown that L-DOPA is therapeutically effective, its main limitation is the occurrence of augmentation (AUG) in the course of long-term treatment. However, most of the evidence is based on retrospective analyses of case series without a common definition of augmentation. In order to evaluate the incidence and clinical characteristics of augmentation, the European Subgroup of the International Restless Legs Study Group has performed a multicentric, prospective study on long-term L-DOPA treatment.

Methods: The study included untreated patients diagnosed with RLS according to NIH criteria and was performed across 6 European countries. Diagnostic procedures consisted of a medical history, laboratory diagnosis and medical evaluation. Patients were treated with an initial dosage of 100/25mg L-DOPA/benserazide (as monotherapy). Clinic visits were performed every week for the first month, and monthly thereafter, and involved systematic assessments on RLS severity (IRLS, RLS-6, CGI), augmentation, and safety measures. AUG was defined as established by NIH-criteria. During each clinic visit, the dosage of L-DOPA was adjusted according to clinical needs. The study was approved by the Institutional Review Board of all centers, and informed consent was obtained from all patients.

Results: Thirty four patients were included in this preliminary analysis; 15 completed the six-month trial and 19 dropped out. AUG occurred in 17 out of 34 patients (50%). Among those that dropped out, AUG occurred in 68.4%, and was the main reason for discontinuation in 36.8%. AUG developed within the first two months in 52%, and within the third month in 76%. The mean dose of L-DOPA was 317 mg/d (SD: 111). However, 88% of AUG had dosages of L-DOPA superior to 300 mg/d. The mean (SD) dosage in patients undergoing AUG was 369 (80) mg/d, against 272 (124) mg/d in Non-AUG. AUG developed within two weeks of the last dose increase in 73% of patients. No relationship could be seen between RLS severity at baseline and propensity to AUG.

Conclusion: Preliminary results suggest that in the course of a six-month treatment period with L-DOPA, AUG occurred 50% of patients. AUG was more frequent when dosages were higher than 300 mg/day and developed in 50% of the cases within the first two months of treatment.

The study was supported by European Subgroup of the International Restless Legs Study Group and was performed with help of an unrestricted grant form Pfizer, Corp.

Opiates For RLS: Assessing Benefit Vs. Risk

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Introduction: Opioid agents for restless legs syndrome (RLS) prove particularly beneficial in patients who have failed or experienced complications from dopaminergic and gabaminergic therapies. Risk of opiates include the serious side effects of addiction, respiratory depression, exacerbation of sleep disordered breathing, constipation/emesis, excess sedation, and withdrawal reactions. A study was conducted to test a clinical model to assess the benefit-to-risk ratio (BRR) of opiates in 24 severe RLS patients.

Methods: The BRR was designed to measure benefit against risk of opiates in RLS patients. The pain literature was used to develop the specific agent property score (SAPS) that is based upon the likelihood of serious side effect multiplied by codeine equivalency. BENEFIT: numerator consists of: (1/IRLS scale score) X 80 + (1/Sleep Latency minutes) X 100 + (ESS/6) X 2 + # observed side effects + (SAPS X milligram dose)/200 + (5-point snoring level to indirectly measure SDB) x 2. Group mean BRR was calculated in the 24 patients (F=13, M=11; age: 57.2 yrs) who took five opiates (SAPS rating): [hydrocodone (20.0), hydromorphone (186.7), levorphanol (400.0) and methadone (70.0), propoxyphene (5.42)].

Results: Propoxyphene (N = 8 patients treated with propoxyphene) produced a mean OTI = 0.843. Hydromorphone (N = 11) had a mean OTI = 0.944. Hydrocodone (N = 11) produced a mean OTI = 1.040. Methadone (N = 7) showed a mean OTI = 1.125. Levorphanol (N = 18) had a mean OTI = 1.197.

Conclusion: Levorphanol and methadone cause more side effects but are more effective than propoxyphene and hydromorphone in improving the IRLS scale, sleep latency and sleep time. Hydrocodone is intermediate in its benefit-risk. BRR >1 indicates greater benefit than risk of opiate therapy and can be applied to both individual RLS patients and groups.
Restless Legs Syndrome (RLS) is characterized by an urge to move the legs, worse at rest and at night, and relieved by movement. It can be primary or associated with conditions such as iron deficiency, peripheral neuropathy (PN) and metabolic disturbances (diabetes, uremia, magnesium deficiency, hypercalcemia). While there is no cure for primary RLS, secondary cases may resolve after treatment of the underlying disorder. There are no established guidelines for the laboratory evaluation of RLS. In view of the wide range of metabolic derangements that can cause secondary RLS (including PN), a cost effective approach is needed. This is a study of the value of routine laboratory studies in RLS.

**Methods:** Adults meeting the International RLS Study Group criteria for RLS were recruited over 2 years. Subjects had complete blood count, ferritin, urea, creatinine, electrolytes (Na+, K+, Ca2+), random glucose, albumin, acute phase reactants, PN or renal impairment. RLS severity scores ranged from 2-38/40 (mean 23.6). Ferritin levels were obtained in 80 patients. Of these, 32 (40%) had values below 50 ug/L, and only 4/32 had low hemoglobin (Hb) and hematocrit (Hct) levels. All 4 had very low ferritin levels(one 20 ug/L, the rest 5-6 ug/L). None of the 82 patients tested had abnormal urea,creatinine, Na+ or K+ levels. Only 4 had elevated or borderline Ca2+ levels. Only 2 of 75 patients tested had abnormal urea,creatinine, Na+ or K+ levels. Only 4 had elevated or borderline Ca2+ levels. Only 2 of 75 patients tested had abnormal urea,creatinine, Na+ or K+ levels. None of the 69 patients tested had paraproteinemia. Vitamin B12 levels were borderline in 2 of 78 patients, neither had known predisposing conditions nor clinical/EMG evidence of PN. All 49 patients tested had normal folate levels. None of the 82 patients tested had abnormal urea,creatinine, Na+ or K+ levels. None of the 82 patients tested had abnormal urea,creatinine, Na+ or K+ levels. None of the 82 patients tested had abnormal urea,creatinine, Na+ or K+ levels.

**Conclusion:** We sampled a range of mild to severe primary RLS patients. Laboratory studies showed clinically significant decreased ferritin levels in 40% of patients. Calcium and TSH derangements were found mainly in patients who also had other suggestive clinical features. Urea, creatinine, Na+, K+ and folate levels were normal in all the patients tested. These findings suggest a role only for routine screening ferritin levels in suspected ‘primary’ RLS patients, Hb/Hct levels were not helpful. Other metabolic studies are indicated only if there are other clinical features to suggest derangement.
0813
Validation Of An Algorithm For The Diagnosis Of The Restless Legs Syndrome (RLS): The Restless Legs Syndrome Diagnostic Index (RLS-DI)
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Introduction: With the RLS-DI, clinically relevant diagnostic criteria of the International RLS Study Group for RLS (n=10) are weighted differently according to their presence or absence in an individual patient and summarized in the RLS diagnostic index score. The RLS-DI (range −25 to +20) was developed to classify the probability of the RLS diagnosis: scores 16 to 20 indicate definite RLS, 10 to 15 highly probable RLS, 4 to 9 possible RLS, 1 to 3 unlikely RLS, 0 to −25 no RLS. The RLS-DI and its cut-offs had been established according to clinical experience. Data from a first validation study of the RLS-DI are presented.

Methods: From the cohort of all patients who were evaluated in our sleep laboratory during the years 2003 and 2004, those patients were invited to participate in a telephone interview who had a final diagnosis of either RLS or any other disease (OTH) with at least partly similar symptoms like RLS patients (insomnia, polyneuropathy, or psycho-reactive sleep disorder). During the interview, the RLS-DI and the IRLS severity scale were completed. A cut-off score of RLS-DI≥+10 identified patients with an at least probable diagnosis of RLS. Sensitivity and specificity were calculated using the final primary diagnosis of one sleep laboratory expert as validation criterion.

Results: N=37 patients with RLS and n=35 with OTH were interviewed. Both groups differed in the RLS-DI score (+16.5±3.1 vs. −12.0±6.0, p<0.001) and in the IRLS total score (30.6±6.3 vs. 5.1±12.6, p<0.001). Sensitivity of the RLS-DI was 100% and its specificity was 91.4%. In 3 false positives of 35 OTH patients, secondary or intermittent RLS was reported as comorbidity.

Conclusion: The RLS-DI is a valid and easy to use method to assure or exclude the diagnosis of RLS, according to very favorable results of this validation study.

0814
Disruptive Periodic Limb Movements And Functional Outcomes
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Introduction: Overall there is limited data on the impact of sleep disorders on daily functional abilities. The Functional Outcomes of Sleep Questionnaire (FOSQ) is a beneficial tool among disorders of excessive sleepiness. Due to a lack of data on the functional effect of disruptive periodic limb movements (PLM’s), our objective was to determine the impact among this population.

Methods: We retrospectively recruited patients that underwent a polysomnogram (PSG) recording at our facility from June - December 2004 without a diagnosis of obstructive sleep apnea. We limited our sample to patients with available demographic data, sleep variables including: total sleep time (TST), sleep efficiency index (SEI), apnea/hypopnea index (AHI), arousal index (AI), arousal for no apparent reason (AFNAR), periodic limb movement index (PLMI), a periodic limb movement arousal index (PLMAI) greater than 5.0, and complete Epworth Sleepiness Scale (ESS) and Functional Outcomes Questionnaire (FOSQ). Scoring criteria for PLM’s was consistent with the Atlas Task Force.

Results: Among our sample (n=41) the distribution of ESS scores were divided into two groups based upon the median, scores below the median constituted the control group (mean= 5.3± 2.3) and scores above the median constituted the sleepy group (mean 12.6± 3.0). Patients were equally distributed among the two groups in respect to age, sex, and sleep variables. We found a significant difference among the control and sleepy group in regard to the activity (p<0.05) and vigilance (p<0.001) FOSQ subscales.

Conclusion: Although we did not observe a significant difference in the FOSQ global score, mean group scores studies suggest that sleepy patients tend to have more functional impairment as opposed to the control group. This possibly indicates that arousals associated with PLM’s may have a deleterious effect upon functional ability. Further investigations with larger sample size would be beneficial in investigating this effect.

0815
A Segregation Analysis Of The Restless Legs Syndrome (RLS) Based On Age-Of-Onset Models
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Introduction: Familial aggregation has long been suspected in RLS, but has received little formal investigation. A segregation analysis done in Germany found a successful fit for a major gene model with dominant inheritance, but only in families having an average age of onset below 30 (Winkelmann et al., 2002). 3 candidate loci have been reported on different chromosomes in distinct populations using different techniques and models. We have now investigated segregation in the families of RLS patients enrolled in a case-control family study that used blinded diagnoses of affected status.

Methods: Probands were consecutive RLS patients presenting to the Neurology and Sleep clinics at Johns-Hopkins Bayview who were willing to have first- and second-degree relatives contacted. An RLS diagnosis was made in those who endorsed the four diagnostic features of RLS and whose symptoms could not be explained by an alternate diagnosis. Those with uncertain diagnoses were excluded from analysis. 77 pedigrees were analyzed with 590 phenotyped subjects including 281 diagnosed with RLS. A conomming analysis was done to determine if there was more than one distribution of ages-of-onset in subjects with RLS. The patterns of inheritance of RLS were examined using RLS as a dichotomous trait and also using age-of-onset models in segregation analyses carried out using the REGD and REGTL subroutines in SAGE 3.1, respectively.

Results: The conomming analysis found two distributions of ages-of-onset: ages-of-onset below 26.35 were more likely to fall into an early distribution. Results of the REGD and REGTL models suggest that neither purely environmental nor major gene models fit these pedigrees.

Conclusion: Our results are consistent with an important genetic contribution to development of RLS, but suggest that the underlying genetic model may be polygenic. Consistent with the three loci previously reported for this disorder, it is likely that multiple susceptibility alleles will be found whose importance may vary in different populations.

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0816

Actigraphy For Plm Detection - The Effect Of Threshold Setting On PLM Indices

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Introduction: Actigraphy is increasingly used to detect periodic leg movement (PLM) in patients with Restless Legs Syndrome (RLS). The aim of this study was to investigate the relation between PLM counts obtained by actigraphy with three different threshold settings compared to polysomnography (PSG) according to standard criteria.

Methods: 10 patients (mean age 60.9 ± 12.0 years) with a PLM index (PLMI) > 5 per hour in a previous polysomnography underwent simultaneous actigraphy from both legs (PAM-RL with Software Version 7.5.3, IM Systems). For analysis, PSG and actigraphy were displayed in simultaneous 1 minute windows. In PSG, PLM were manually counted according to standard criteria. Actigraphic PLMIs were obtained for time in bed. The On-Off threshold, the factor to translate the PLM count to acceleration units, was set at 160/100 (default), 120/80 and, manually and individually on the basis of a typical PLM for each patient.

Results: The polysomnographic PLMI was 37.0 ± 30.7 PLM/hour (h); the actigraphic PLMI with default threshold 160/100 was 63.6 ± 39.3 PLM/h, with 120/80 71.0 ± 43.1 PLM/h and individually for each patient 44.9 ± 27.6 PLM/h. The difference between PLMIs derived from actigraphy with the threshold 160/100 (p=0.009, Wilcoxon test) and 120/80 (p=0.005, Wilcoxon test) and PLMIs in PSG was significant, whereas with individual and manual threshold setting it was no longer significant (p=0.074, Wilcoxon test). Correlation between all 3 threshold setting was high (Spearman's r=0.939, p<0.001).

Conclusion: Actigraphy overestimated PLM in comparison with PSG, but threshold settings of the actometer influenced significantly the results. The most reliable results were obtained for actigraphy with manual threshold setting for each individual patient.

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0817

Management Of RLS Augmentation By Levodopa Withdrawal — A Case Report

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Introduction: Augmentation is defined as earlier onset and/or increased severity of symptoms in RLS patients on dopaminergic treatment (Allen R, 2003).

Methods: A 65 year old women was referred for severe RLS refractory to treatment. Most severe RLS symptoms were present throughout the day and the night, despite around-the-clock levodopa dosing (1200 mg/d). The patient had been pretreated with levodopa for 18 months. The initial dose was 200 mg, but gradual dosage increase had occurred, because of progressive shortening of effect, and earlier onset of symptoms. During levodopa withdrawal and switch to pramipexole, three consecutive nights of polysomnography (PSG) were performed and a modified IRLS applied (Walters AS, 2003).

Results: Levodopa was suspended 14 hours before PSG, and clonazepam 0.5-1 mg administered on demand. In the first night, PSG showed a severely reduced sleep efficiency (66.4%). Night sleep was interrupted by 5 prolonged wake episodes, with body rocking and waking around. PLMS were present during the whole night (PLMS index > 50/h). Two days later, pramipexole 0.35 mg was instituted at bedtime. Sleep efficiency was 82.6%, and PLM index below 5/h. The IRLS primarily increased from 32 at presentation, to 39 during withdrawal, and subsequently fell to 3 after withdrawal and switch to pramipexole.

Conclusion: Levodopa withdrawal led to a brief exacerbation of symptoms, which was partially covered by administration of clonazepam and physical countermeasures. Two days after withdrawal, dopaminergic treatment was reassumed with pramipexole on a once-daily basis and at a low dose, with very good success. This case supports the contribution of pharmacodynamic mechanisms in augmentation of RLS. It demonstrates that withdrawal of dopaminergic substances is essential in its management, and treatment should be re-instituted at much lower dose levels. In some patients, switch to opioids will be necessary (Allen R, personal communication).

0818

Peak Circadian Occurrence Of PLMS During The Biological Nighttime

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Introduction: Periodic leg movements of sleep (PLMS) are characterized by repetitive, stereotyped movements, usually in the beginning of the night. The related movement disorder Restless Legs Syndrome (RLS) has been shown to have a circadian pattern of expression. To assess whether PLMS truly exhibit a circadian pattern, we conducted a study in which sleep was scheduled at all circadian phases after a similar duration of wakefulness.

Methods: We studied 3 healthy subjects with PLMS (PLMI 28-56) in a month-long circadian rhythm study. After 3 baseline nights, subjects lived on a 20-h “day” for 30 cycles (26 calendar days). Each scheduled sleep episode lasted 6.7h, following 13.3h awake. On 12 of the 30 nights, subjects received melatonin before lights out. Melatonin data remain blind. Sleep was polysomnographically recorded, including left and right anterior tibialis EMG. The circadian period of each subject and the circadian phase of each epoch of sleep was assessed using core body temperature, and we then analyzed the sleep and leg movement data in 8 circadian phase bins of ~3 h.

Results: We restricted our analysis to Stage 2 sleep, with >24,000 epochs of Stage 2 averaging >1000 epochs at each of the 8 circadian phases (579-1718 epochs/circadian phase/subject). PLMI per hour of Stage 2 varied significantly with circadian phase in all subjects (p<0.01). The pattern of circadian variation was similar across subjects, with fewest leg movements during the phases corresponding to late morning/early afternoon under entrained conditions and most during the phases corresponding to biological nighttime.

Conclusion: We observed a significant, consistent, circadian rhythm in PLMS per hour of Stage 2 sleep with a peak during the biological nighttime, a pattern consistent with RLS symptoms recorded during sleep deprivation. Together, these studies suggest an underlying circadian component contributing to both movement disorders. While this pathophysiology remains unknown, circadian rhythms of dopamine may play a role.

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Insomnia and Daytime Sleepiness: Risk Attributable To RLS And Behavioral Factors In A Community Sample

**Introduction:** Insomnia, daytime sleepiness, and Restless Legs Syndrome (RLS) are common complaints which may be impacted by personal behavior. The goal of this research was to estimate the prevalence of insomnia, daytime sleepiness, and RLS; and the proportion of insomnia and sleepiness which are attributable to RLS or behavioral factors in a representative community based sample.

**Methods:** Using random digit dialing techniques, a cross-sectional telephone survey was conducted in five N.E. Ohio counties. The survey included measures of insomnia, day time sleepiness, RLS, behavioral factors (smoking, alcohol, caffeine, exercise, obesity), use of health services, and diagnosis of sleep complaints.

**Results:** The response rate among eligible respondents was 32%. The mean age for the 202 respondents was 67 and 63% were female. The prevalence of moderate or severe insomnia was 10%, severe daytime sleepiness was 33%, and RLS was 14%. Thirty-five percent of respondents had a BMI over 30. For insomnia, the attributable risk (AR) for BMI > 30 = 53% (p<.0001); the AR for evening caffeine consumption = 20% (p = 0.06); and for severe RLS = 10% (p = .04). For daytime sleepiness, the AR for male gender = 40% (p<.0001); for severe insomnia = 12% (p=.0004); and for RLS = 11% (p=.03). Other behavioral factors were unrelated to sleep complaints. All those with severe insomnia had sought medical help; 83% reported receiving a diagnosis or treatment. Thirty-six percent of those with severe daytime sleepiness had sought help; 24% reported a diagnosis or treatment. Fifty percent of those with RLS had sought help; 29% reported a diagnosis or treatment. While 10 patients reported a diagnosis of sleep apnea, no patient reported a diagnosis of RLS.

**Conclusion:** Attributable risk, which combines risk factor prevalence with relative risk, illustrates the relative contribution of obesity, gender, and RLS to insomnia and daytime sleepiness.

Supported by a Research Challenge grant from the Ohio Board of Regents.

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**Evaluation Of The Periodoc Led Movement Index After Maximum Effort Test**

**Introduction:** Periodic leg movement (PLM) is defined as the occurrence of periodic episodes of repetitive and highly stereotyped limb movements during sleep. Interventions not pharmalogics are an alternative for the best one in the quality of the sleep. Most studies regarding exercise and sleep have been concerned with the influence of exercise on sleep architecture and efficiency, and not on its effects in the prevention and treatment of sleep disorders. The aim of our present study was evaluate to incidence of PLM after a maximum effort test.

**Methods:** Twenty-one patients (13 women, 8 men) with index of PLM ≥5h, were submitted to two Polissonografy: baseline and night after the maximum effort test. After baseline PSG, the volunteers were tested in a cycle ergometer. The test followed the sequence of 3 minutes of rest on the cycle ergometer, followed by increments of 25Watts every 2 minutes. The parameters of sleep evaluated were Total Sleep Time (TST/min), Total Wake Time (TWT/min), Total Slow Wave Sleep (SWS/min), REM sleep (min), Sleep Latency (SL/min), Number of Arousal (NA), index of Periodic Leg Movements (PLM/h), among others.

**Results:** The results found in the night after the maximum effort test demonstrated increase of the TST of 310,05 for 351,05 (p≤0,01), REM of 57,23 for 71,73 (p≤0,01) and decrease of PLM/h 44,46 for 27,78 (p≤0,05).

**Conclusion:** Our results suggest a decrease in the index of PLM after maximum effort test with improvement in the quality of the sleep and an increase in the REM. The REM increase itself could be related to a better consolidation of sleep due to the decrease of the index of PLM.

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**Polysomnographic Evaluation Of Idiopathic Restless Legs Syndrome Patients:**

**Introduction:** Insomnia and daytime sleepiness are common among patients with Restless Legs Syndrome (RLS). The goal of this research was to estimate the prevalence of insomnia and daytime sleepiness, and to estimate the contribution of RLS and other behavioral factors to these complaints in primary care patients.

**Methods:** Telephone interviews were conducted with 1761 patients recruited at 12 VA primary care clinics in Ohio. Measures of RLS, insomnia, daytime sleepiness, alcohol dependence, smoking and BMI were included. Logistic regression was used to obtain odds ratios that were used with risk factor prevalence to estimate attributable risks (AR).

**Results:** Patients were aged 22 to 92. Eighty percent of the sample were male, 41% had a BMI of 30 or over, and 46% had post high school education. The prevalence of RLS symptoms at least once per week was 21% for women and 13% for men. Moderate or severe insomnia was more common in women (27% compared to 14% for men). Both genders had a 7% prevalence of daytime sleepiness. In predicting insomnia, the attributable risk was 22% (p<.0001) for RLS, 27% (p=.003) for a BMI of 30 or over, 4% (p=.007) for alcohol dependence, and 6% (p=.12) for smoking. In predicting daytime sleepiness, the AR for insomnia was 28% (p<.0001) and 7% (p=.006) for RLS. Obesity, smoking, and alcohol dependence did not have a significant relationship to daytime sleepiness beyond their effects on insomnia. Only 10 of the 243 patients who reported RLS symptoms had been diagnosed with RLS.

**Conclusion:** RLS, obesity, alcohol dependence, and gender, are significant risk factors for insomnia. Insomnia, in turn, is a significant risk factor for daytime sleepiness. RLS is a significant risk factor for daytime sleepiness, even after controlling for insomnia. Despite the impact of RLS on insomnia and daytime sleepiness, few patients are diagnosed with RLS by their physicians.

This research was supported by DAMD17-03-1-0082 from the US Army Medical Research and Materiel Command and an unrestricted grant from Pfizer Pharmaceutical Corporation.
Introduction: low doses of pramipexole are a well known treatment for RLS. Aim of our study was to evaluate the first night effect of a single dose of pramipexole in consecutive patients affected by idiopathic RLS that never received dopaminergic treatment before.

Methods: patients underwent the following: clinical evaluation, visual analogical scale (VAS) for RLS symptoms, hematological screen, ENG/EMG examination, and two consecutive nights of full-PSG (first night=baseline; second night=treatment). Only patients who met the international diagnostic criteria for RLS and with a PLMS index greater than 10 as well as an RLS rating scale greater than 25 were included. Before the second night, all patients received at 9.00 pm the same dose of pramipexole (0.25 mg).

Results: 16 patients (mean age 61.4 SD 12.2, M/F=4/12) were included. In all patients RLS symptoms subjectively improved after the first night of treatment (VAS). No significant differences between the baseline and the treatment nights were observed in: sleep latency (33 SD 38 min vs 19 SD 26); total awakenings (16 vs 19); % of S1 (5.4 SD 3.4 vs 4.4 SD 3.1), S2 (62.1 SD 15.9 vs 62.9 SD 12.1), SWS (16.5 SD 9.1 vs 16.1 SD 8.8), REM (15.6 SD 8.8 vs 16.6 SD 5.8); and REM latency (150 SD 67 min vs 154.1 SD 108). Significant differences were observed in: WASO (168 SD 92 min vs 61 SD 37, p<0.05), sleep efficiency (55.8 SD 22.5 vs 76.8 SD 14.3p<0.005) and total sleep time (299 SD 65 min vs 394 SD 65, p<0.05), PLMS index dropped from 70 SD 23 to 12 SD 23 (p<0.001). PLMS index dropped from 70 SD 57 to 12 SD 23 (p<0.001). PLMS index dropped from 70 SD 57 to 12 SD 23 (p<0.001).

Conclusion: single low doses of pramipexole in RLS naive patients improved symptoms and sleep parameters, already after one night of treatment. Moreover, pramipexole determined a significant drop of PLMS, without a significant change in the CAP rate. However, pramipexole seems to induce, as possible acute effect, a relative REM and slow wave sleep inhibition.

References


0823 Results From The First Active Controlled Trial To Investigate Efficacy Of Cabergoline Compared To Levodopa In The Treatment Of Patients With Severe Restless Legs Syndrome

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Introduction: The dopamine agonist cabergoline was compared to levodopa as therapy for RLS in a double-blind, multi-center efficacy trial. The aim was to demonstrate (a) non-inferiority in symptom relief of the DA cabergoline (CAB) compared to levodopa / benserazide (LEV) after 6 to 8 weeks of short-term treatment and (b) superiority of CAB over LEV after 30 weeks of long-term therapy with respect to discontinuation from treatment due to lack or loss of efficacy or augmentation.

Methods: Methods: Patients with idiopathic RLS were treated with fixed daily doses of 2 mg CAB or 200 mg LEV; in the event of insufficient efficacy after six weeks, dose was increased to 3 mg CAB or 300 mg LEV. Efficacy was assessed by changes in the IRLS total score from baseline to week 6 or 8 to evaluate non-inferiority of CAB versus LEV; the non-inferiority margin was set to be more than 3 points. For long-term superiority evaluation, time to discontinuation of treatment due to lack/loss of efficacy or augmentation according to investigators assessments was analyzed.

Results: The adjusted mean change from baseline in IRLS sum score in the short-term period was d= less than 16.4 in the CAB group and d= less than 10.1 in the LEV group. The 95% confidence interval of the adjusted mean difference between both treatments at the end of the short-term period, [-8.4; -4.3, point estimate:-6.4] demonstrated not only non-inferiority, but also a clinically significant superiority of CAB over LEV (p<.0001). During the total treatment period of 30 weeks, more patients of the LEV group (24.0%) than of the CAB group (11.9%) discontinued due to lack/loss of efficacy or augmentation (p=0.0029, log-rank test, Wilcoxon scores).

Conclusion: This first large-scale active controlled study in RLS showed superior efficacy of cabergoline versus levodopa after short- and long-term therapy. Discontinuation from treatment due to loss of efficacy or augmentation less frequent under cabergoline than under levodopa. Cabergoline again demonstrated its favorable efficacy in the treatment of RLS with a low risk for augmentation or inefficacy. For levodopa, the rate of augmentation or poor efficacy over a 30-week period was surprisingly low (24%) in this active controlled double-blind comparative trial.

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0824 Population-Based Confirmation Of The 12q RLS Locus In Iceland

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Introduction: Restless Legs Syndrome (RLS) affects 5-10% of the US and European populations is associated with poor general and mental health, and negatively impacts upon sleep and daytime alertness. Epidemiologic and genetic linkage studies demonstrate that genetic factors contribute to RLS. Identification of genes that contribute to RLS would therefore have an enormous impact on its understanding and treatment.

Methods: We enrolled 1257 Icelanders, 559 of whom endorsed 4 consensus RLS criteria (RLS4 group). Complete phenotypes that include nocturnal periodic leg movement counts are available for 795 subjects of whom 488 are classified as positive or probably positive for RLS (PLM group). All affecteds and some of their family members have been genotyped with a 1100 marker microsatellite set.

Results: Classification as PLM-positive was excellent at discriminating real RLS: 98% positive predictive value, 97% specificity, and 73% sensitivity. Multiple regression analysis demonstrated that PLMi > 10 was a predictor of true RLS (OR= 29.7; 95% CI 3.4-255.5). 382 of the RLS4 patients cluster in 126 families. Genome-wide linkage revealed a LOD score of 2.4 on chromosome 12 at the same locus previously reported in a French-Canadian family. Using PLM criteria to define affected status yielded 328 patients in 108 family clusters (including 2nd cousins). A genome-wide scan with these families revealed a linkage peak on 12q that coincided with the RLS4 peak (LOD = 3.9; p-value of 1.02 x 10-5, Zln 4.25) that increased to 4.2 with additional markers, thereby surpassing Lander-Kruglyak criteria for genome-wide significance (p = 4.76 X 10-6, Zln 4.427).
RS Foundation

0825
Management Of Augmentation In Patients With Restless Legs Syndrome

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Introduction: Dopaminergic therapy is the treatment of first choice in patients with restless legs syndrome. However, the most important adverse event in longterm treatment with either levodopa or rarely dopamine agonists (DA) is the occurrence of augmentation. Augmentation is defined as an earlier onset of RLS symptoms during the day, a possible involvement of other body parts and an increased severity of symptoms (Allen et al, Sleep Med 2003; 4:101-119) after the beginning of a dopaminergic medication in RLS patients.

Methods: Within 6 months we collected data of consecutive RLS patients with augmentation, who were admitted as inpatients to our hospital because of severe augmentation. Demographic and clinical data, laboratory tests, RLS severity, treatment regimen and treatment outcome were documented.

Results: 24 patients with idiopathic (n=17) and secondary (iron deficiency; 5; polyneuropathy and diabetes: 2) RLS (18 f; 6 m; mean age: 65.0 years; range: 42-82) were admitted with a disease duration between 1 and 55 years (mean: 15 years). All patients fulfilled the criteria of augmentation (Allen et al 2003), severity of RLS was greater than 30 on the IRLS (RLS severity scale), and had received either levodopa monotherapy (n=21) at a mean dosage of 567.5mg (range:100 to 1500mg), pramipexole monotherapy (n=1; dosage: 0.77mg), pergolide monotherapy (n=1; dosage: 2mg) or a combination of pramipexole levodopa (n=1), 3 patients took additional opioids. In all patients earlier switches of medication have failed. The agent, that caused augmentation was immediately stopped by hospital admission in 20 patients, in 4 patients the dosage was tapered down for 3 days, all patients were offered soluble opioids (tildine or tramadol) on demand. In 15 patients levodopa was replaced by a dopamine agonist, 7 patients needed a combination treatment of a DA plus an opioid, 2 patients received other medication (i.e. iron because of severe iron deficiency; DA opioid benzodiazepine because of benzodiazepine use). The outcome after 2 weeks was estimated as very good (n=11), good (n=10) and was still pending in 3 patients according to patients opinion.

Conclusion: Augmentation can become a severe problem requiring hospital admission and cessation of levodopa or DA therapy. Some patients could not be treated sufficiently with dopamine agonist monotherapy after being augmented and needed additional opioids.

0826
Racial And Ethnic Patterns In Patients Diagnosed With Restless Legs Syndrome (RLS)

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Introduction: It is commonly reported that RLS patients are overwhelmingly Caucasian. Despite obvious genetic and social significance there has been no prior documentation of the racial features of RLS patients.

Methods: A consecutive case series of patients diagnosed with RLS at a sleep-disorder outpatient service was evaluated for racial-ethnic characteristics determined by clinic interview. RLS was classified as either primary or secondary. Assuming no significant racial differences in occurrence of RLS permits using the 2000 census sample to predict the percentage of the diagnosed cases that should occur for each group. The difference between this predicted and the observed number provides a test of the null hypothesis of no racial differences.

Results: The total sample of 259 diagnosed with RLS was almost exclusively (95.8%) Caucasian non-Hispanics. The observed number in each racial-ethnic category compared to that predicted from the census data were: Asian 2 vs. 10, Hispanic 3 vs. 11, African American 6 vs. 72, Caucasian non-Hispanic 248 vs. 161. (chi squared= 120.7, p<0.0001). The percentage of the RLS cases diagnosed with secondary RLS was 0 for Asians and Hispanics, 67% for African Americans, and 48% for Caucasian non-Hispanics. A significantly larger percentage of RLS was diagnosed for African-Americans compared to Caucasian non-Hispanics. For the 135 with primary RLS in this sample 2 (1.5%) were Asian, 3 (2.2%) Hispanic, 2 (1.5%) African American and 128 (94.8%) Caucasian non-Hispanic. The patients diagnosed with other sleep disorders such as sleep apnea did not show this large proportion of Caucasians.

Conclusion: Although RLS is reported to be more common in lower social economic classes it appears to be not only uncommon among African Americans but when it occurs it is likely to be a secondary form of RLS. Cultural, environmental and genetic differences between the races may inform about factors producing RLS.

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0827
Csf Ferritin Is Less For Earlier Than Later Age Of Symptom Onset Of Restless Legs Syndrome

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Introduction: Early-onset (before age 45) and late-onset of RLS symptoms has been reported to define differing phenotypes of RLS with differing disease progression and genetic factors. These suggest biological differences possibly relating to iron status. If the biological factor is more prominent for early- vs. late-onset RLS than the iron abnormality may also be greater (lower ferritin and higher transferrin) for the early -onset RLS.

Methods: Patients with idiopathic RLS over age 45 with daily symptoms, PLMS >20/hour and no iron-deficiency were studied for 3-days in the GCRC after abstaining from all RLS medications for at least two weeks. CSF and serum samples were obtained at 10:00 PM on the last day in the study. Clinical history obtained RLS severity on the Johns Hopkins RLS severity Scale (JHRLSS) and age-of-onset of RLS symptoms. Averages , standard deviations are presented.

Results: 15 early- and 15 late-onset patients (7 males and 8 females in each group) were studied. The mean age slightly younger for the early-onset than the late-onset (58.6,8.1 vs. 66.2,9.6). However, the patients age did not correlate with iron measures. Early- compared to late-onset RLS showed significantly lower CSF ferritin (2,1.0,6 vs. 2.8,0.7 mcg/l t=3.0, p<0.005) and marginally higher CSF transferrin (5.4,2.1 vs. 4.4,1.4 mg/dl t=1.6 p=0.06) but there were no differences in serum iron measures. The age at which symptoms first started correlated with both CSF ferritin (r=0.49, p<0.006) and CSF transferrin (r= -0.37, p<0.05) but not with any serum values. These correlation were strongest in the early-onset group (CSF ferritin r=0.65, p<0.005; CSF transferrin r= -0.47, p<0.04) but were not significant for the late-onset phenotype.

Conclusion: The CSF measures indicate that the degree of CNS iron deficiency in later life is greater for early- than late-onset RLS and the degree of iron deficit may determine the age RLS symptoms start.
Anti-Histamines And Benzodiazepines Exacerbate Daytime Restless Legs Syndrome (RLS) Symptoms

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Introduction: Two sedating medications have been reported to have opposite effects on RLS, anti-histamines exacerbate while benzodiazepines may reduce RLS symptoms. Neither have been adequately evaluated for effects on RLS symptoms.

Methods: Twelve RLS patients reporting adequate treatment for their RLS using only dopamine agonists underwent 3 consecutive days of drug challenges while on treatment. The same dose of the same drug was administered IV twice each day at 3 and 5:45 PM and a 60 minute suggested immobilization test (SIT) followed each dose. The 2nd day was always placebo. The doses on the 1st and 3rd days were either diphenhydramine (25 mg) or lorazepam (0.5 mg) given following double-blind procedures. The same drug dose was repeated each day. The patient was blind to which day the placebo was given. The SIT test was measured for periodic limb movements per hour (PLMW/hr). Sleepiness was assessed as the time to the first sleep epoch (Sleep Lat) and the number of times that patient was awakened from sleep to continue the 60-minute SIT. Subjective ratings of RLS symptoms were also obtained.

Results: Preliminary analyses showed that PLMW/hr were greater for each patient for each of the diphenhydramine doses compared to comparable lorazepam doses (p<0.005) and in contrast the measures showed non-significantly greater sleepiness for lorazepam than diphenhydramine. Comparison with placebo showed PLMW/hr was significantly greater for diphenhydramine (p<0.005) and marginally significantly greater for lorazepam (p=0.10). Subjective ratings of RLS severity showed similar significant differences. There were no significant differences for the measures of sleepiness although the direction of change was that expected.

Conclusion: The results are consistent with daytime sedating anti-histamines severely exacerbating RLS more than expected for their sedating effects. Daytime benzodiazepines contrary to expectations also moderately increase RLS symptoms.
0829

Sleep Disorders In Children With Epilepsy

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Introduction: As epilepsy and sleep-wake disorders are common conditions in childhood, it is possible they may occur in the same patient by coincidence or on the basis of related pathophysiology. The prevalence of sleep disturbances in children with specific seizure types has not been extensively evaluated. Our objective was to evaluate sleep-wake complaints in sub-groups of childhood seizure disorders.

Methods: Forty five consecutive families of children with known or suspected seizures were surveyed. Thirteen of the 45 (28.9%) had non-epileptic events like migraine and movement disorders, and served as controls. The characteristics of sleep complaints in the remaining children with seizures are described.

Results: Among the 32 children with seizure disorders, 15 (47%) had generalized seizures (GS), 13 (41%) had simple partial (S) and 4 (12.5%) had complex partial (CPS) seizures. Nineteen of 32 epilepsy subjects (59%) reported sleep-wake problems as compared to 4/13 (23%) of the controls (p= 0.0241). The breakdown was 8/15 (53%) in the GS, 8/13 (61.5%) in the SPS and 3/4 (75%) in the CPS category. The most common symptoms in these 19 subjects with disturbed sleep were: difficulty falling sleep in 4/8 (50%) with GS, 6/8 (75%) with SPS and 1/3 (33%) with CPS. Difficulty staying sleep was reported in 8/19 (42%) total, with 3 being in the GS, 4 in the SPS and 1 in the CPS category. Non-restorative sleep was reported overall in 11/19 (57%) with sleep disturbance, specifically in 5/8 (62.5%) with GS, 4/8 (50%) with SPS and 2/3 (66%) with CPS. Habitual snoring was present in only 3/19 (15%).

Conclusion: Sleep onset / sleep maintenance insomnia and non-restorative sleep are common co-morbid symptoms in children with seizure disorders. There was no correlation of sleep disturbance to seizure type.

0830

Kleine-Levine Syndrome (KLS) And The Thalamus

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Introduction: KLS is a periodic hypersomnia with onset during teenage years that has been proven to be resistant to many treatment trials and is little understood.

Methods: Systematic prospective studies of 7 boys 11 to 17 years at onset of periodic hypersomnia, followed up to 13 years. With EEG, polysomnography, CT-scan, MRI and finally Tc-99m ECD single photon emission tomography (SPECT) obtained during day 4 or 5 and at least 1 month away from the symptomatic period, SPECT (with subtraction) were analyzed blind to condition (normal/hypersomnia period)

Results: Clinical evaluations, polysomnography, and systematic follow-up investigations affirm KLS. All imaging tests but SPECT were normal. SPECT: Two/7 subjects withdrew consent for further imaging study during symptomatic and aggressive periods during wakefulness but 5 underwent testing. All 7 patients ended having SPECT performed during asymptomatic period. Hyperperfusion of both thalami was seen during the symptomatic period that completely disappeared during the asymptomatic period in the 5 patients studied during and after post hypersomnic period. Other more variable hyperperfusion regions were also noted. They persisted during the asymptomatic period in 2 cases: over the temporal lobe (2/7 cases), frontal lobe (1/7 cases) and basal ganglia (1/7 cases). The largest amount of persistent hypoperfusion was seen in the subject with longest clinical evolution.

Conclusion: Hypoperfusion of the thalamus is a consistent finding during the symptomatic period, and disappear at the end of the symptomatic period; but other perfusion abnormalities may persist even during the asymptomatic period. The longer the duration of the syndrome, the more extended the hyperperfusion regions during asymptomatic period. Clinical presentation of KLS patients is similar to clinical presentation of young adults with bilateral paramedian thalamic stroke and pseudo-hypersomnia. In both syndromes patients were apathetic, behavioral aspect of sleep with sleep posture, aggressive and disinhibited behavior.

0831

Long Term Outcome Of Treatment Trials Of Kleine-Levin Syndrome (KLS)

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Introduction: Very long term of treatment trials in KLS is not reported. We carefully followed 9 teen-agers with KLS for a mean of 5.5 years (range 2-13 years)

Methods: 9 teen agers-2 with associated mild seizure disorder- had clinical evaluations, polysomnography, MSLT and systematic follow-up investigations. Patients received the following treatment trials covering at least 2 episodes and sometime over 3 years of periodic hypersomnia: lithium, imipramine, fluoxetine, moclobemide, risperidone, acetazolamide, carbamazepine, valproic acid and influenza type A vaccine. The stimulants modafinil and methylphenidate were administered at the first symptoms of periodic hypersomnia.

Results: Frequency of episodes varied from 2 to 6 time/year. All patients presented typical symptoms of KLS with abnormal behavior during the hypersomnic period with hyposexuality, dis-inhibition, bulimia , burst of aggressiveness followed by apathetism. Polysomnography and MSLT during the asymptomatic period eliminated any other sleep disorder. Only 2 of these Asian patients were HLA-DQB1-0601. Seizure disorder was unchanged during symptomatic period and well controlled by treatment. Symptomatic period was very stereotypic in duration from episode to episode in each subject and oscillated between subjects from 7 to 10 days. None of the treatment trial had any impact on the recurrence or duration of the hypersomnic episode. Stimulants never improved subject's clinical presentation during hypersomnic episode.

Conclusion: None of the treatments mentioned in the literature had long term effect and avoided re-occurrence of stereotypic periodic hypersomnia, and none of the stimulants helped during the hypersomnic episode. As already reported seizure can be seen in association with KLS but its appropriate treatment do not impact on KLS. The predominance of HLA DQB1-0602 is not verified in this Chinese subjects.

0832

Exploratory Polysomnographic Evaluation Of Pregabalin On Sleep Disturbance In Patients With Epilepsy

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Introduction: The incidence of sleep disturbance in epilepsy is higher than in matched controls and is related to significant impairment of quality of life. Relationships between seizures, drug treatment and sleep disturbance are complex. It has been suggested that antiepileptic drugs (AEDs), that consolidate disturbed sleep, may confer benefits beyond seizure control. Adjunctive pregabalin is highly effective in refractory partial seizures and in neuropathic pain (NeP), and reduces sleep interference in NeP. The effects of adjunctive pregabalin 300 mg/day versus placebo on polysomnographic (PSG) variables in patients with well-controlled partial seizures and subjectively reported sleep disturbance were evaluated.

Methods: An exploratory, 4-week, double-blind study was conducted in patients with well-controlled partial seizures on AED monotherapy and objectively reported sleep disturbance (as per Sleep Diagnosis Questionnaire evaluating sleep in prior 6 months). Mean changes from baseline to endpoint in PSG and subjective sleep variables in patients on adjunctive pregabalin 300 mg/day (n=8) were compared with patients on placebo (n=7). PSG-sleep efficiency was the primary efficacy measure. Secondary efficacy parameters included other PSG variables and subjective assessments (e.g. MOS Sleep Scale).

Results: Baseline PSGs indicated clinically relevant sleep disturbances due to sleep fragmentation. Mean (SE) sleep efficiency improved significantly in the pregabalin group from 73.7% (6.16) at baseline to 80.8% (3.27) at endpoint (p<0.05) and was not significant in the placebo group. Differences between baseline-endpoint changes were not statistically significant between groups. Pregabalin was associated with a significant reduction in number of awakenings (p<0.05) and improvement in wake-time-after-sleep-onset approached significance (p=0.055). Significant improvement of MOS subscales with pregabalin: 16.9 on the sleep disturbance and increased sleep duration by 1.5h (both p<0.05). The most common AEs were dizziness and somnolence.

Conclusion: This exploratory study indicates that pregabalin is well tolerated and improved sleep continuity in patients with clinically relevant sleep disturbance. The effect appears independent of seizure control. The effects of pregabalin on disturbed sleep and seizures and their interrelationships warrant further study.

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Nocturnal And Diurnal Seizures In Mesial Temporal Lobe Epilepsy
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Introduction: Previous studies of sleep-related partial seizures have lacked precise localization of the epileptogenic focus. We studied the influence of sleep on partial seizure type and duration in well-localized mesial temporal lobe epilepsy, hypothesizing that sleep-onset seizures are longer and generalize more frequently than wake-onset seizures.

Methods: We retrospectively identified consecutive patients with a seizure-free outcome following anterior temporal lobectomy (ATL) from 1993-2001 with video-EEG captured seizures in both sleep and wakefulness. We analyzed each seizure for sleep stage at onset, ILAE seizure type by ictal semiology, and seizure onset and offset times. Sleep stage was determined by Rechtschaffen and Kales criteria modified as follows: no chin EMG was utilized, frontotemporal and anterior temporal leads were used to determine eye movements, bipolar montage was used to determine slow wave amplitude, and NREM stages 3 and 4 were grouped together as slow wave sleep.

Results: 23 (10 men and 13 women) had a total of 335 (176 right and 159 left) temporal onset seizures. 106 (32%) arose from sleep. Sleep seizures were evenly distributed between Stages 1 (54 seizures) and 2 (51 seizures) sleep, with a single seizure from slow wave sleep and none in REM. Seizure types (sleep (%), awake (%)) were: 57 simple partial (22 (39%), 35 (61%)); 255 complex partial (73 (29%), 182 (71%)); and 23 complex partial with secondary generalization (11 (48%), 12 (52%)). The rate of complex partial seizures undergoing secondary generalization was significantly higher in sleep (12.8%, CI 6.62-23.33) than wake onset (5.9%, CI 2.72-12.42) seizures (OR 2.33, p=0.0091).

Conclusion: We found that sleep-onset mesial temporal lobe seizures arise almost exclusively from light NREM sleep, that there was no significant difference in duration between sleep and wake onset mesial temporal seizures, and that sleep influences mesial temporal lobe seizure propagation by increasing the likelihood of secondary generalization. Limitations of our study include lack of electrocorticography, and our inability to reformat the existing analog longitudinal bipolar montage recordings, which may have lead to underestimation of tonic REM and slow wave sleep stages at seizure onset, respectively. Future prospective studies of surgically localized epileptic foci utilizing video-EEG polysomnography are needed to more optimally determine the influence of sleep on partial seizures in other epilepsy syndromes.

0834
The Quantification Of Disrupted Sleep In Migraine Via Actigraphy: A Pilot Study
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Introduction: Ambulatory actigraphic monitoring may provide an objective, reliable, and non-intrusive method to monitor the course of episodic clinical events such as migraine headaches. This ongoing study explores the use of the actigraph as a quantitative measurement tool for migraine headache. The study is aimed at defining specific actigraphic signal characteristics of migraine such as hypo-kinetic activity and altered sleep patterns and expands the computational methods applied to the analysis of actigrams.

Methods: Episodic migraines were recorded by a headache calendar and continuously monitored by Trimode Actigraphy for a minimum of 16 days, recording ZCM, TAT, and PIM. Data were scored for sleep and then partitioned into separate Wake and TIB Interval segments, and the full data set was broken into 1-hour segments for analysis of ultradian rhythms. Each segment was then analyzed to quantify several statistical parameters and quantitative descriptors.

Results: Six migraine episodes were recorded over the study period. Suppressed activity levels were apparent across all channels shortly following the onset of migraines which were visually distinguishable from normal wake and sleep patterns. There were significant decreases in PIM (p<.003), ZCM (p<.001), and TAT (p<.001) for Wake periods with migraine compared to those without migraine. Standard analyses of sleep (TST, Latency, WASO) showed no change, but there were significant differences for TIB close to migraine episodes in terms of ZCM (p=0.007) and TAT (p=0.05), suggestive of sleep disruptions on migraine days. Ultradian rhythms were not changed according to Complex Demodulation for individual frequencies, except for the 4 cycle-per-day rhythm, which was suppressed during days involving migraines.

Conclusion: Preliminary data suggests that actigraphy may be a viable tool for quantifying migraine syndrome. The actigraph record indicates that there was suppression of activity during migraine episodes and a number of movement characteristics changed during both Wake and Sleep.
High Prevalence Of Obstructive Sleep Apnea Among Patients With Pseudotumor Cerebri
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Introduction: There are some common features between obstructive sleep apnea (OSA) and pseudotumor cerebri (PC), i.e., obesity and morning headache. However, the prevalence of OSA among PC patients is not well studied, and the relationship between these two diseases is not widely recognized in current medical practice. In this study, we want to determine the prevalence of OSA among our patients with PC and hopefully to increase the awareness of OSA in this patient population.

Methods: 42 patients were identified at Kaleida Health System for possible PC and 36 patients were included for the study according to PC diagnosis criteria. By reviewing the charts, we determined how many patients who already had nocturnal polysomnography (NPSG) and diagnosed with PC, then we interviewed patients who have not had NPSG and obtained the related demographic data, and then underwent NPSG to find out how many patients who have unrecognized OSA among them. OSA diagnosis criteria: respiratory disturbance index (RDI) > 5 and excessive daytime sleepiness.

Results: 36 patients were satisfied the PC diagnosis criteria and qualified for the study (all female except one, age=40.8+/-3.6 y). 7 of the 36 (19.4%) already had a NPSG done; 6 of the 7 patients had OSA (85.7%). Among the remaining 29 patients, 16 patients were able to contact and willing to participate the study, and 8 of the 16 patients were interviewed and undergone NPSG. 7 of the 8 patients were diagnosed with OSA (87.5%). Of all 15 patients with NPSG, 13 patients were diagnosed with OSA (86.7%). Their average BMI=40+/-2.3 (range 25-54), ESS =8.8+/-1.8 (range 0-17), RDI=22.7+/-7.6 (5.1-78), REM-sleep RDI=39.2+/-12.2 (4.6-96), Min SaO2=84.7+/-4.4 (51%-95%).

Conclusion: Our preliminary data indicates a very high prevalence of OSA among patients with pseudotumor cerebri (PC). The benefit of CPAP treatment for PC and OSA is in progress.

Sleep Disturbances In Neurometabolic, Degenerative And Genetic Medical Conditions. The Neurometplus Approach
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Introduction: It is not uncommon to find sleep disorders in neurometabolic, degenerative and genetic conditions. Literature is not easily available on this topic. NeurometPlus offer a practical approach in the search for information on sleep disturbances in these conditions.

Methods: NeurometPlus is an educational and diagnostic software database program, used for diagnosis and management of neurometabolic, degenerative and genetic medical conditions in children and adults. Over 430 conditions are included in the database at this moment, with updates and expansion of information every 3 months. Three relational databases including 70 fields of symptoms and signs, as well as 32 abnormal laboratory fields and different ages of onset are searchable by combining different fields. Sleep abnormalities when present are described for the conditions included in the program.

Results: By using the powerful searching capabilities of the program including the field “Sleep abnormality” on the search, as well as the text find box, all neurometabolic, degenerative and genetic medical conditions associated with sleep disturbances are found.

Prevalence Of Significant Central Apnea On Polysomnography With Vagal Nerve Stimulation In Patients With Chronic Epilepsy
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Introduction: Vagal Nerve Stimulation (VNS) using an implanted stimulator (Cyberonics, Houston, TX, U.S.A.) is now an accepted treatment modality in refractory epilepsy. Though the exact mechanism of action of the vagal stimulation is still unclear, it is believed to act by modulating vagal input to the nucleus tractus solitarius and brain stem reticular formation. The vagal input in turn is believed to interrupt the synchrony of cerebral electrical activity that occurs with seizures. Though VNS has been shown to both worsen obstructive apneas in some patients and decrease respiratory effort and airflow in others, frank central apneas have never been reported.

Methods: Polysomnographic, VNS and clinical data from 9 patients (mean age 39 years) was analyzed retrospectively. All polysomnograms were reviewed by board certified polysomnographers for significant obstructive, mixed and central apneas. Mixed apneas were classified along with obstructive group. Significant central apnea was defined as central apnea lasting >=10 secs associated with arousals or unexplained desaturations below 88% in the absence of any detectable cause.

Results: Five patients (55.6%) had significant obstructive sleep apnea (mean RDI=25.74). One patient (11.1%) had significant central apnea with unexplained desaturations down to 86% occurring rhythmically, associated with VNS stimulator firing artifacts. Demographic stimulator, and polysomnographic data from the groups with obstructive and central apnea will be compared.

Conclusion: Though mild decrease in respiratory airflow and effort during sleep has been reported with VNS pulse generator activity, significant central apneas are rare. As reported by others, we also found obstructive sleep apnea to be more common. The exact cause for the significant central apneas in our case is unclear but it is possible that increased vagal tone and/or inhibition of the respiratory centers induced by VNS firing may have contributed to this unusual phenomenon.

Hypersomnia Following Traumatic Injury
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Introduction: Traumatic brain injury (TBI) can cause post-traumatic hypersomnia. Injury severity and location are important, with many non-cranial trauma patients also endorsing sleepiness. Patients often improve over time but longitudinal studies are lacking.

Methods: We investigated excessive sleepiness in representative TBI cases enrolled at the time of injury and prospectively followed for 1 year. TBI cases (n=514), non-cranial trauma controls (TC, n=132), and healthy friend controls (HC, n=102), answered the following 4 questions from the Sickness Impact Profile related to their current state of sleepiness at 1
month and 1 year post-injury: 1) I am sleeping or dozing most of the time, day and night; 2) I sit around half-asleep; 3) I sleep or nap more during the day and; 4) I sleep longer during the night. For example go to bed earlier, get up later. Sleepiness severity was defined by number of endorsed items. TBI severity was defined by time from injury to follow simple commands as follows: ≤24 hours, 1-6 days, 7-13 days, 14-28 days, ≥29 days. Statistics include ANOVAs and Tukey post-hoc analyses.

**Results:** At 1 month, 52% of TBI (mean age 30, 73% male), 41% of TC (mean age 31, 72% male) and 3% of HC subjects (mean age 25, 64% male) endorsed ≥ 1 sleepiness item (p<.001). After 1 year, 27% of TBI, 23% of TC, and 1% of HC subjects endorsed ≥ 1 sleepiness item (p<.001). Post hoc analyses at 1 month indicated TBI patients were sleepier than both TC and HC subjects (p < .05). At 1 year, TBI subjects remained sleepier than HC subjects (p < .05) but not TC patients. TBI patients were sleepier than TC patients when divided into time to follow command groups at 1 month (p < .001) and 1 year (p = .002) post-injury. Post hoc analyses revealed that TCI patients at 1 month were less sleepy than both the 1-6 day and 7-13 day TBI time to follow command groups (p < .05). In addition, the ≤24 hour TBI time to follow command group was less sleepy than the 7-13 day TBI time to follow command group (p < .05). At 1 year, post hoc analyses revealed the ≤24 hour TBI time to follow command group was less sleepy than the 14-28 day time to follow command group (p < .05). At 1 year sleepiness improved in 45% of TBI patients as compared to 32% of TC patients (p < .05).

**Conclusion:** Sleepiness is most common following traumatic brain injury although a large percentage of non-cranial trauma patients also endorse this symptom. Improvement is typical, with symptoms persisting as a function of injury severity.

**0839 Sleep Disordered Breathing In Children With Head And Neck Plexiform Neurofibromas**

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**Introduction:** Neurofibromatosis Type 1 (NF-1) is a common genetic disease, affecting 1 in 3000. Plexiform neurofibromas (PNs) represent one of the most significant complications of NF-1. These benign tumors, which form along nerves, may become large and compress visceral structures. Neurofibromas involving the head and neck are common, and may lead to significant sleep disordered breathing.

**Methods:** The study population included children with severe, progressive PNs that were referred to the neuro-oncology clinic at The Children’s Hospital of Philadelphia between September 1999 and July 2002. From a population of 737 NF-1 patients, 156 were found to have PNs; 84 of these had head/neck involvement. In this retrospective study, we analyzed overnight polysomnography (PSG) performed in our lab on 14 children with head/neck PNs, ranging in age from 3 to 18 years. The indication for referral to a PSG was clinical concern for sleep disordered breathing.

**Results:** At the time of their PSG, 5 patients already had some surgical intervention. Sleep related abnormalities were seen in 12 of 14 patients. Two subjects had obstructive sleep apnea, with an elevated apnea/hypopnea index (>5), however, 11 subjects had nocturnal hypoxemia, with average oxyhemoglobin saturations of 88% +/- 5%. 3/14 also had hypoventilation. All patients exhibited paradoxical breathing during PSG, and eight patients snored during their studies. 6 had alterations in sleep architecture: increased arousals/awakening index (>15/hr), and prolonged REM latency (mean 118 minutes).

**Conclusion:** We noted sleep disordered breathing in a high percentage of NF-1 subjects with head/neck PNs referred for evaluation. The most common abnormalities included nocturnal hypoxemia, hypoventilation, and overt OSA. Our findings warrant further investigation of children with severe head and neck PNs, as the prevalence and incidence of sleep disordered breathing in this population is still unknown.

**0840 Obstructive Sleep Apnea On Polysomnography In Patients With Parkinsonism**

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**Introduction:** Nocturnal sleep fragmentation is reportedly common in patients with Parkinsonism and is multifactorial in origin. As obstructive sleep apnea is a potentially reversible cause of sleep fragmentation (and ensuing daytime sleepiness), its recognition is of great clinical significance. The prevalence of obstructive sleep apnea in patients with Parkinsonism is unclear, although some studies place it at about 20%.

**Methods:** Demographic and Polysomnographic data from 46 patients (mean age 68.5 years) studied over the last 3 years at our AASM accredited laboratory was reviewed. All patients had been referred for snoring, daytime sleepiness, apneas, or multiple awakenings by neurologists. Board certified polysomnographers scored the studies using conventional criteria. The number of patients who had respiratory disturbance indices (RDI) greater than or equal to 5/hr and 15/hr were calculated separately. Sleep efficiency, percentages of slow wave and REM sleep, periodic limb movements, Epworth scores and mean sleep onset latencies on MSLT were also analyzed.

**Results:** The mean sleep efficiency for the group was 60.76%. Slow wave sleep and REM sleep were 2.68% and 9.05% respectively. 38/48 (82.6%) had an RDI of >=5 and 22/46 (47%) had an RDI >15/hr. 18/46 (39.13%) had periodic limb movements. Obstructive sleep apnea seemed to be far the most common apnea type.

**Conclusion:** The occurrence of Obstructive sleep apnea in Parkinsonism seems to be much higher than would be expected in a similar population. Sleep efficiency, slow wave and REM sleep appear to be reduced in this patient group, and could be due to many causes (including medication effects). Although this sample may have been affected by referral bias since only symptomatic patients were studied, obstructive sleep apnea and polysomnography need to be considered in all patients with Parkinsonism and sleep symptoms.

**0841 Excessive Daytime Sleepiness In Parkinson’s Disease**

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**Introduction:** Excessive daytime sleepiness (EDS) has been documented in up to 70% of patients with Parkinson’s disease. Underlying causes include altered sleep-wake regulation, side effects of dopaminergic drugs and comorbidities such as sleep-disordered breathing, period leg movements. The objectives were to determine the prevalence rate of EDS according to the Epworth Sleepiness Scale (ESS) score ≥10 in an idiopathic Parkinson’s disease (IPD) population sample and its PSG correlates.

**Methods:** Thirty five consecutive IPD subjects (12F/23M; age=67.37±6.83; BMI=25.30±4.47; disease duration/DD=7.54±4.65; Hoehn-Yahr scale(HYS)=2.31±0.76 completed the ESS. Patients demographics data of subjects with ESS≥10 were compared(Z test) with ESS<10 subjects. Subjects with ESS≥10 performed an all-nigh PSG.

**Results:** Seventeen subjects showed ESS≥10 (3F/14M; age=67.35±4.80; BMI=25.83±3.08; DD=6.0±3.84; HYS=2.29±0.69) and 18 subjects showed
Introduction: Patients with Myotonic Dystrophy type 1 (DM1) exhibit sleep abnormalities that are reminiscent of Narcolepsy, such as excessive daytime sleepiness (EDS) and abnormal REM sleep. Given that these abnormalities occur in Narcolepsy in association with Hypocretin (Hcrt) deficiency, it is possible that patients with DM1 exhibit Hcrt deficiency as part of the complex DM1 phenotype. An initial study from a Stanford/Spanish collaboration provides data that supports this hypothesis. The present study was undertaken to further evaluate the possibility that the sleep abnormalities that occur with DM1 are associated with abnormally low levels of Hcrt in the Cerebrospinal Fluid (CSF).

Methods: To date 7 patients with genetically confirmed DM1 and the complaint of EDS have been recruited through our neuromuscular clinic. Patients completed an ESS and underwent a lumbar puncture between 8 and 9 AM. CSF was immediately frozen. Hcrt levels were measured using a direct radioimmunoassay. HLA-DQB1*0602 type was determined. Overnight polysomnograms and MSLTs were also performed (results are reported elsewhere in this volume).

Results: 3 females and 4 males, age range 36-53 (mean 43) were evaluated for the present analysis. The number of CTG repeats ranged from 338 to 885. ESS ranged from 3 to 17 (mean 13). Two of the patients were HLA-DQB1*0602 positive. Hcrt CSF levels were in the normal range (mean 243 pg/mL), except for one subject in the intermediate range (193 pg/mL).

Conclusion: Despite sleep disturbance similarity with Narcolepsy, EDS in DM1 does not seem to be associated with Hcrt deficiency in this limited series of patients. Because these results differ from the preliminary study we are 1) evaluating how the studies differ with respect to methodological issues (e.g., time and type of assay, subjects characteristics, etc.) and 2) increasing our sample size to explore whether only a limited subset of DM1 subjects exhibit Hcrt abnormalities.

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Concomitant Sleep Disorders In A Series Of Patients With Myotonic Dystrophy
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Introduction: Patients with Myotonic Dystrophy type 1 (DM1) complain of excessive daytime sleepiness (EDS) and have abnormal sleep regulation. Some have suggested that the sleepiness may be a result of sleep related breathing disorders, especially as the disease progresses to affect the respiratory musculature.

Methods: To date 9 patients (4F & 5M; mean age 41 [25-55]) with genetically confirmed DM1 and the complaint of excessive daytime sleepiness (EDS) have been recruited through our neuromuscular clinic. Each subject underwent a standard overnight PSG and MSLT to assess for the presence and severity of intrinsic sleep disorders. (The sleep continuity and architecture results are reported elsewhere in this volume).

Results: The mean AHI for the group was 6.1 with a range from 0.1 - 22.0 events per hour. Of the nine patients, three met PSG criteria for Obstructive Sleep Apnea Syndrome. The mean PLMI was 9.4 with a range of 0.0-21.0; four of these subjects met criteria for mild to moderate Periodic Limb Movements of Sleep. (The sleep continuity and architecture results are reported elsewhere in this volume).

Conclusion: The majority of the subjects in this sample did not exhibit significant sleep pathology. Moreover, the severity of the sleep disorders for the majority of subjects was in the mild range. Thus, the excessive daytime sleepiness seen in Myotonic Dystrophy does not appear to be primarily related to sleep related breathing disorders or periodic limb movements. Furthermore, given that the subjective complaints of sleepiness...
often occur in DM1 prior to the onset of muscular symptoms, it seems likely that a central mechanism is, at least in part, responsible for the EDS that occurs in association with DM1.

**0845**

**PSG And MSLT Sleep In Patients With Myotonic Dystrophy**

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**Introduction:** Patients with Myotonic Dystrophy (DM) exhibit daytime fatigue and sleepiness and have been shown to have increased REM pressure. In this study we present preliminary data from a PSG/MSLT study of 10 patients with DM.

**Methods:** Subjects were evaluated over a 24 hour period with a PSG and a MSLT. The PSG study included 6 EEGs, 2 EOGs, a mentalis EMG, 2 tibial EMGs, nasal/oral airflow, thoracic and abdominal effort, and blood oxygen saturation. Nocturnal sleep was recorded during the patients’ preferred sleep phase and subjects were allowed to sleep ad libitum. The MSLT study was comprised of 4 nap opportunities.

**Results:** The mean age of the group was 40.8 yrs +/- 9.8 and 60% of subjects were male. The mean time in bed was 485.4 min. +/- 32.5. Sleep latency was, on average, prolonged at 23.4 min. +/- 41.6, although 60% of the subjects had sleep latencies below 10 minutes. Wake after sleep onset was increased at 76.4 min. +/- 58.7, where 80% of the subjects had WASO values longer than 30 minutes in duration. Sleep efficiency was low at 78.9% +/- 17.1%, where 60% of the sample has SE% below 90%.

With respect to sleep architecture, the sample exhibited a low to average proportion of SWS 4.7% +/- 5.9% and an usually high percentage REM sleep (28.4% +/- 9.4%). 60% of the sample exhibit more than 30% REM sleep. REM latency was not found to be reduced (107.4 +/- 93.1). On the MSLT, the MD subjects were not found to be excessively sleepy (mean nap SL = 12.1 +/- 6.1) and only 1 subject exhibited pathologic sleepiness. This same subject had 2 naps with REM sleep.

**Conclusion:** These data suggest that patients with DM, as a group, exhibited significant sleep continuity and sleep architectural disturbance.

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**0846**

**Kleine-Levin Syndrome (KLS): A Meta-Analysis Of 122 Cases In The Literature**

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**Introduction:** KLS is a rare disorder with periodic hypersomnia and cognitive/behavioral disturbances. Large series of patients are lacking.

**Methods:** In this meta-analysis, we compiled symptoms and treatments response from 122 cases reported in 80 primary articles (1962-2004). Duplicate cases (n=39) and large case series without adequate clinical description for every case were excluded.

**Results:** Secondary cases were rare (n=12), with less male predominance (58% men) and had later onset (26±17 years, p=0.0002 vs primary). Primary KLS (n=110) was described worldwide. Almost all cases (96%) were sporadic and most (72%) were men. Onset was 16±7 year old (mean±SD, range 9-53, 85% during the second decade); disease duration (median) was 3.5 years (range 0.5-27). A precipitating factor was found in 56.4%: infection or fever (38.2%), head trauma, psychological and physical exertion (9%), or excessive/first alcohol consumption (5.4%). Patients reported a median of 7 episodes, lasting 10 days, and recurring every 3 months (median values). During episodes, patients slept 18 hours a day (median) with polysomnography resembling narcolepsy (27%) or harmonious idiopathic hypersomnias (73%). The most prevalent symptoms were (i) hypersomnia (100%); (ii) cognitive disturbances (41%), including mental slowness, impaired speech (19%), disturbed concentration and memory (14%), confusion (16%), depersonalization and altered perception (14%), hallucinations or delusions (6.4%); (iii) eating disturbances (67%), including megaphagia (39%), craving for sweets (9%), compulsive food searching (8%), inability to restrain eating in the presence of food (4%); (iv) hyper-sexuality (35%); (v) compulsive/aggressive behavior (17%). Encephalograms showed slow activity during the attacks in 61%, disappearing between attacks. In 38 patients where treatment was attempted (90 trials), lithium, used in 55%, was the most successful in preventing relapses (62% success rate), followed by stimulants (mainly dextroamphetamine, 36%), carbamazepin 33%, antidepressants 6% and neuroleptics 0%.

**Conclusion:** Our meta-analysis confirms the existence of unique syndrome and suggests lithium as the most effective treatment.

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**0847**

**Prevalence And Clinical Characteristics Of Restless Legs Syndromes In Japanese Patients With Parkinson’s Disease**

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**Introduction:** It has been reported that restless legs syndrome (RLS) is highly prevalent among Caucasian patients with Parkinson’s disease (PD). However, the prevalence of RLS in Asian PD patients and the influence of the disorder on subjective sleep quality have not been well elucidated. In order clarity these issues, we investigated the prevalence of RLS among Japanese PD patients and compared the clinical characteristics between secondary RLS in PD and idiopathic RLS.

**Methods:** One hundred and thirty-five PD patients, age and sex matched 131 healthy controls and 22 idiopathic RLS patients were subjected in this study. On all the subjects, diagnosis of RLS was made based on clinical interviews, and subjective sleep quality was assessed by using Pittsburg Sleep Quality Index (PSQI).

**Results:** The prevalence rate of RLS was significantly higher in PD patients than control subjects (12% vs. 2.3%, p<0.01). PSQI score was significantly higher in the PD patients with RLS than both the PD patients without RLS and the controls. The clinical background variables including PD severity, doses of the drugs used for the treatment of PD and the serum values of both iron and ferritin did not differ between the two groups with and without RLS. While compared with the idiopathic RLS patients, the PD patients with RLS showed significantly milder RLS severity. However, PSQI score was not statistically different between the two groups.

**Conclusion:** Our results impressed the etiological linkage between RLS and PD even in Japan, and the existence of RLS was thought to be one of the important aggravating factors of subjective sleep disturbance in PD despite the low RLS severity. Moreover, our results indicated that iron deficiency might not play a pathogenetic role on the occurrence of the disorder in PD patients.
0848

Vivid Dreams, Hallucinations, REM Sleep Disorders (Status Dissociatus) And Hypocretin In Guillain-Barre Syndrome (GBS)

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Introduction: Hallucinations, REM sleep behavior disorders and hypocretin deficiency have been independently described in some patients with GBS, an auto-immune disorder of the peripheral nervous system. We looked for their association in a series of GBS patients and controls placed in intensive care unit.

Methods: We studied prospectively the nature, frequency and determinants of psychotic signs in 133 GBS patients. In addition, we examined the association of hallucinations and REM sleep during night and day using continuous sleep monitoring in 11 GBS patients. In addition, we examined the association of hallucinations and REM sleep without GBS, in ventilated in ICU (controls).

Results: Psychic signs without confusion were experienced by 40/133 (30%) patients. They appeared a median 9 days after GBS onset (range 0-32 days, during the progression or the plateau of the disease), and lasted a median 10 days (range 1-132 days). They included vivid dreams (13%), illusions (26%), hallucinations (59%), and delusions (69%), mostly paranoid. Hallucinations were visual (33.3%), somesthetic (10.2%, including an illusory body tilt), auditory (13%), and frequently hypnagogic. Six patients experienced hallucinations before their admission to the ICU. Fifty-five percent patients under ventilation experienced psychotic signs vs. 8.6% non-ventilated patients (p<0.0001). Autonomic dysfunction, severity of the disease and high CSF protein levels were significant risk factors for psychic signs. Cerebrospinal fluid hypocretin levels, measured in 17 patients, were normal at GBS onset. During sleep monitoring, total sleep time and REM sleep latencies tended to be shorter in GBS hallucinators than in other groups. Only hallucinators had sleep onset in REM sleep periods (n=4/6), abnormal and frequent REMs during non REM sleep (n=4/6), REM sleep completely without atonia (n=6/6, 100% tonic, vs. 20% on other groups), and REM sleep behavior disorders (n=1/6), resembling a status dissociatus. These abnormalities were not related exclusively to ICU conditions, and were reversible, disappearing almost completely when the patients recovered from the psychotic episode.

Conclusion: Vivid dreams, hallucinations, and psychosis occurred in one third of GBS patients and were associated with severe GBS forms and autonomic dysfunction. Sleep studies suggest that they are wakeful dreams caused by a status dissociatus.

0849

Nightly Variability In Perceived Sleep Quality Of Parkinson Disease (PD) Patients Is Reflected In Polysomnography

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Introduction: PD is associated with disturbed sleep, though patients often experience considerable variability in the quality of their sleep. This study compared customary PSG measures (TST, SE, REM%, RDI, PLMSI) between two consecutive lab nights in which rated global quality differed on a 5-point scale.

Methods: PD Patients were (n = 52) studied for 3 consecutive nights with overnight PSG as part of a randomized pharmacologic trial. We divided pts into those whose reported sleep quality on Nights 2 and 3 differed by at least 1 point on the 5-point scale (N = 37) versus those who reported identical sleep quality on those nts (n = 15). For the first group, we compared the good versus bad night regardless of whether they derived from nt 2 or nt 3. For the second group, we compared nt 2 and nt 3, since they were identical in perceived sleep quality.

Results: Good night/bad night comparisons indicated statistically significant differences in TST (good = 314.3 mins, SD = 79.6; bad = 282.3 mins, SD = 93.8), t = 2.12, p = .04) and SE (good = 75.9%, SD = 15.8; bad = 71.6%, SD = 15.5, t = 2.03, p = .05). Neither REM%, RDI, nor PLM differentiated better or worse nights. In the group with identical sleep quality on both nts, comparison of all PSG derived variables were NS.

Conclusion: These data suggest that, among a pt population with severely disturbed sleep, gross PSG measures (TST, SE), were responsive to perceived sleep quality, thus arguing that these metrics should be sensitive to results from the clinical trial yet to be determined because of blinding. The results also suggest that neither RDI nor PLMSI show an obvious relationship with nt-to-nt sleep quality in this population.

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0850

Association Of Vascular Distribution Of Stroke In Insomnia

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Introduction: We investigate whether anterior circulation strokes manifest different sleep complaints to posterior strokes, using Insomnia Severity Index (ISI), Epworth Sleepiness Scale (ESS), and Sleep Disorders Questionnaires (SDQ). Evidence links sleep with stroke aapnea, insomnia, and daytime sleepiness. Abnormalities in sleep architecture result from brain damage (strokes). It is unclear whether strokes with specific vascular origin or laterality (right vs left) manifest different patterns of sleep complaints.

Methods: 38 patients were admitted with ischemic or hemorrhagic strokes. Age, sleep aapnea portion of SDQ, ESS, ISI, and tobacco/coffeeine were obtained. Abnormal scores for: SDQ > 32 (females), > 36 (males); ESS > 10. ISI scores: 0-7 no significance, 8-14 subthreshold, 15-21 moderate, and 22-28 severe clinical insomnia

Results: 38 patients had average age of 64 yo (range 32-91). 33/38 had ischemic strokes; 5/38 hemorrhagic. Average scores: SDQ 32 (range 17-53), ESS 9 (range 0-22). ISI: 7 (range 0-24 SD 7). Of 38 patients, 11(30%) had some indication of insomnia (3/38 subthreshold, 7/38 moderate, 1/38 severe). 27/38 had no clinical significance of insomnia. There was significant correlation between anterior circulation strokes (n=16) and each component of ISI and total score: Difficulty falling asleep (r =0.41), staying asleep (0.37), waking up early (0.50), dissatisfaction with sleep (0.64), interference with daily life (0.55), noticeably to others (0.53), worried about sleep (0.49), and total ISI (0.54). Posterior strokes (n=16) had significant negative correlation to components and total ISI. Neither anterior nor posterior strokes had correlation with ESS or SDQ. No correlation between right/left sided strokes and ISI/ESS/SDQ was seen. There was no correlation between tobacco, caffeine, and insomnia.

Conclusion: These findings demonstrate that patients with strokes have evidence of insomnia. Patients who endorsed insomnia were likely to have anterior rather than posterior strokes. Although we did not control for affective disorders, this is potential mechanism that needs exploration.

0851

Sleep Disordered Breathing (SDB) In Parkinsons Disease (PD)

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Introduction: Upper airway abnormalities and decreased lower lung
function are well known in PD and might be expected to contribute to a higher prevalence of SDB in such patients. Conversely, the rarity of obes-
ity in PD and the potential beneficial influence of dopaminergic agents
(by peripheral or central enhancement of respiratory muscle function or
baroreceptor downregulation) might be protective. A substantial amount
of PD PSG data in, collected in the Baseline phase of a clinical trial,
afforded the opportunity to examine SDB.

**Methods:** Idiopathic PD patients (n= 52) (X [SD] age = 61.7 [9.2]) were
studied for 3 consecutive lab nights. Breathing events were scored manu-
ally using conventional criteria with regards to O2 saturation levels to
compute the RDI.

**Results:** Mean (SD) RDIs for Nights 1, 2 and 3 were 7.3 (9.2), 9.3 (11.4),
and 7.9 (11.1), respectively, with modest internight reliabilities, ranging
from .58 to .79. Mean (3-nt) RDI correlated with age (r =.39, p < .005)
but not BMI (r =.24, p = .09). Mean (SD) BMI was 26.7 (4.0), suggesting
minimal obesity. RDI was higher among individuals who used cardiovas-
cular (CV) Rx or CV Hx (12.1 [10.7] vs 5.4 [7.4], t = 2.56, p < .02), but
not among those with Hx of poor voice control (t = .53, NS). Neither levo-
dopa (n = 27) nor dopamine agonists (n = 39) were associated with lower
RDIs. Prevalences exceeding RDIs of 5 (49%) or 15 (16%) events per
hour were comparable to threshold values reported for 50 and 60 year-
olds in SHHS.

**Conclusion:** These data do not suggest that idiopathic PD confers
increased risk for SDB, despite age-dependence and association with CV
disease. These patients had no overt autonomic dysfunction suggestive of
multi-system atrophy, which might be expected to impact breathing in
sleep adversely.

**AT-00611**

**0852**

**Epidemiological And Neuroradiological Features Of Restless Legs
Syndroms In Multiple Sclerosis**

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**Introduction:** Although Multiple Sclerosis (MS) is recognised to be often
associated with sleep complaints and with periodic legs movements dur-
ing sleep,1 no data are available about the possible coexistence between
Restless Legs Syndrome (RLS) and MS.

**Methods:** A prospective study, which included a consecutive MS patients
observed at the Neuroimaging Research Unit during the last year was car-
ried out. Each patient underwent a medical history interview, a neurolog-
ical examination with the assessment of the Expanded Disability Status
Scale (EDSS), a brain and cervical cord MRI, a structured telephone
interview to verify the presence of the standard diagnostic criteria for
RLS and the patient sleep habits. During MRI analysis, the following
variables were considered: global and regional (cerebral hemisphere, cérébelleum, brainstem) dual-echo lesion load, number of cervical cord
lesions, brain mean diffusivity (MD) and fractional anisotropy (FA) his-
tograms derived metrics of the normal-appearing white (NAWM) and
gray (NAGM) matter, MD and FA histograms metrics of the cervical
cord.

**Results:** Eighty-two subjects (mean age=43.2 SD 12.1; M/F=35/47) were
included in the study. Mean duration of MS was 10.7 SD 7.1 yrs, the
mean EDSS score was 4.2 SD 2.9. Twenty-seven patients resulted affect-
ed by RLS (prevalence rate 35.4%). In 7 patients (8.5%), the RLS preceded
the clinical MS onset, while in the remaining cases (24.4%) the RLS
followed or was simultaneous with the clinical MS onset. When compar-
ing the RLS group with the group without RLS, no significant differences
were found in MS duration, age, and gender. The primary progressive MS
course was more represented in the RLS group, which showed also an
higher EDSS score with a particular impairment of pyramidal system.
Among the MRI metrics analyzed, significant differences were found
between patients with and without RLS in terms of brain average FA of
the NAGM (significantly reduced in patients without RLS, p=0.01) and
cervical cord average FA (significantly reduced in patients with RLS,
p=0.02).

**Conclusion:** RLS symptoms are very common in MS patients. This form
of RLS should be considered as symptomatic. RLS seems to be associat-
ed with an higher disability of the pyramidal system, and with a progress-
ive MS course. Neuroradiological results demonstrated that the cervical
cord damage represents a significant risk factor for RLS among MS
patients.

References 1. Ferini-Strambi L, Filippi M, Martinelli V, Oldani A, 
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multiple sclerosis: correlations with clinical and brain magnetic reson-

**0853**

**Axonal Damage In Congenital Central Hypoventilation Syndrome
Revealed By Diffusion Tensor Imaging Procedures**

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**Introduction:** Congenital Central Hypoventilation Syndrome (CCHS) is
characterized by an impaired drive to breathe during sleep, reduced CO2
and hypoxia sensitivity, and aberrant autonomic control. Previous magnet-
ic resonance imaging studies showed neural tissue loss and functional
deficits in CCHS within regions containing fiber bundles or areas traversed
by fibers. Affected structures lay in critical regions for breathing and car-
diatic regulation, including fibers from cerebellar Purkinje areas to deep
nuclei, a set of structures which coordinate autonomic and somatic motor
outflow, and major fiber bundles interconnecting limbic structures involved
in cardiovascular control and the perception of breathlessness (air hunger).
We assessed possible axonal injury in CCHS patients using a technique
optimized for assessing fiber integrity, diffusion tensor imaging (DTI).

**Methods:** A set of 10 CCHS patients (15 ± 2.5 yrs) ventilatory-depend-
ent during sleep but not waking, and 20 age- and gender-matched control
subjects were subjected to DTI procedures in a Siemens 3.0T Trio scan-
ner. We evaluated fractional anisotropy (FA) maps, which provide an
assessment of the coherent organization and quantity of axons, voxel-by-
voxel. After spatial transformation, FA values at each voxel across groups
were compared using ANOVA (age as a covariate), with P < 0.05, correct-
ed for multiple comparisons (false discovery rate).

**Results:** Reduced FA values appeared in CCHS patients within multiple
areas that mediate breathing and cardiovascular control, including fibers
of the brachial conjunctivum, extending near the deep cerebellar nuclei,
the preoptic area, the dorsal caudal temporal lobe, a site which earlier
showed multiple functional deficits in CCHS blood pressure and breath-
ing challenges, a portion of the body and tail of the caudate nucleus, and
the amygdala.

**Conclusion:** The findings suggest that neural damage in CCHS partially
consists of a reduction or maldevelopment of axons between structures.
Communication between these structures would be altered, leading to
deficient physiological responses.

**HD-22695**
Cluster Headache Patients Have Normal Circadian And Sleep Time Autonomic Nervous System Function

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Introduction: Cluster headache (CH) is a rare primary headache with severe pain attacks associated with autonomic changes such as lacrimation, conjunctival injection, nasal congestion and rhinorrhea. Attacks are likely to occur during sleep and sleep related breathing disorders are recognized as a possible trigger. Time-frequency decomposition (TFD) of instantaneous Heart Rate Variability (HRV) is a widely accepted non-invasive tool of investigation of the autonomic nervous system providing the following: VLF - vasomotor, LF - both sympathetic and parasympathetic, HF - mainly parasympathetic activity and LF/HF - sympathovagal balance. Our objective was to estimate the autonomic features of CH and their connection to sleep.

Methods: Subjects: (1) 10 with episodic CH during an attack period, (2) 8 patients during a quiet period, (3) 3 normal volunteers. All subjects were males with similar age, BMI and smoking history. All completed a sleep diary, and underwent continuous 24h ECG recording. TFD was applied to the ECG, and spectral components and mean heart rate (HR) were obtained for the 24h period and for bedtime.

Results: No significant difference between groups was found in mean HR, VLF, LF, HF and LF/HF, when those variables were compared for the overall 24 hours recording time and for the bedtime. In all groups mean HR decreased significantly during bedtime, irrespective of the occurrence of episodes during sleep. VLF, LF and HF increased while LF/HF decreased significantly in all subjects during bedtime. The change in LF/HF was more accentuated (not significantly) in patients.

Conclusion: No difference in autonomic function was detected in cluster headache patients during quiet or exacerbation periods. All groups presented significantly lower mean HR and predominantly parasympathetic autonomic balance during bedtime. Episodic surges in HR and VLF suggest that some subjects might have sleep-related breathing disorder and this correlates well with the BMI. Although CH episodes present with autonomic features, patients have no significant abnormality in circadian and sleep autonomic function.
0855
Using The Epworth Sleepiness Scale As Screening Tool For Sleepiness In Sarcoidosis
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Introduction: Sarcoidosis, a granulomatous disease of unknown etiology that involves multiple organ systems, often presents with constitutional symptoms such as somnolence. Fatigue or disturbed sleep, while common complaints, are often sub-optimally addressed due to clinicians’ need to focus on more life-threatening medical issues. The true incidence of fatigue in Sarcoidosis is unknown but has been estimated to vary between 30-70% (OP Sharma). In addition, Turner et al, in a series of 83 consecutive patients with Sarcoidosis, diagnosed sleep apnea in 17%. The goals of this study are to determine the prevalence of Excessive Daytime Somnolence (EDS) in patients with Sarcoidosis.

Methods: The Epworth Sleepiness Scale (ESS) is a self-administered eight-item questionnaire that is a measure of EDS. Subjects with an ESS >9 are categorized as meeting criteria for EDS (Johns et al). It also been subsequently validated as a good screening test for Sleep Disordered Breathing (SDB). The Division of Pulmonary Diseases of The Mount Sinai School of Medicine administered the Epworth Sleepiness Scale (ESS) to 451 patients with biopsy-proven sarcoidosis.

Results: One-hundred and three subjects (22.8%) had an ESS > 9. Eight of these patients underwent NPSG for symptoms consistent with SDB. All of the patients who screened positive on ESS for SDB and who underwent NPSG’s were found to have sleep apnea. The average ESS of these 8 patients with OSAS with ESS > 9 is 12.1.

Conclusion: Based on the results of this study 22% of subjects with biopsy-proven sarcoidosis manifest EDS as defined by an ESS > 9. Sleepiness is underrecognized in this population. Of the 8 patients who underwent NPSG, all were found to have OSAS. We plan to perform additional NPSG’s on a larger sample of patients with sarcoidosis to clarify the role of ESS as an inexpensive and facile screening tool for SDB in this patient population.

0856
Impaired Slow-Wave Activity Response To A 4-Hour Sleep Delay In Chronic Fatigue Syndrome: Preliminary Findings Of A Monoyzotic Co-Twin Control Study
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Introduction: Chronic fatigue syndrome (CFS) is a disorder of unknown etiology. Unrefreshing sleep is one criterion in the case definition for CFS but the pathophysiological basis of this symptom is not clear. In our previous study of CFS discordant monozygotic (MZ) twins we observed few differences in standard polysomnography derived variables. In this follow-up study, we used a sleep delay challenge to test the integrity of sleep homeostatic mechanisms in CFS.

Methods: Fourteen sets of MZ twins discordant for CFS participated in the study. Habitual sleep time was established for each twin pair from 2-week sleep logs. Each set of twins spent 3 consecutive nights in the lab: one adaptation night, one baseline night, and one sleep delay night. On the third night bedtime was delayed by 4 hours. Polysomnography was scored visually according to standard criteria. Central and parietal EEG data were digitized and subjected to power spectral analysis to determine slow-wave activity (SWA). Data were partitioned into successive NREM periods (successive epochs of stage 2,3 or 4) according to previously published criteria. Currently, complete data are available on 9 pairs of twins. Repeated-measures ANOVA were computed on SWA power with health status (CFS or healthy) and baseline versus delay as within-subject measures.

Results: There were no significant differences in sleep architecture or efficiency on the baseline night and no significant twin by delay interaction in mean slow-wave (stage 3 + 4 min) sleep time (F=2.95, df=1,8, p=.12). SWA did differ between twins. The healthy twins showed the expected SWA enhancement in response to sleep delay, with an approximate 300 mV increase in SWA in the first NREM period. In contrast, the CFS twins SWA was reduced by 100 mV in response to the sleep delay. ANOVA revealed a significant CFS effect on SWA after sleep delay (F=8.04, df=1,7, p<0.03); and the twin by sleep delay interaction approached significance (F=4.4, df=1,7, p<0.08). More detailed analysis of the time course of SWA in each set of twins is underway.

Conclusion: These preliminary findings suggest the homeostatic sleep drive is impaired in CFS. Impaired sleep drive may relate to subjective complaints of poor sleep in patients with CFS.

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0857
Increased Fatigue In Breast Cancer Patients Is Related To Desynchronized Circadian Rhythms During Chemotherapy
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Introduction: Breast cancer patients often experience fatigue before, during, and after chemotherapy. A few studies have suggested a relationship between circadian rhythms and fatigue. As a part of larger study on fatigue, sleep and circadian rhythms in breast cancer patients, we report the results of fatigue, circadian rhythms, and their correlations from data collected before and during cycle 1 of chemotherapy.

Methods: Forty women diagnosed with stage I to IIIA breast cancer, scheduled to receive at least 4 cycles of adjuvant or neoadjuvant anthracycline-based chemotherapy were studied. Fatigue was assessed using the Short Form of Multidimensional Fatigue Symptom Inventory (MF-SI-SF). Sleep/wake (rest/activity) circadian rhythms were recorded with wrist actigraphy (AMI).

Results: Cancer patients reported significantly (p=0.0005) more fatigue during the 3 weeks of chemotherapy than before treatment, with reports of fatigue deteriorating on the total MF-SI-SF and on the General, Physical, Mental, and Vigor subscales from before the start of chemotherapy to cycle 1. Circadian rhythms were synchronized before chemotherapy, but became desynchronized during chemotherapy, specifically in measures of amplitude, minimum, slope, and F-statistic. Both fatigue and circadian rhythms significantly improved during week 3 compared to week 1 within cycle 1 (all p<0.05). Fatigue was significantly correlated with measures of circadian rhythm desynchronization (particularly with acrophase, amplitude and minimum), and with a more delayed circadian phase (t=0.38, p=0.016).

Conclusion: Although cause and effect can not be determined from these data, fatigue and circadian rhythms were related, with correlations sug-
In the model.

These findings can provide a foundation for ostomy-specific interventions to improve quality of sleep and fatigue. These findings can provide a foundation for ostomy-specific interventions to improve quality of sleep and fatigue. These findings can provide a foundation for ostomy-specific interventions to improve quality of sleep and fatigue. These findings can provide a foundation for ostomy-specific interventions to improve quality of sleep and fatigue.

Supported by a grant (IIR 02-221-2) from the health Services Research and Development Service, Department of Veterans Affairs (R. Krouse) and, in part, NIH NHLBI cooperative agreement U01HL53938-07S1 (CM Baldwin).
bidity were migraines (30%), hypertension (22%), asthma (20%), depression (18%), GERD (17%), hypothyroidism (13%), arthritis (10%), chronic low back pain (6%) and diabetes (6%). Sixty-eight percent of patients were on antidepressants for treatment of fibromyalgia or depression. The PSG data showed a mean sleep latency of 21 minutes (0 to 105 minutes). The mean % of slow wave sleep was 5.5% (0 to 30%). The average % of REM sleep was 14.5%. The mean sleep efficiency was 76% (17 to 98%). Obstructive sleep apnea (OSA) (AH1>5/hr sleep) was present in 81% of the patients (24% with mild OSA, 35% with moderate and 22% with severe OSA). Mean AH1 was 22.5 events/hr sleep (0 to 144). Periodic limb movements in sleep (PLMS) were seen in 54% of patients, 30% of whom had an arousal PLMS index >5/hr sleep. PSG data of 92 patients was available for evaluation of measurable alpha delta sleep. This pattern was present in 18%.

Conclusion: Patients with FM have an increased prevalence of intrinsic sleep disorders. Our data supports that a thorough sleep history should be obtained in all patients with FM with a polysomnogram if clinically indicated. Specific treatment for concomitant sleep disorders may improve quality of life in this patient population. A prospective trial to determine this effect is ongoing.

0861 Is CPAP An Effective Treatment For Gastroesophageal Reflux Disease?
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Introduction: Patients with obstructive sleep apnea (OSA) have a very high incidence of gastroesophageal reflux disease (GERD). Previous studies have shown that the use of continuous positive airway pressure (CPAP) reduces the frequency of reflux events, but the studies only assessed the effect of a single night of treatment. The aim of this study was to assess the effect of one week of CPAP treatment on gastroesophageal reflux in patients with objectively documented OSA and GERD.

Methods: Sixteen patients with suspected OSA and GERD were recruited. Polysomnography (PSG) and 24-hour continuous esophageal pH monitoring were performed at baseline. Patients with an apnea-hypopnea index (AHI) > 20 per hour and a 24-hour acid contact time of at least 6% were included. As part of the PSG qualifying evaluation, all patients had a CPAP titration to reduce the AHI to < 10 events/hour. Patients were then sent home on nasal CPAP for one week. After approximately seven nights of CPAP treatment, the PSG and esophageal pH monitoring were repeated.

Results: The average AHI was reduced from 59.4 to 2.5 (p < .001). The total acid contact time (ACT) was reduced from 13.9% to 5.6% (p < .001). The upright ACT was reduced from 12.4% to 6.8% (p < .05), and the supine (during the sleeping interval) ACT was reduced from 16.3% to 3.8% (p < .01). 81% of the patients had a reduction in supine ACT to within the normal range (less than 4%).

Conclusion: One week of treatment with CPAP did reduce GER during the sleeping interval, as well as during wakefulness. In OSA patients with significant heartburn complaints, CPAP would appear to be an efficacious approach to the treatment of both disorders.

0862 Association Between Enhanced Pain Perception And Sleep Disturbance
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Introduction: Ample clinical and empirical evidence has shown that sleep disturbance is often associated with enhanced pain sensitivity. Nevertheless, the basic mechanisms underlying the relationship between sleep and pain are not clearly understood. Measures of pain perception include quantitative sensory testing (QST), and personality characteristics such as pain catastrophizing, that influences the emotional and cognitive aspects of pain processing. Indeed, pain complaints and catastrophic worry about the consequences of disturbed sleep are common phenomena among patients with primary insomnia. Only few studies have evaluated the association between pain processing and sleep quality using advanced psychophysical measures. The present pilot study aims to evaluate the relationships between sleep disturbance, perception of noxious stimuli and pain catastrophizing in healthy individuals.

Methods: The study included a sample of 27 healthy men and women, (mean age 35.1±13.7). Sleep quality was measured by the Pittsburgh Sleep Quality Index (PSQI). Pain perception was assessed via QST using a thermal sensor analyzer including heat pain threshold and magnitude estimation of supra-threshold phasic painful stimuli at an intensity of 47°C (TSA 2001) (Medoc, Israel). The painful stimuli were applied to the forearm. The level of catastrophizing was assessed by the Pain Catastrophizing Scale (PCS).

Results: Pearson correlation coefficient revealed that sleep disturbance was negatively correlated with heat pain threshold (r= -0.48, p=0.020), and positively correlated with enhanced pain scores for the supra-threshold phasic stimuli (r=0.426, p=0.043). In addition, higher sleep disturbance was associated with greater level of pain catastrophizing (r=0.54, p=0.016).

Conclusion: Increased pain sensitivity and catastrophizing may be associated with greater sleep disturbance. Pain reactivity as well as sleep quality may both be attributed to psychological and physiological hyperarousability. Further studies are needed to explore the role of sensory hyperarousability as a possible underlying mechanism that bonds disturbed sleep and pain.

0863 Attitudes Towards Cancer And Sleep Complaints In A Community-Based Sample
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Introduction: This study investigated the association of sleep complaints and cancer concerns in an ethnically diverse sample.

Methods: We recruited 1440 women for the study (White=25%, mean age=60.09 ± 6.29 yrs; Black=63%, mean age=59.27 ± 6.66 yrs; and Hispanic=12%, mean age=58.30 ± 6.17 yrs). We conducted an interview assessing cancer concerns with the Cancer Attitude Inventory. This addressed concerns about developing breast cancer, thinking about personal risk of developing cancer, concern about how it affects daily activities, and how it affects moods. Data on history of cancer and tumor/abnormal growth were also provided. We assessed sleep complaints with the sleep disorder subscale of the Comprehensive Assessment and Referral Evaluation.

Results: Of the sample, 5% reported a history of cancer (breast or others) and 18% reported having had an abnormal growth or tumor. Altogether, 60% reported being concerned about developing breast cancer, 29% indicated that they thought about personal risks of cancer every day. Of those concerned about cancer, 37% indicated that it affected their daily activi-
ties and 41% indicated that it affected their mood. Of those reporting that they thought about personal risk of cancer every day, 45% indicated that it affected their daily activities and 51% indicated that it affected their mood. Regarding insomnia complaints, 56% reported either DIS, DMS, or EMA. Women reporting a cancer history had greater insomnia complaints than those who did not [76% vs. 55%; χ² = 12.36, p < 0.001], and women who reported an abnormal growth also reported greater insomnia complaints [77% vs. 52%; χ² = 58.07, p < 0.001]. The rate of insomnia complaints was also significantly greater among women reporting being concerned about cancer [61% vs. 49%; χ² = 20.01, p < 0.001] and among those thinking about personal risk of cancer every day [70% vs. 50%; χ² = 49.56, p < 0.001].

Conclusion: These findings support previous reports on sleep complaints among cancer patients. Interestingly, cancer concerns, expressed either as anxiety about developing cancer or worry about personal risk factors, were associated with insomnia complaints. This study suggests that there is a strong likelihood that even individuals who have had an abnormal growth or tumor might experience sleep difficulties. Thus, approaches to provide supportive therapy to alleviate sleep problems should be directed not only at cancer patients but also at individuals with abnormal findings based on screening tests.

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0864

SWS In Napping And Subsequent Nocturnal Sleep Among Women With Significant Premenstrual Symptoms

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Introduction: Women with severe premenstrual symptoms tend to have a more disturbed sleeping pattern and higher daytime sleepiness during the late-luteal phase of their cycle, compared to women with minimal symptoms. The goal of this study was to examine the potential beneficial effects of a mid-afternoon nap among women with severe symptoms. More specifically, we report here on whether the presence of SWS in naps has an effect on the SWS of subsequent nocturnal sleep.

Methods: Four women (age range 25 to 35) with severe premenstrual symptoms, according to the Premenstrual Tension Rating Scale, and who were not using any contraceptive medication and had regular and ovulatory menstrual cycles, participated in this study. These women took a mid-afternoon nap of a maximum of 30 minutes during the late-luteal phase of their cycle, and returned to the laboratory that night for a nocturnal sleep recording. A second nocturnal sleep recording was performed during the late-luteal phase, on a day that participants had not taken a nap.

Results: The naps contained an average of 11.75 minutes of SWS. The number of minutes of SWS during nocturnal sleep was not significantly different when participants took a nap (mean 77.1 min) compared to when they did not take a nap (mean 85.9 min) (p > .05). More specifically, one participant showed a marked increase, two showed a marked decrease and one did not change. Similarly, onset latency of SWS was not significantly different between these two conditions (mean 20.6 and 15.6) (p > .05) and followed the same pattern as for the amount of SWS.

Conclusion: While data obtained from more participants will provide a better picture, these results suggest that a mid-afternoon nap containing SWS, taken during the late-luteal phase of the cycle by women with severe emotional premenstrual symptoms, does not consistently affect SWS of the subsequent night, while potentially counteracting the effect of daytime sleepiness.
were screened for anxiety with the State/Trait Anxiety Scale (STAI) and depression with Beck's Depression Inventory (BDI), after completing a number connection test (NCT-A) to screen for encephalopathy. As controls, twelve chronic renal failure patients (ages 37-79) followed the same protocol.

Results: Individual diagnostic components of the GSAQ were not significantly different but the composite mean scores (23.9 vs. 29.2) showed poorer sleep quality for cirrhotics (p=.029). Total sleep time and daytime fatigue were not significantly different (p=.17, p=.27), yet cirrhotics rated their sleep quality significantly lower (means .67 vs. 1.55, p=.029) on the sleep logs and the ESS (means 7.92 vs. 13.6, p=.005).

Conclusion: Patients with liver cirrhosis consistently reported poorer sleep quality than the control group. However, both groups had very similar total sleep times and daytime fatigue ratings, and indistinguishable sleep disorder diagnostic ratings. These results indicate the possibility of a direct relationship between sleep disturbance and liver cirrhosis which could be confirmed by further physiological sleep studies.

0867 Effect Of Smoking On Smoker's Subjective Quality Of Sleep
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Introduction: Little is known about the effects of smoking and sleep. We studied tobacco cessation and its impact on participants' subjective quality of sleep. We hypothesized that smoking was associated with disturbed sleep architecture and hence heavy smokers will report subjectively poor quality of sleep.

Methods: A smoking cessation program consisting of six weekly sessions that emphasize behavior modification and pharmacologic interventions. Data was collected from questionnaires focusing on smoking, medical history, and self-assessment of sleep patterns. A Likert scale of 1-5 (1=poor sleepers) was used to assess sleep quality before and after quitting. Epworth Sleepiness Scale, Fagerstrom Scores and sleep quality after quitting were compared in smokers with poor and good sleep at night before quitting. Quit status was confirmed with CO levels. Continuous factors were compared using the Mann-Whitney test. Data are presented as mean±SD. Associations between sleep groups and categorical factors were examined using the Fisher's Exact test.

Results: 402 Participants (210 poor sleepers; 192 good sleepers; before quitting) were studied. CO levels varied from <20 to 73 PPM on day one. There was no significant difference between poor and good sleepers for age(46±11.7 vs 47.9±12.6), carbon monoxide levels(23.0±12.7 vs 21.2±12.2) or ESS (7.3±5.5 vs 6.8±5.5) at pack years. Poor sleepers had higher Fagerstrom Scores (6.0±2.4 vs 5.3±2.4; p<0.01) and were more likely to report alcohol/substance abuse (9.5% vs 3.1%; p<0.02). Poor sleepers were also more likely to report daytime sleepiness (60.1% vs 41.0%; p<0.001) and waking up in the night to smoke (33.2% vs 12.2%; p<0.001). There was no difference in self-report of cardiac morbidities. Poor sleepers were more likely to self-report depression/use of anti-depressants (24.3% vs 15.1%; p<0.03). They were more likely to smoke their first cigarette within 30 minutes of waking (81.4% vs. 69.6%; p<0.01). They were more likely to smoke if ill in bed (62.9% vs. 48.7%; p<0.005) and more likely to smoke >20 cigarettes per day (54.3% vs 41.8%; p<0.02).

Conclusion: The reported sleep quality correlates with severity of addiction as measured by Fagerstrom Scores. It is possible that nocturnal nicotine craving is the reason behind smoker's propensity to wake up in the night to smoke. The qualitative effects of pharmacological agents (nicotine replacement therapy) used for tobacco dependence and their effect on sleep need further investigation in terms of preventing the nocturnal awakenings observed amongst smokers.

0868 Sleep And Subclinical Cardiovascular Disease: The Swan Heart Study
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Introduction: Many otherwise healthy persons who complain of sleep disturbances fear that poor sleep will have detrimental effects on their health. In fact, sleep disturbances and disorders may be associated with earlier onset of subclinical cardiovascular disease (SCD). However, the effect of sleep on SCD could be related to confounding factors associated with sleep that also contribute to cardiovascular morbidity. We examined whether sleep is associated with indices of SCD above and beyond hormones and other sociodemographic, lifestyle and health variables in a cohort of middle-aged women.

Methods: This cross-sectional analysis was designed to examine the relationship between self-reported sleep and indices of SCD in a sample of 170 African-American and 318 Caucasian women, aged 45-58 years (mean±SD=50.3±2.8), participating in SWAN Heart, an ancillary study involving participants at the Chicago and Pittsburgh sites of the Study of Women's Health Across the Nation (SWAN). Sleep was measured with the Pittsburgh Sleep Quality Index (PSQI) global score. SCD measures included carotid intima-media thickness (IMT), common carotid adventitial diameter (CDIAMA), and aortic (Ascore) and coronary artery (Cscore) calcification. Covariates included ethnicity, a measure of androgen excess, age, study site, education, Framingham Risk Score, body mass index (BMI), physical activity score, smoking, and chronic medical conditions. We used linear regression models to assess the relationship between the PSQI score and IMT and CDIAMA measures. A survival type of analysis was used to assess the relationship between the PSQI score and the 2 calcium scores.

Results: The mean PSQI score was 6.0±3.6. The ethnicity-adjusted PSQI score was significantly associated with IMT (p<0.04), CDIAMA (p<0.003), and Ascore (p<0.001), but not with the Cscore (p=.18). However, after multivariate adjustment, the PSQI score was only marginally associated with CDIAMA (p<0.07) and not significantly associated with the other three SCD measures. In the adjusted models, BMI was highly significantly associated with all four measures of SCD (all p<0.001) and the Framingham Risk Score was significantly associated with CDIAMA (p<0.04) and Ascore (p<0.007).

Conclusion: Sleep may not have a direct effect on measures of SCD. However, sleep disturbance may exert an indirect effect that is mediated by other health factors.

The Study of Women's Health Across the Nation (SWAN) was funded by the National Institute on Aging, the National Institute of Nursing Research, and the National Institutes of Health Office of Research on Women's Health. SWAN-Heart was funded by the National Heart, Lung, and Blood Institute.
Introduction: Atrial fibrillation (AF), one of the most common cardiac arrhythmias, is associated with a number of disabling symptoms. Among the most common are disrupted sleep and inactivity, problems that can be mutually perpetuating. Thus, the purpose of this preliminary study was to describe and examine relationships among nocturnal sleep, daytime sleepiness, and activity patterns in a sample of these patients.

Methods: A convenience sample of nine patients (5 males and 4 females; mean age 70.2 ± 13.6) with a history of permanent AF was recruited from an anticoagulation clinic. Participants wore a wrist actigraph for 96 hours. At the end of the monitoring period, subjects also completed the Epworth Sleepiness Scale (ESS; range 0 to 24; high score=greater daytime sleepiness) and the Pittsburgh Sleep Quality Index (PSQI; range 0-21; high score=greater sleep disturbance). Descriptive statistics and correlations (Spearman’s rho; rs) were computed.

Results: Mean (± SD) scores were: 7.9 ± 2.8 for the ESS (22.2% > 10 indicating significant sleepiness), and 8.6 ± 2.6 for the PSQI (89% > 5 indicating significant sleep disturbance). The mean total nocturnal sleep time was 384.9 ± 71.0 minutes with a mean sleep efficiency of 89.1 ± 6.8%. The mean sleep latency was 12.6 ± 11.7 minutes. In comparison to normative data, daytime activity level (mean 114.0 ± 100.7 counts per 1-minute epoch) was decreased and nighttime activity level (19.3 ± 18.2) was increased. A higher score on the PSQI was significantly associated with increased nighttime activity (rs = 0.812, p = .014). No significant relationships were noted between ESS and daytime or nighttime activity or between PSQI and daytime activity.

Conclusion: These preliminary results suggest that sleep/wake and activity pattern disturbances are prevalent in patients with AF and may be related. Further examination of these relationships is warranted in order to develop targeted interventions designed to improve clinical outcomes.

Sleep Disruption In Breast Cancer Patients Post-Chemotherapy

Introduction: Women with breast cancer often report disturbed sleep but there have been few objective sleep studies. Additionally, it is unknown if specific sleep disorders, such as periodic limb movements in sleep (PLMS) or sleep apnea contribute to the reported disturbed sleep. This study looked at sleep disorders in women just completing chemotherapy for breast cancer.

Methods: Thirty six women (mean age=51.2 years, SD=10.5) diagnosed with stage I to IIIA breast cancer, scheduled to receive at least 4 cycles of adjuvant or neoadjuvant anthracycline-based chemotherapy were studied. Fatigue was assessed using the Short Form of Multidimensional Fatigue Symptom Inventory (MFSI-SF). Objective sleep was recorded using wrist actigraphy (AMI, Ardsley, NY). Data from 4 time points were reported: before and during week 1, week 2, and week 3 of cycle-one chemotherapy. All subjects had both fatigue and actigraphy sleep data for all of the four time points.

Results: During the first week of cycle 1 chemotherapy compared to before treatment, women reported significantly more General fatigue (p=0.0098), and based on actigraphy were significantly less alert during the day with less time spent awake (p=0.0015) and longer naps (p=0.0065). During treatment, more Physical, Emotional and Mental fatigue and less Vigor were significantly correlated with more daytime sleep and longer nighttime wake duration (r values 0.33-0.48; p values 0.047-0.0028).

Conclusion: Increased fatigue is associated with increased napping during the day and more awakenings at night during chemotherapy among breast cancer patients. Cause and effect can not be determined from this study; however, studies examining the effect of improving night time sleep on daytime fatigue may be warranted.

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0872
Unique REM Rebound Following Sleep Restriction In Fibromyalgia Patients Compared To Rheumatoid Arthritis And Healthy Controls
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Introduction: Due to reports that patients with fibromyalgia (FMS) have increased wakefulness during sleep and increased alpha intrusion during sleep, FMS is hypothesized to be a disorder of hyperarousal. To test this hypothesis we challenged FMS and rheumatoid arthritis (RA) patients with sleep restriction and examined aspects of recovery sleep.

Methods: Thirteen FMS, 6 RA, and 5 healthy, normal controls (NC) completed a sleep diary at home for 2 weeks and were then compared in the lab for 4 nights of PSG: Night 1 = lab adaptation (8 hours TIB), Night 2 = baseline (8 hours TIB), Night 3 = sleep restriction (bedtime delayed by 4 hours and limited to 4 hours TIB), and Night 4 = recovery (8 hours TIB).

Results: There were no differences between the groups on Nights 2 and 3 in terms of total sleep time (TST), minutes of REM (REM m) or stage REM as a percent of TST (REM %). On Night 4 there continued to be no significant group differences in TST (FMS = 436 minutes, RA = 410 minutes, and NC = 432 minutes). However, on Night 4, FMS patients had significantly more REM m (FMS = 116, RA = 69, and NC = 95) and REM % (FMS = 26%, RA = 17%, and NC = 22%). In post-hoc comparisons of REM m and REM %, FMS patients differed significantly from RA (REM m p = .002 and REM % p = .004) and NC (REM m p = .04 and REM % p = .03). Finally, for FMS patients, Night 4 REM m and REM % were significantly elevated relative to their own Night 2 values (p = .001 and p = .003 respectively).

Conclusion: These data show a REM rebound after 1 night of sleep restriction in FMS patients but not in RA or NC. FMS patients are super sensitive to the loss of REM sleep.

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0873
Fatigue, Pain And Sleep EEG Cyclical Alternating Pattern (CAP) In Chronic Post SARS Vs. Fibromyalgia Syndrome
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Introduction: Patients who remain disabled following Severe Acute Respiratory Syndrome (SARS) report persistent fatigue, generalized myalgia and nonrestorative sleep. We hypothesized that chronic post SARS subjects share similar EEG sleep and somatic features with fibromyalgia syndrome (FMS).

Methods: 11 female healthcare workers (mean age 48 ± 12y.) with persistent impaired health 12 to 17 months after hospitalization/quarantine for SARS (mean duration =20 ± 9 days) were compared to aged-matched female FMS subjects (n=19, mean age 42.4 ± 11.8 y.) with standard self-rating scales of musculoskeletal pain (0-30), fatigue (1-7) and sleepiness (6.1 ± 4.2, vs. 10.9 ± 5.7, p<.0005) and post-sleep (5.5 ± 4.5, vs. 11.8 ± 6.5, p<.0005) and less pre-sleep sleepiness (2.8 ± 1.1, vs 4.3 ± 1.1, p<.01) they had similar moderate sleepiness post-sleep (3.4 ± 1.9, vs. 3.9 ± 1.1, n.s.). The high CAP rate of post SARS and FMS (mean = 71.2 ± 13.4, vs. 70.4 ± 15.6, n.s.) is similar to the findings in FMS by Rizzi M et al, 2004 (mean 68 ± 6, vs. 45 ± 11 in controls, p<.001). There were no other differences between the groups in any other measure of sleep including stages, respiration, and movements.

Conclusion: Chronic post-SARS is similar to fibromyalgia in severity of fatigue, nonrestorative sleep with elevated sleep EEG CAP rate, but with less musculoskeletal pain as in patients with Chronic Fatigue Syndrome.

0874
Fatigue, Muscular Symptoms And Disordered Sleep In Chronic Post Sars
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Introduction: Severe Acute Respiratory Syndrome (SARS) emerged as a major global health problem in early 2003 with 247 probable SARS cases and 44 deaths occurring in Ontario. Although there were no new cases after June 2003, health problems persisted in a cohort of SARS patients. This is the first report of the long-term effects of SARS on sleep, somatic and mood symptoms.

Methods: 11 of 18 female health care workers (mean age 48 ± 12y., B.M.I. = 26 ± 5.9), who were 12 to 17 months after hospital care and/or quarantine for SARS (mean duration = 20 ± 9 days) and had persistent impaired health, participated in the study of their sleep and symptoms. The Post SARS group were compared to a healthy group of 8 females (mean age 30 ± 6.7 y., B.M.I.= 24.8 ± 6.1) by employing standard self-ratings on the Whaler Physical Symptom Inventory (WPSI), Beck Depression Inventory (BDI), the Sleep Assessment Questionnaire (SAQ), and of pain, fatigue and sleepiness before and after an overnight polysomnography, followed by the MSLT. Bonferroni corrections were performed on the multiple t-tests.

Results: Post-SARS subjects reported more symptoms on the WPSI (mean 10.6 ± 5.0 vs. 0.4 ± 0.5, p<.0001) having tiredness, difficulty sleeping, myalgia and muscular weakness on most days. They had more depressive symptoms (B.D.I. mean = 13.3 ± 9 vs.0.86 ± 1.5, p<.0001), more sleep disturbances on the SAQ (mean = 30.9 ± 5 vs 10.9 ± 3.4, p<.0001), more fatigue post-sleep (p<.05), and more myalgia pre- and post-sleep (p<.01). Post SARS subjects showed a higher REM related apnea/hypopnea index (mean 14.5 ± 14.5, vs. 0.0, p<.01) and more alpha EEG sleep (1.5, mean = 2.9 ± 0.5 vs.1.6 ± 0.8, p<.005). Five post SARS subjects had variable sleepiness on the MSLT. Bonferroni corrections were performed on the multiple t-tests.

Conclusion: Chronic post-SARS is characterized by persistent fatigue, myalgia, weakness, depression, and nonrestorative sleep with associated REM related apneas/hypopneas and alpha EEG sleep disorder. These clinical and sleep features of chronic post SARS are similar to chronic fatigue syndrome/fibromyalgia.

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0875
Sleep Disruption In Lung Cancer Survivors Compared To Noncancer Controls
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Introduction: Sleep disruption is a common complaint amongst lung cancer survivors, yet little is known about this condition. We examined sleep parameters in long-term elderly lung cancer survivors relative to elderly noncancer controls.

Methods: Lung cancer survivors at least 5 years from diagnosis (N=76) and noncancer controls (N=48) participated. The Pittsburgh Sleep Quality Index (PSQI), demographic and additional questions were completed by telephone survey.

Results: Among the 124 participants, the mean age was 74 (SD=6.6; range=61-89), with 64% female, and 90% Caucasian. Mean lung cancer survival was 7.8 years (SD=1.6; range=5-11); 89% received surgery only. Lung cancer survivors (LCS) spent more hours in bed (8.7 vs. 7.7, p<.006), despite spending a similar amount of time asleep (6.5 vs. 6.8, p=0.24); they thus had a markedly lower sleep efficiency (77% vs. 89%, p<.001). Global PSQI was significantly higher in LCS (5.9 vs. 4.5, p<.04), consistent with poorer sleep quality in LCS. Sleep latency was similar (24 min vs. 22 min, p=.71). LCS reported using medication to help them sleep more often than NCC (p<.001). LCS had more problems with sleep latency, nocturnal awakenings, nocturia, dyspnea, coughing/snor- ing, and legs twitching/jerking compared to NCC (p<.05). LCS had more sleep disruption from pain or feeling too hot than LCS (p<.05). Dyspnea was significantly worse in LCS (2.6 vs. 1.3, p<.03) while pain was significantly worse in NCC (3.3 vs. 2.1, p<.04). However, the amount of distress from sleep difficulties in LCS, while higher than NCC (analog scale, 2.6 vs. 2.4, p=.62) was not significantly different.

Conclusion: These results demonstrate robust differences in sleep parameters between LCS and NCC. While sleep efficiency showed prominent differences between groups, differences of a smaller magnitude were documented as the most common cause of transient or short-term insomnia, which plays an important role in health status. The aim of this report was to describe the hemodialysis patients' objective and subjective sleep disturbances and the relationship to stress levels.

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0877
Perceived Stress And Sleep Disturbances Among Hemodialysis Patients: A Preliminary Report
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Introduction: Sleep disturbance is a common complaint among hemodialysis patients, yet studies in hemodialysis patients' sleep problems focused on psychosocial stress are rare, although stress has been documented as the most common cause of transient or short-term insomnia, which plays an important role in health status. The aim of this report was to describe the hemodialysis patients' objective and subjective sleep disturbances and the relationship to stress levels.

Methods: As part of a randomized clinical trial, data was collected in a nine-month period. This analysis reports on the 14 hemodialysis patients during their first three months, pre-randomized phase data. Three sets of data were collected: 1) demographic data, 2) Perceived Stress Scale (PSS), Hemodialysis Stressor Scale (HSS), and Pittsburgh Sleep Quality Index (PSQI), and 3) total sleep time (TST) and sleep efficiency (SE) averaged from five nights of wrist actigraphy monitoring.

Results: All 14 subjects were African-American with a mean age of 57.9 (SD=42.2); mean scores for the HSS and PSS were 52.21 (SD=23.3) and 12 (SD=6.1) respectively. The total score of HSS was significantly correlated with PSS (r=59, p<.03). Average SE over the five nights was 68.35% (SE= 5.78), and the average TST was about six hours (M=305.5minutes, SE= 31.74). The global PSQI score was 5.29 (SD=3.69), indicating severe sleep disturbance. Patients who scored a higher HSS reported a higher global PSQI score (r=.67, p<.01) and a higher sleep disturbance from the PSQI (r=.58, p<.03). Patients who perceived higher global stress scores (PSS) reported a lower sleep quality in the PSQI (r=.65, p=.01). From the actigraphy data, a higher HSS score was correlated with lower SE (r=.63, p<.02) and less TST (r=.85, p<.001).
Conclusion: The preliminary data suggest an important relationship between stress and sleep quantity and quality.

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0878
National Nocturia Survey
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Introduction: The objective was to analyse nocturia prevalence and features of a representative sample of the French population with nocturia aged between 18 and 65.

Methods: A cross-sectional survey conducted by phone between December 2003 and January 2004 on a sample of 4,331 individuals. Epworth self-administered questionnaire was used to assess effects on sleepiness.

Results: The prevalence of nocturia was found to be 23.6%, higher in women (25.8%) than in men (21.0%). Prevalence rises steadily with age, from 13.5% to 42.9%. Among individuals with nocturia, 12.4% got up twice on average, 4.4% got up three times and 0.9% got up four or more times. Overweight and obesity are more frequent in nocturia group vs controls (p<0.05). More people experience difficulties falling sleep, staying asleep or having non-refreshing sleep at least 3 times a week and note impacts in everyday life in nocturia group (p<0.001). People with nocturia experience more pathological or severely pathological daytime sleepiness. 19.5% have a pathological Epworth score (>10), compared with 10% in the control population (p<0.001) and 5.0% have a severely pathological score (>15) compared with 1.0% (p<0.001). People with nocturia use healthcare services and medication at higher rates than those who do not have nocturia: 20.2% of them take psychotropic drugs compared to 3.8% of people who do not have nocturia (p<0.001). People with nocturia experience more pathological or severely pathological daytime sleepiness. 19.5% have a pathological Epworth score (>10), compared with 10% in the control population (p<0.001).

Conclusion: The prevalence of nocturia rises with age and is higher in women only up to the age of 50. Sleep complaints and an increase of BMI are more frequent in nocturia. People with nocturia experience more daytime sleepiness than people who do not wake up in the night. They also use healthcare services and take psychotropic drugs at higher rates.

0879
Correlates Of Excessive Daytime Sleepiness In Asthma
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Introduction: Prior studies have shown a high prevalence of excessive daytime sleepiness (EDS) and sleep disruption in asthma, but the underlying reasons are not well known. We hypothesized that unrecognized sleep-disordered breathing (SDB) may contribute to EDS in asthma.

Methods: Patients at routine appointments for follow-up at a tertiary Asthma Clinic, and not under treatment for SDB or other lung conditions, completed the Sleep Apnea scale of Sleep Disorders Questionnaire (SA-SDQ, Douglas et al, 1994), Epworth Sleepiness Scale (ESS), question items about asthma symptom frequency (National Asthma Education and Prevention Program guidelines), and peak flow measurements (for prior 2 months). Medical records were reviewed to identify asthma severity (step 1 to 4), comorbid diagnoses, and medications.

Results: Among the 99 subjects, age (mean±standard deviation) was 47±13.2 yrs (range 20-72); 68 (69%) were women; body mass index (BMI) was 30±6.6; forced expiratory volume in one second (FEV1) was 2.63±0.85 liters (88.4±20.5% predicted); 27 subjects (27%) were in asthma severity step 1, 17 (17%) in step 2, 23 (23%) in step 3 and 32 (32%) in step 4. The SA-SDQ score was 30±8.2 (range 13-51), ESS score was 9.8±5.5 and 49% of the subjects had ESS scores≥10. The ESS score correlated with SA-SDQ score (Spearman rho=0.39, p=0.0001), frequency of snoring (rho=0.29, p=0.004), male gender (rho=0.27, p=0.007), asthma severity step (rho=0.22, p=0.03), and diurnal (rho=0.25, p=0.01) and nocturnal (rho=0.21, p=0.03) asthma symptom frequency. No correlation was seen between ESS and age, BMI, FEV1, history of allergic rhinitis, GERD, psychiatric disorders, inhaled long-acting bronchodilator or corticosteroid use. The ESS score was predicted by SA-SDQ (p=0.001) but not asthma step, or daytime or nighttime asthma symptom frequency, after adjustment for each of these variables.

Conclusion: Sleepiness is common in asthmatics and may reflect comorbid occult SDB more than the asthma itself.

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0880
Sleep Patterns Of Women At Risk For The Development Of Preterm Labor
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Introduction: Elevated cytokine levels are believed to play important roles in the initiation of preterm labor. These cytokines are also known to induce changes in sleep, suggesting a possible association between sleep pattern changes and preterm labor. To examine this potential relationship, subjective nocturnal sleep quality and daytime sleepiness were measured in pregnant women. Later, gestational age at delivery was observed.

Methods: A convenience sample of 220 women completed the Pittsburgh Sleep Quality Index (PSQI), the Epworth Sleepiness Scale (ESS), and the Perceived Stress Scale (PSS) during routine office visits in the second trimester of pregnancy. Delivery outcome data identified those subjects who delivered preterm.

Results: No difference was observed between the mean PSQI scores of the term and preterm groups: term 6.71(SD + 3.22), preterm 6.81(SD + 2.50), p = 0.63. Sleep latency, a component of the PSQI, differed between the 2 groups (p=0.03) with subjects who delivered preterm reporting longer sleep latency (26.09 minutes, SD + 19.91) than those who delivered at term (18.53 minutes, SD + 12.45). Daytime dysfunction, another component of the PSQI, also differed between the groups. Subjects who delivered preterm reported less of a problem with daytime dysfunction than their term counterparts (preterm 0.91 SD + 0.64, term 1.16 SD + 0.68, p = 0.03). No other differences were detected between the groups in the total scores of the other primary variables (ESS and PSS), in the other sleep variables measured by the PSQI (sleep efficiency, total sleep time), or in the other component scores of the PSQI.

Conclusion: These data suggest a possible relationship between sleep onset insomnia and preterm birth. Additional research to identify those factors that may delay sleep onset in pregnancy and their role in the development of preterm labor is warranted.
0881
Do Polysomnographic Findings Explain Sleepiness Or Pain In Fibromyalgia Syndrome?

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Introduction: Polysomnography in fibromyalgia syndrome (FMS) often shows alpha-delta, K-alpha, or cyclic alternating (CAP) patterns, but the extent to which these signs of disturbed sleep correlate with sleepiness or pain is not known.

Methods: Female rheumatology clinic FMS patients and normal female age-matched volunteers completed a 2-week pain diary and the Gracely Box Scale (psychophysiological pain perception). Subjects with sleep apnea on polysomnography were excluded; the remainder had second polysomnograms and Multiple Sleep Latency Tests. One investigator masked to FMS status visually assessed records for any clear (1) alpha-delta sleep, (2) K-alpha complexes, or (3) cyclic alternating pattern (CAP).

Results: The FMS (n=16) and control (n=14) subjects had a mean age of 43±13 years (without group difference, p=.92). Pain diary and perception scores were substantially higher among FMS subjects (p<0.0001), but sleepiness was not (mean sleep latency=11.6±4.7 vs. 13.1±5.1 minutes, p=.39). The FMS subjects had more frequent stage shifts (p=.035) and somewhat less percent stage 2 sleep (p=.072) but did not differ in arousal frequency, other sleep stages, sleep efficiency, or rates of periodic leg movements (all p>0.10). The alpha-delta pattern (n=12 subjects), K-alpha complexes (n=7), and CAP (n=9) were each somewhat more common among FMS patients, but not significantly (chi-square p>.10 for each). Sleepiness was not associated with any of the above polysomnographic or pain measures (Spearman rho, p>.05). Higher pain diary and perception scores were associated with increased stage shifts (p<.01 for each) and trended inversely with percent stage 2 sleep (p=.06 for each), but showed no association with other measures. No new association reached significance when controls were excluded.

Conclusion: Patients with FMS have some objective evidence of sleep disturbance, but sleep architectural features described in FMS may not always distinguish these patients from controls, or explain pain or sleepiness that FMS patients report.

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0882
Sleep Characteristics And Menopausal Symptoms In A Post Adjuvant Treatment Breast Cancer Sample

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Introduction: Sleep disturbances are frequently present in women diagnosed with breast cancer (BRCA). Few studies have investigated and described the nature of these sleep disturbances. Prior studies have primarily assessed general sleep quality. There are many factors that may be responsible for sleep difficulties, including chemotherapy-induced menopause and/or the use of the anti-estrogen drug Tamoxifen, which may itself induce menopause. The purpose of this study is to investigate and describe subjective and objective sleep parameters in a BRCA population, with a focus on menopausal symptoms and Tamoxifen use, in order to further understand sleep disturbances in this population.

Methods: Eighteen women (aged 34-67 years) diagnosed with stage I-III breast cancer were studied. All women were participants in a larger cognitive behavioral stress management study. All were at least 2 months post adjuvant treatment for BRCA. Demographic data were collected, as well as type and duration of both adjuvant and post-adjuvant treatments. Actigraphy and sleep diary data were collected for 7 consecutive nights.

Results: Total sleep time (TST) as measured by actigraphy (mean = 401.70 min, SD = 56.79) and sleep diary data (mean = 411.84 min, SD = 56.79) were calculated. Mean actigraphy sleep efficiency (SE) was 82.15% (SD = 7.35); mean sleep diary SE was 84.01% (SD = 9.47). Correlations showed that women who report a higher degree of sleep disturbance from hot flashes (HF) have decreased TST (r = -.56; p = .02), and that decreased TIB is correlated with both number of HF (r = -.50; p = .03) and reported degree of sleep disturbance by HF (r = -.56, p = .02). Both TIB and TST were regressed on Tamoxifen status, age, and degree of disturbance from HF; with 76% of TIB variance (F = 7.39, p = .01), and 60% of TST variance (F = 5.05, p = .02) accounted for by this model.

Conclusion: Data provide evidence of disrupted sleep in women with BRCA. Tamoxifen use and HF are associated with sleep difficulties. This may implicate the role of estrogen deficiency in sleep problems; further investigations are warranted.

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0883
Comparison Of Sleep-Wake Patterns In Two Groups Of Late Stage Cancer Patients And Healthy Adults

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Introduction: Although sleep-wake disturbances are common in cancer patients, there may be differences in subjective sleep quality among cancer groups. However, few studies have focused on homogeneous samples. Therefore, we studied patients with late-stage lung and colorectal cancer and healthy adults to examine and compare subjective nocturnal sleep quality and daytime sleepiness.

Methods: The sample included 116 outpatients (43 lung, 37 colorectal, 36 healthy adults) who were cognitively intact, had no history of a sleep, neurologic, mood, anxiety or psychotic disorder, or known cerebral metastases. Groups were equivalent relative to age, gender, and race. Subjects completed the Pittsburgh Sleep Quality Index (PSQI) and the Epworth Sleepiness Scale (ESS). Group differences in sleep-wake variables were analyzed with Kruskal-Wallis tests.

Results: Cancer subjects reported significantly poorer sleep quality than the healthy adults (mean PSQI global score lung 9.26, colorectal 7.86, comparison 5.83, p<.001) including longer sleep latency (p<.01), lower sleep efficiency (p<.02), and more sleep disturbances (p<.01). Lung cancer participants recorded the poorest sleep, used significantly more sleep medication (p<.01), and had more daytime dysfunction (p<.01) than the other study groups. While there were no statistically significant differences in sleep disturbances between cancer groups, each displayed a different pattern of disturbances when compared to the healthy adults: lung patients reported significantly more breathing difficulty (p<.001), cough (p=.02), nocturia (p<.01), and awakenings (p<.01); colorectal patients more pain (p<.01) and feeling hot (p<.01). Forty-four percent of lung and
38% of colorectal participants scored more than 10 on the ESS compared to 14% of the comparison group (p<.01), indicating a significant problem with daytime sleepiness in the cancer groups.

Conclusion: Sleep-wake disturbances were prevalent in patients with advanced cancer. There were differences in the pattern of sleep disturbances among all study groups, suggesting that underlying cancer pathologies may contribute differentially to disturbed sleep-wake patterns.

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0884

Elderly Patients Receiving Hemodialysis Showed Disturbed Sleep Architecture Compared With Healthy Elderly Control

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Introduction: It has been reported that insomnia is highly prevalent among elderly patients with end-stage renal disease (ESRD) receiving hemodialysis (HD). However, it has not been elucidated whether sleep architecture of elderly HD patients is disturbed even without subjective sleep complaints. The aim of the study was to identify the characteristics of sleep architecture among the elderly HD patients.

Methods: 30 patients (16 men, 14 women, age 69.1±4.8) receiving HD due to ESRD with the age ranging from 60 to 80 years old who does not have subjective sleep problems were enrolled in this study (HD group). 35 normal elderly (17 men, 18 women, age 69.4±5.0) who does not have subjective sleep complaints were recruited for comparison (control group). Overnight polysomnography (PSG) was recorded on all subjects and PSG parameters were compared between the two groups.

Results: Apnea hypopnea index was significantly higher in the HD group (34.1±27.6/hour) than in the control group (10.3±9.5/hour). Periodic limb movement during sleep (PLMS) defined as PLM index >5/hour was more prevalent in the HD group (50.0%) than in control (28.6%), but the PLM index did not show any statistical difference between the two groups. Sleep latency was longer in the HD group (53.0±36.6 min) than in the control group (13.2±10.0 min), and the sleep efficiency was lower in the HD group (69.6±16.7 %) than in control (81.3±10.3 %). Arousal index was higher in the HD group (55.5±19.4/hour) than in control (22.7±12.6/hour). Although the index of spontaneous arousal and respiratory arousal were significantly more frequent in the HD group, the PLM index did not show any statistical difference between the two groups.

Conclusion: Sleep architecture among HD patients were disturbed even without subjective sleep complaints. Sleep disordered breathing seemed to contribute more to the sleep disturbance in HD patients than PLMS.

0885

Sleep Apnea/Hypopnea In Patients With Acromegaly

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Introduction: Sleep apnea/hypopnea (SAH) has been consistently reported in patients with acromegaly. Both obstructive and central respiratory events occur. Upper airway region soft tissue overgrowth might be correlated with severity of sleep apnea. Treatment with octreotide can decrease tongue volume and improve sleep-disordered breathing. Anecdotal reports show improvement of SAH after neurosurgical treatment.

Methods: 11 patients recently diagnosed with acromegaly (6 male, 5 female, mean age 49.1 years, range 32-65; BMI 29.8(3.3); IGF-1 1068.6(592.1) microg/l; GH 27.5(40.8) microg/l (mean[sd]), GH median 20), were submitted to polysonomographic study on baseline and 1 month after acromegaly treatment. According to clinical severity criteria, 7 patients were recruited to receive octreotide acetate (Sandostatin LAR 20-30 mg every 4 weeks I.M.) and 4 were selected for neurosurgical treatment. GH and IGF-1 levels were assessed 1 month later.

Results: At baseline, all except one patient presented respiratory disturbance index (RDI) > 5 events/hr (29.2/hr) and 6 out of 11 subjects presented central sleep apnea. One month of treatment (surgery or octreotide), produced no significant RDI difference 28.8(21.1) (mean[sd]). However, a significant reduction in GH (9.7(17) median 1.2, p<0.05) and IGF-I (684.1 (595.2) p<0.05) levels was observed and IGF-I levels in 45% of patients were normalized within the age-adjusted normal range.

Conclusion: A high prevalence of sleep-disordered breathing was found at baseline in this sample of severely affected acromegaly patients. No difference was observed on RDI after one month of treatment with either octreotide or surgery. The current one-month data challenge previous studies with 6-month octreotide treatment showing a clinically significant RDI improvement. Positive airway pressure treatment is warranted for these subjects up to six-month follow-up.

0886

Cancer Pain And Its Relationship To Sleep Disturbances And Depression

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Introduction: Three factors interfering with optimal quality of life for cancer patients are pain, depression, and sleep disturbances. However, there is little data classifying the sleep disturbances experienced by hospitalized cancer patients. The purpose of this study is to explore the degree of subjective sleep disturbances in an inpatient cancer population.

Methods: 14 subjects (8 females) with varying cancer diagnoses were recruited from inpatient oncology floors. Mean age was 50.5 years (±15.9) with a mean time since cancer diagnosis of 2.5 years (± 6.02). Subjects completed an extensive battery including the Brief Pain Inventory (BPI) short form, the Center for Epidemiological Studies-Depression Scale (CES-D), and the Pittsburgh Sleep Quality Index (PSQI).

Results: As expected, this sample reported much higher levels of psychological distress on the CES-D (24.4 ± 9.29) compared to the average population (9.25). According to the BPI subjects reported an average pain score of 4.35 (± 1.34) characterizing moderate pain, which is consistent with reported pain scores within the inpatient cancer population. PSQI global mean score was 11.28 (± 3.09) indicating increased sleep disturbances in this population. Patients scored higher on the PSQI components of sleep latency, sleep dysfunction, and daytime dysfunction. A positive trend existed between higher pain scores and increasing subjective sleep complaints (rs= .50, p=.06).

Conclusion: Cancer patients tend to have poor subjective sleep quality regardless of self-reported pain levels. Patients with higher pain scores...
Introduction: Chronic Fatigue belongs to medically unexplained illnesses. The most prevalent complaint among fatigue subjects is unrefreshing sleep, but a well-described abnormal pattern has not yet been demonstrated.

Methods: Thirteen female fatigue patients (41.1± 9.8) were selected. They scored positively in 2 fatigue scales, underwent a polygraphic recording including esophageal pressure monitoring. Fourteen normal control subjects (31.6 ± 10.2) were also monitored. Heart Rate Variability using Time and Frequency Domain techniques was performed for a stable 5-minute period, during Stages 2, 3 and 4 Non-REM and REM sleep. ANOVA and Pearson correlation coefficient were used with p≤ 0.01.

Results: Significant differences were found between fatigue and controls in Krupp Scale (44.2 - 11.9 vs 31.6 - 10.2), RDI (4.7 - 3.3 vs 1.0 - 1.4), Sleep Efficiency (82.2 - 91.1 vs 90.6 - 4.6) and Slow wave sleep percentage (13.9 - 7.2 vs 25.4 - 6.7). There was a significant negative correlation between Sleep Efficiency and Krupp Scale scoring (r = -.56, p=0.01). Regarding Heart Rate Variability, there were no significant differences between fatigue and controls for Time Domain (Mean RR Interval, SDNN, RMSSD, SDSD, NN50, pNN50) and Frequency Domain (VLF, LF, HF, LF/HF, and Total Power) parameters.

Conclusion: Fatigue complaint, was associated with decreased SWS and Sleep Efficiency, and significant increased, but still normal RDI. HRV parameters, Epworth Scale scoring, and microarousal index did not differentiate fatigue from normals. The lack of ANS alteration may be due to the small number of subjects or the small window for HRV analysis.

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0888
The Relationship Between BMI And Sleep Apnea In Stable Hemodialysis Patients
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Introduction: Sleep apnea is a common problem in the hemodialysis (HD) population, but risk factors for this disorder have been poorly characterized. In particular, there is no consistent evidence suggesting a relationship between sleep apnea severity and obesity in this group. Thus, the purpose of this study was to examine the relationship between respiratory disturbance index (RDI) and body mass index (BMI; kg/m2) in a sample of these patients.

Methods: The sample included 46 stable HD subjects (mean age 51.6 ± 10.8 years) with no known history of sleep apnea (24 men and 22 women; 36 Black and 10 White). BMI was calculated using the patient’s estimated dry weight at time of consent: data were categorized according to criteria defined by Center for Disease Control & Prevention (overweight 25.0 - 29.9, obese ≥ 30.0). The sample included (41.3 %) normal weight, (34.8 %) overweight and (23.9 %) obese subjects (mean BMI 26.76 ± 5.6). Subjects underwent overnight laboratory-based polysomnography. RDI was measured as number of apneic events per hour of sleep. Descriptive and nonparametric correlational procedures were used for data analyses.

Results: BMI was significantly and positively related to RDI (rs=0.32, p<0.03) but explained only approximately 10% of the variance in RDI. Conclusion: These findings indicate that obesity maybe a risk factor for sleep apnea in stable HD patients but that numerous other factors likely contribute to the high prevalence of this disorder in this population.

0889
Sleep Disordered Breathing And Pulmonary Hypertension
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Introduction: Sleep disordered breathing (SDB) is known to cause mild pulmonary hypertension (PH), but the prevalence of SDB in patients with more severe PH is unknown. We examined the overall prevalence of SDB in PH patients referred to the sleep laboratory.

Methods: A retrospective review of PH patients suspected of having SDB at our tertiary academic center between 1/03 and 10/04 was performed. PH was divided into pulmonary arterial hypertension (PAH) (eg scleroderma, idiopathic, congenital heart disease, anorexigenics) or non-PAH; severity was defined as mild/moderate (mean pulmonary arterial pressure (MPAP) 26-44 mmHg by catheterization or right ventricular systolic pressure (RVSP) 41-59 mmHg by echocardiography), or severe (MPAP ≥ 45 mmHg or RVSP ≥ 60 mmHg). Definitions of SDB: obstructive sleep apnea (OSA) = apnea-hypopnea index (AHI) ≥10; central sleep apnea (CSA) = central apneas ≥ 10/hour; nocturnal desaturation (ND) = > 30% total sleep time (TST) SaO2 < 90% or > 5% TST SaO2< 90% and nadir < 85%; and REM apnea (REMA) = REM AHI twice the total AHI. Comparisons of subjects were performed using Fisher’s exact test or Student’s t-test.

Results: Twenty-three PH subjects were identified; 10 (43.5%, 95%CI 23.2%-63.7%) had PAH. No significant differences existed between PAH vs. non-PAH for gender (males 40% vs. 46.2%, p=0.10), race (white 60% vs. 46.2%, p=0.68), or body-mass index (30.9 vs. 31.9 kg/m2, p=0.86). Overall SDB prevalence was high (82.6%, 95%CI 67.1%-98.1%). SDB was common in patients with and without PH (70.0% vs. 92.3%, p=0.28): OSA (53.8% vs. 40.0%, p=0.68); CSA (10.0% vs. 7.7%, p=1.00); ND (40.0% vs. 38.5%, p=1.00); REMA (33.3% vs. 50.0%, p=0.64). There was no trend in the prevalence of SDB in patients with mild/moderate vs. severe PH (100.0% vs. 69.2%, p=0.10): OSA (60.0% vs. 38.5%, p=0.41); CSA (10.0% vs. 7.7%, p=1.00); ND (30.0% vs. 46.2%, p=0.67); REMA (71.4% vs. 20.0%, p=0.06).

Conclusion: PH patients referred for sleep testing have high rates of SDB. Future studies should focus on exploring the association of SDB and PH by comparing the prevalence of SDB in patients with and without PH and the impact of SDB treatment on morbidity and mortality.

0890
Sleep Disorders In Intractable Pain Patients -A Retrospective Analysis
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Introduction: A retrospective analysis was undertaken to investigate the outcome of polysomnographic (PSG) evaluations of chronic pain patients. We reviewed and compared data from various sources, including PSG evaluation, standardized scales, and diagnostic criteria between patients with intractable pain (IP) referred by pain management specialists and a non-pain (NP) control group.

Methods: Random selection of 126 patients (63 IP; 63 NP) evaluated with PSG using standard techniques for acquisition and scoring between January and May of 2004.

Results: No difference (p<0.5) was noted between groups in the degree of sleepiness measured by the Epworth Sleepiness Scale score. There was a significant difference in obesity between the IP group (BMI of 27.55) and the NP group (BMI of 33.9) (p<0.0002). Mean Apnea/Hypopnea Index (AIH) of the IP group was 12.9/hour compared to 25.8/hour in the NP group (p<0.001). Both groups experienced significant oxygen desaturation associated with respiratory events with a mean nadir of 84.9% in the IP group and 81.9% in the NP group (p<0.02). Among patients who qualified for treatment with continuous positive airway pressure (CPAP), a higher percentage of IP patients (54.4%) were prescribed CPAP (NP patients 44.4%). Maximum therapeutic CPAP level in both groups was 14 cm H2O. Analysis of period limb movements during sleep (PLMs) indicated that the majority of those in the IP group did not experience PLMs during PSG evaluation.

Conclusion: Patients with intractable pain experience significant disruption in their sleep architecture. In our study, the degree of respiratory disturbance varies between patients with intractable pain and non-pain controls. Patients with IP are more likely to be taking medications that impact sleep disturbance, (2) improve overall sleep quality, and (3) reduce pain-related symptoms. Sleep apnea (SA) occurs in some FM patients. Elevated tonic alpha is characteristic of the sleep in FM patients. In FM, poor sleep quality is associated with pain intensity. It was hypothesized that by treating patients with FM/SA with CPAP, that this may (1) reduce alpha during NREM sleep, (2) improve overall sleep quality, and (3) reduce pain-related symptoms.

Methods: Participants were 40 females (age 25-65). Half the participants were diagnosed with FM and SA, and half with SA only. Two overnight polysomnographic studies were conducted including a baseline night and subsequent CPAP trial. CPAP was administered to all patients on the second night. The percent duration of alpha activity was measured from O1 (referenced to A2) in the first 10-epochs of uninterrupted Stage2 sleep. CPAP pressure for all participants during this interval was maintained at 5cmH2O. The effectiveness of CPAP treatment was measured by respiratory disturbance index (RDI).

Results: Following CPAP treatment, the FM/SA group had a significant decrease in alpha activity from the baseline (M=29.69, SD=5.89) to CPAP trial (M=14.39, SD=2.48) night (t(19)=10.93, p<.0001). CPAP treatment was effective in improving respiration as indicated by a reduction in RDI (t(19)=4.16, p=.001).

Conclusion: These findings suggest that CPAP treatment may be an effective way to reduce arousal-related disordered sleep indicated by elevated alpha activity in patients with FM/SA. The data presented here are preliminary results from the larger study described above. The analysis of alpha in the SA only group will be compared to the FM/SA group to determine whether the effects of CPAP on alpha are specific to FM. Further analyses will investigate if there is improved sleep quality, a reduction in pain symptoms in patients with FM following CPAP treatment and whether the reduction in alpha is correlated with the changes in pain symptoms.

0892
Exercise Capacity In Congestive Heart Failure And Sleep-Disordered Breathing
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Introduction: This study investigates exercise capacity in patients with congestive heart failure (CHF) and sleep-disordered breathing (SDB) on an optimal medical regimen.

Methods: 105 consecutive patients were recruited through our Heart Failure Clinic. Patients were aged 18-82yrs, NYHA class II-IV, clinically stable, and LVEF<40%. Patients underwent in-home testing (StarDust device: nasal pressure, thoracic excision, pulse oximetry). Cheyne-Stokes Respiration (CSR) was defined as at least 3 cycles of symmetrical crescendo-decrescendo breathing pattern, with 30-to-90-second periodicity. Primary CSR was considered >33% of total recording time (TRT). Primary OSA was defined as an AHI>15 (events/hour of TRT) and CSR-time <33%. Patients also underwent cardiopulmonary exercise testing.

Results: 34 patients had primary CSR, 31 had primary OSA, and 40 had no SDB. No significant differences between groups were observed for age, BMI, diabetes, CHF etiology, or medications (88% diuretics, 85% ACE inhibitors, 73% beta blockers). Peak pressure-rate product (pPRP:systolic pressure x HR) was lower in CSR than non-CSR, (Median[CI], 15178[12791-15902] vs. 16532[12384-20300], p=0.02), and in CSR vs. OSA (16292[14768-20496], p=0.05). Peak respiratory exchange ratio (pRER: VC02/VO2) was higher in CSR than non-CSR (Mean±SEM, 1.125±.017 vs. 1.074±.015, p=0.05). There were no significant differences for pPRP and pRER between OSA and no SDB, or between any groups for peak VO2. Patients with CSR had worse heart failure by NYHA Class than non-CSR (Class III in 31% of CSR and 69% of non-CSR, p=0.01). LVEF was lower in CSR than in OSA (15%[15.0-25.0] vs. 27.5%[20.0-32.0], p=.002).

Conclusion: Lower pPRP in CSR than other groups and higher pRER in CSR than non-CSR implies there may be differences in autonomic or metabolic control in CSR. Further work is needed to determine whether these findings contribute to the poor outcome of CSR patients.

Respironics, Inc.

0893
Sleep And Heart Rate Variability In Patients With Chagas Disease, Preliminary Data
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Introduction: Chagas disease is an infection caused by the Trypanosoma cruzi. Twenty million people are thought to be infected with the parasite. There are different chronic forms of the disease including cardiomyopathy (CC). Impaired HRV is an independent predictor of malignant arrhythmia in patients with ischemic cardiomyopathy. Objective-To evaluate the differences in 24-hour HRV and sleep in...
patients with Chagas disease according to ventricular tachycardia induction during the electrophysiological study (EPS).

**Methods:** Seventeen CC patients underwent EPS to investigate previous episode of syncope or sustained ventricular tachycardia (SVT), divided in two groups: patients who induced SVT (group 1, n - 9) and did not induce SVT (group 2, n - 8). Subjects were monitored with polysomnography, and 24-hour holter monitoring, to assess HRV. HRV was obtained during 24-hours, and for stable 5-minute period, during SWS and REM sleep.

**Results:** Patients presented similar age, BMI and left ventricular ejection fraction (EF). There was a reduction in rMSSD and pNN50, during 24 hours, SWS and REM sleep in group 1. SWS% was higher in group 1. The other parameters of HRV and PSG were similar in both groups. Group 1 vs Group 2 (Mean-SD): (age 50.7-5.1 vs 55.5-6.9); (EF 0.4-0.1 vs 0.6-0.1). (PNN50 24-hours 8.1-4.6 vs 22.3-10.5); (PNN50 SWS 7.3-9.3 vs 24.8-12.7); (PNN50 REM 9.7-9.0 vs 28.6-19.7); (SWS 27.8-8.1 vs 16.4-5.3), p<0.04, all.

**Conclusion:** The reduction in parasympathetic during sleep in patients with CC who induce SVT occurred despite their highest amount of SWS (sleep state in which parasympathetic tone is the highest). These findings suggest that a parasympathetic disautonomy may play a role in the genesis of reincident SVT in CC patients. Larger sample of patients should be studied, and a normal control group is already been selected, to assess whether or not group 2 (chagasic patients who did not elicited SVT) have normal parasympathetic tonus during sleep.

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**0894**

**Slow Wave Activity And Heart Rate Variations Are Less Dominant In Fibromyalgia And Chronic Pain Patients Than In Controls**

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**Introduction:** Sleep efficiency in chronic pain and fibromyalgia patients is reported to be lower than in normal subjects (Okura et al., Sleep-APSS 2004). In the present study we looked at EEG and EKG spectral analysis during sleep in patients with chronic pain or fibromyalgia and in normal subjects.

**Methods:** 10 normal subjects were matched for age and gender (5F/5M) to 10 fibromyalgia and 10 chronic pain patients referred to the sleep laboratory. The heart rate variability (HRV), estimated as low frequency / (low frequency + high frequency) ratio, was used to assess sympathetic cardiac activity. Slow wave activity (SWA) from the central EEG lead (C3/A2) and HRV from the D-1 EKG lead were calculated using power spectral analysis over the first 3 consecutive non-REM to REM cycles. Fifteen-minute samples of data were chosen from wake, non-REM sleep (stage 2, delta sleep), and REM sleep for HRV spectral analysis.

**Results:** Univariate analysis of variance (ANOVA) procedures conducted indicated significant differences between the groups on autonomic activity during non-REM sleep. Specifically, the IBS-D and IBS-C group had greater sympathetic dominance compared to the IBS-A during non-REM sleep stages (p < .05). These differences were not observed during REM or waking.

**Conclusion:** 1. The IBS-D and IBS-C groups were physiologically distinct with regard to autonomic functioning compared to IBS-A group. 2. Sleep appears to unmask differences in autonomic activity suggesting this may serve as a biological marker that distinguishes different subgroups of IBS patients.

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**0896**

**Sleep Disturbances, Fatigue, Depression, And Heart Rate Variability In Menopausal Women With And Without RA**

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**Introduction:** Women with rheumatoid arthritis (RA) experience sleep disturbances, fatigue, depression and inflammation. The heightened inflammation increases cardiovascular risk. An indicator of cardiovascular risk, heart rate variability (HRV) sharply declines during menopause in healthy women. HRV was lower in one study of males and females with RA. Little is known about HRV in peri and postmenopausal women with RA. Therefore, this study investigated differences in HRV, sleep, and fatigue in postmenopausal women with and without RA.

**Methods:** This descriptive/comparative study consisted of a sample of 38 peri and postmenopausal women (RA and healthy) with a mean age of 57.8 (SD 8.8). Measures included subjective sleep estimates (general sleep disturbance scale, sleep quality, wake after sleep onset (WASO) in minutes, fatigue, and depression. Heart rate was measured for 15 minutes

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with paced breathing for the analysis of HRV.

**Results:** RA women were older with more depression, both of which affect HRV, thus age and depression were used as covariates in all analyses. The standard deviation of the RR interval (SD RR), a measure of HRV, was significantly lower in RA women. While WASO initially was almost equal, after controlling for age and depression, women with RA rated WASO lower than healthy women. Other subjective sleep ratings indicated moderate sleep disturbances in women but did not differ by group. Fatigue also was moderate in women but did not differ by group.

**Conclusion:** After controlling for age and depression, compared to healthy women RA women had lower HRV, perhaps indicating a higher risk of future cardiovascular events. Women had moderate sleep disturbances and fatigue, however women with RA recorded lower WASO than healthy women. RA women may have become accustomed to poor sleep over time, thus in a future study of sleep and HRV, sleep should be measured objectively as well as subjectively.

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**0897**

Heart Rate During Sleeping And Waking In Symptom Subgroups With Irritable Bowel Syndrome

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**Introduction:** Previous research from our laboratory has suggested that cardiac autonomic regulation as measured by heart rate spectral analysis is altered during rapid-eye movement (REM) sleep in patients with irritable bowel syndrome (IBS). Other studies have suggested autonomic dysregulation in patients with IBS utilizing resting heart rate responses to stressful stimuli. Little work has been done examining autonomic functioning in the three major subgroups of IBS: constipation-predominant, diarrhea-predominant, and patients alternating between constipation and diarrhea symptoms.

**Methods:** Three groups of women who met Rome criteria for IBS were studied: 21 diarrhea-predominant (IBS-D), 32 constipation-predominant (IBS-C), and 20 alternating (IBS-A), as well as 21 women who were community controls. Fifteen-minute segments of resting heart rate were selected from non-REM (NREM), REM, and waking conditions.

**Results:** Univariate analysis of variance (ANOVA) procedures revealed significant differences between the groups on resting heart rate during NREM, REM, and waking periods. Pairwise comparisons showed that controls had significantly lower heart rate compared to both diarrhea-predominant and constipation-predominant patients during NREM sleep (p < .05). During waking and REM only, the diarrhea-predominant group was significantly different from controls (p < .05).

**Conclusion:** 1. Heart rate levels during NREM sleep are consistently higher in IBS-C and IBS-D patients, but there is no differentiation among the IBS-A and control groups. 2. Elevated heart rate in IBS-C and IBS-D patients suggests overall autonomic activation reflective of an underlying physiologic characteristic of these IBS symptom subgroups. 3. Autonomic activity during NREM sleep reflects potentially important physiological differences between IBS symptom subgroups.

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**0898**

Evaluation Of Sleep In End-Stage Renal Failure Patients With Secondary Hyperparathyroidism (HPT)

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**Introduction:** Previous studies of normal subjects have shown an in-phase association between intact parathyroid hormone (iPTH) levels and stage 3, 4 (delta) sleep. We hypothesized that daytime tiredness in patients with HPT might be related to induced changes in sleep quality, specifically delta sleep or other sleep disorders. The relationship between iPTH and sleep in patients with elevated levels of iPTH due to secondary HPT has not been studied. We theorized that there might be an association between iPTH levels and sleep quality in patients with HPT, causing fatigue.

**Methods:** We reviewed data collected prospectively in 17 subjects (6 female, 11 male) with secondary HPT due to end-stage renal disease. All 17 subjects underwent nocturnal polysomnography (NPSG) at an accredited Sleep Center. Serum iPTH levels were collected within 30 days of NPSG. Objective data included sleep efficiency; sleep stages; apnea-hypopnea index; periodic limb movements (PLMs); minutes of wake after sleep onset (WASO), number of stage shifts, and total arousal index. Subjective data included Epworth Sleepiness Scale, Beck Depression Index, and the subjective assessment of the sleep problem. The data were analyzed using ANOVA, and Pearson Correlation Coefficient.

**Results:** There was no statistically significant relationship between PTH and sleep efficiency, sleep stages, REM sleep, Epworth score, PLMs, stage shifts, sleep-disordered breathing, or WASO. A trend of an inverse relationship was noted between iPTH and delta sleep.

**Conclusion:** The fatigue experienced by patients with secondary HPT cannot be explained by an association between iPTH and sleep abnormalities recognized by standard NPSG. This data does not support a relationship, causal or otherwise, between iPTH and fatigue or poor sleep in this patient population.

**0899**

Shifting Costs To Patients Discourages Specialty Evaluation For Non-Breathing Related Sleep Disorders

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**Introduction:** Although diagnosis and treatment of sleep disorders have been shown to be cost effective, steadily rising costs have motivated health insurers to shift more costs to patients through increased premiums and co-payments for services. In 2003, Mayo Clinic employees accounted for 15% of visits to the Sleep Disorders Center (SDC), a multi-specialty sleep practice. Beginning January 1 2004, employee co-payment for covered services changed from none to $25 for specialty visits and averaged $250-$350 for polysomnography. We hypothesized that this would lead to a decrease in the employee utilization of the SDC.

**Methods:** We examined and compared the clinical and medical accounting data from employee SDC visits from January 1 to March 31, 2003, with that of January 1 to March 31, 2004. The presenting clinical features, polysomnographic findings, diagnoses, and appointment patterns were retrospectively analyzed.

**Results:** The total number of patient services in the first quarters of 2003 and 2004 was similar (638 vs. 624, p = 0.98). Snoring, restless legs symp-
0900
High Arousal Index And Weak Labial Closure Force Observed In A Rheumatology Clinic
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Introduction: Since a tendency of weak labial closure force (LFC) and high arousal index (AI) of polysomnogram (PSG) were observed among the patients of a rheumatology clinic, the correlations between LCF and the results (including AI) of PSG were examined.

Methods: One hundred and seventy eight female patients of age between 44 to 88 who were suffering from various rheumatic diseases such as rheumatoid arthritis (120), systemic sclelosis (20), systemic lupus erythematous (11), polymyositis (5) and others (22) were examined. PSG was performed in a sleep laboratory using a standard 14-channels apparatus.Recordings were analyzed manually by fully trained technicians. LCF was measured using a strain-gauged cantilever beam assembly attached with two lip holders. LCF value was expressed by Newton (N) and the mean LCFs of age and sex mached controls was 12.63, SD2.74N.

Results: High Al (mean 23.03, SD 9.76) and weak LCFs (mean 10.40, SD 3.02) were observed in these 178 patients. A significant correlation between LCF and AI (r=-0.202, P<.01, N=178) has been observed. However, no correlations (r=0.159, P<.05) has been also observed. However, no correlations between LCF and AHI(apnea hypopnea index) and DI(desaturation index) were found.

Conclusion: The change in insurance policies did not decrease total utilization, but shifted the spectrum of diagnoses seen at the SDC toward more symptomatic patients with co-morbidities and SRBDs. Patients with other sleep disorders may be less willing to spend their money for speciality diagnosis and management.

0901
Increased Sleep Disturbances In Patients With HIV Related Painful Neuropathy
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Introduction: HIV+ patients who are otherwise asymptomatic experience subtle subjective and objective sleep abnormalities, but few studies have examined HIV+ patients with other medical co-morbidities such as pain. Here, we examined subjective sleep patterns in HIV+ patients diagnosed with painful distal, sensory polyneuropathy (DSPN) and compared these patterns to those in age matched normal controls.

Methods: Subjective sleep measurements were examined in 10 patients (ages: 39-50, all male) diagnosed with HIV DSPN and 10 normal controls (ages: 34-56, 6 female, 4 male) drawn from separate, but contemporary, studies. All participants completed sleep diaries assessing sleep quantity and quality for at least 4 days, Epworth Sleepiness Scale (ESS), Horne and Ostberg Morningness-Eveningness Questionnaire (MEQ), and a sleep questionnaire designed to qualitatively identify the causes and effects of sleep disruption.

Results: There were no significant differences between the groups in age, chronotype, habitual bedtime and habitual wake time. HIV DSPN patients reported significantly longer sleep latency, lower sleep efficiency, lower total sleep time, and a trend for greater wake after sleep onset. Patients also reported a significantly greater variety of factors leading to nighttime sleep disturbances. With respect to daytime sequelae, patients showed a trend feeling less refreshed upon awakening, and reported a significantly greater number and duration of naps. There were no differences in ESS scores. Finally, patients reported having “a typical night of sleep” significantly less often than controls.

Conclusion: The HIV DSPN patients reported experiencing significantly more disturbed sleep than normal controls, along with less refreshing sleep and more daytime naps. The lack of significant differences in the ESS scores suggests that napping may help patients offset daytime sleepiness. These results may be influenced by gender differences but the effect sizes suggest this is not a major contributing factor.
for both modality of treatment (p=0.78).

**Conclusion:** Hydrotherapy is as effective as conventional physiotherapy to improve quality of life of patients with fibromyalgia when analyzed through SF-36, however hydrotherapy showed to be more effective in the improvement in Total Sleep Time.
Sleep Change And Depression In Adolescence

Danner FW

Introduction: Insufficient sleep among adolescents has repeatedly been associated with depressed mood and poor psychological functioning (Acebo & Carskadon, 2002; Dahl & Lewin, 2001; Roberts et al., 2002) but rarely has this association been directly studied over time (Patten et al., 2001). The present study assessed changes in depression over time among adolescents as a function of changes in sleep.

Methods: Sleep and depression were analyzed from two consecutive years of the National Longitudinal Study of Adolescent Health. A total of 5,114 adolescents who reported at least 8 hours of sleep per night during Year 1 were selected for study. They were then divided into those who maintained at least 8 hours of sleep in Year 2 and those who dropped below 8 hours. Depression was assessed in both years using the CES-D scale (Radloff, 1977) and cut-off scores of 24 for females and 22 for males (Roberts et al., 1991). Logistic regression was used to calculate the odds of being depressed at Time 2 as a function of moving from good sleep (8 or more hours) to less than good sleep (<8 hours). Sex, age, and Time 1 depression status were entered prior to adding the coded sleep change score.

Results: Sex, age, and depression at Time 1 were all significant predictors of Time 2 depression with higher odds ratios of 2.03 (females), 1.16 (older adolescents), and 8.76 (previously depressed). After controlling for these strong predictors of Time 2 depression, the odds of being depressed were 1.98 times higher for those whose hours of sleep declined. There was also a significant Sex X Sleep Change interaction, with males more strongly affected by less sleep.

Conclusion: Moving from 8 hours of sleep per night to less than 8 hours during adolescence nearly doubled the probability of depression, and this effect was more pronounced for males.

Depression As A Correlate Of Sleep Hallucinations, Sleep Paralysis, Cataplexy-Like Episodes, And Automatic Behavior In The Wisconsin Sleep Cohort Study

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Introduction: Sleep paralysis (SP), hypnagogic/hypnopompic hallucinations (HH), cataplexy-like episodes--Rapid Eye Movement (REM) sleep phenomena--and automatic behavior (AB), though typical narcolepsy symptoms, have been reported in population-based and non-narcoleptic samples. A case study by Hudson et al. found that nightmares in post-traumatic stress disorder were associated with SP, hypnagogic hallucinations, and REM sleep pathology, while epidemiologic studies by Ohayon et al. have found that depression is linked to hypnagogic hallucinations and SP. Symptoms' psychiatric correlates, particularly depression, merit further attention in community samples.

Methods: The sample consisted of 812 participants, studied 1998-2002, from the Wisconsin Sleep Cohort Study, who completed a mailed questionnaire measuring outcomes and ≥1 overnight sleep protocol including polysomnography and Zung Self-Rating Depression Scale. Outcome presence referred to ever experiencing any item ≥1/month: Cataplexy was defined as muscle weakness in legs or buckling of knees when laughing and/or angry and/or telling-hearing joke; SP, as being unable to move or feeling paralyzed upon awakening a.m. and/or during night's sleep; HH, as hearing or seeing strange or frightening things or people during sleep onset p.m. and/or upon awakening a.m. and/or when drowsy; AB, as blank spells when driving and/or sitting. Four multivariate logistic regression models were run with depression (Zung≥50) as main predictor, adjusted for age, gender, antidepressant use, body mass index, and sleep-disordered breathing (measured by apnea-hypopnea index).

Results: After adjustment for covariates, depression was positively associated with 2.0-fold (95% CI, 0.66-5.8), 2.1-fold (1.2-3.7) and 5.1-fold (1.6-15.5) increased ≥1/month HH, AB, and SP odds, respectively, and 1.3-fold (0.22-7.2) increased ≥1/month cataplexy-like episode odds. Depression was significantly, positively associated with all outcomes >few times ever (not shown), including 4.2-fold (1.7-11.0) elevated cataplexy odds.

Conclusion: Our epidemiologic findings suggest depression may contribute to AB and REM-related disturbances, which may be additional sleep symptoms of depression. Longitudinal studies are warranted to investigate whether depression leads to development of these sleep disturbances.

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EEG Activity During REM Sleep In Autism: Primary Vs Non-Primary Visual Areas

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Introduction: Neuropsychological, EEG and brain imaging studies point toward enhanced low-level visual perception in High Functioning Autism (HFA). Asperger Syndrome (AS), a variant of autism without language delay, do not present peaks in the visual modality. Our group has recently reported low spectral values for EEG Beta activity over visual cortex in patients with ASD during REM sleep (Daoust et al., 2004). We tested the hypothesis of an atypical distribution of EEG activity across primary and non-primary visual areas during REM sleep in persons with autism.

Methods: 10 HFA (9M, 1F ; 20.8 ± 3.7 years), 8 AS (8M; 23 ± 3.1 years) and 16 control participants (15M, 1F ; 21 ± 4.3 years) were recorded for two consecutive nights. Spectral analysis of REM sleep Beta EEG activity (13.0 to 19.75 Hz) was performed on primary (O1, O2) and non-primary (T5, T6) visual areas. Left and right relative spectral amplitude was calculated using the formula: [(primary electrode/ non-primary electrode) * 100]. The three groups of participants were compared using a one-way ANOVA for each of the two activity ratios.

Results: The three groups showed comparable REM sleep parameters. Beta activity was consistently greater over primary areas (O1 and O2) than secondary areas (T5, T6) within each of the three groups. Both HFA and AS groups displayed less absolute spectral Beta amplitude for O1 and O2 electrodes than controls but T5 and T6 were not different. HFA participants showed lower O1/T5 ratio compared to controls (p<.04) and AS participants (p<.04). No group differences were observed in the right hemisphere.

Conclusion: There is a decreased contrast between activation of left primary and secondary visual areas in HFA, suggesting that an atypical EEG distribution over visual areas in REM sleep occur only in HFA. Further study should investigate if this correlates with the visual performance.

Primary Visual Areas

Introduction:

Comparison of EEG spectral power between Asperger Syndrome (AS), High Functioning Autism (HFA), and controls in primary (V1, V2) and secondary visual areas (T5, T6) using frequency-domain analysis of REM sleep. Several studies have shown EEG differences in high functioning autism with atypical distribution of EEG activity predominantly left hemisphere. In contrast REM sleep in Asperger Syndrome and High Functioning Autism do not show these left hemisphere differences.

Methods:

10 AS (8M; 23±3.1 years), 10 HFA (9M, 1F; 20.8±3.7 years), and 16 control participants (15M, 1F; 21±4.3 years) were recorded for two consecutive nights. Spectral analysis of REM sleep Beta EEG activity (13.0 to 19.75 Hz) was performed on primary (O1, O2) and non-primary (T5, T6) visual areas. Left and right relative spectral amplitude was calculated using the formula: [(primary electrode/ non-primary electrode) * 100]. The three groups of participants were compared using a one-way ANOVA for each of the two activity ratios.

Results:

The three groups showed comparable REM sleep parameters. Beta activity was consistently greater over primary areas (O1 and O2) than secondary areas (T5, T6) within each of the three groups. Both HFA and AS groups displayed less absolute spectral Beta amplitude for O1 and O2 electrodes than controls but T5 and T6 were not different. HFA participants showed lower O1/T5 ratio compared to controls (p<.04) and AS participants (p<.04). No group differences were observed in the right hemisphere.

Conclusion:

There is a decreased contrast between activation of left primary and secondary visual areas in HFA, suggesting that an atypical EEG distribution over visual areas in REM sleep occur only in HFA. Further study should investigate if this correlates with the visual performance.

Canadian Institutes of Health Research
0906
Characteristics Of Sleep In Depressed And Non-Depressed Pregnant Women
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Introduction: Sleep disturbance is common during pregnancy and it is a diagnostic symptom of Major Depressive Disorder (MDD). During pregnancy, women tend to wake up more frequently than before becoming pregnant, and in comparison to non-pregnant women. This study explores the contributions of pregnancy and depression to sleep disturbances in pregnant women with and without MDD.

Methods: Sleep data was collected from 106 women between 10-35 gestational weeks. Sixty-one met MDD criteria and 45 did not. Analysis was performed on early, middle, and late insomnia (the latter focusing on the 2 hours preceding planned rising time) items from a structured depression interview (Hamilton Rating Scale for Depression-HRSD). Additionally, when a sleep problem was endorsed, a follow-up question inquired about the extent to which pregnancy contributed to the disturbance.

Results: The presence and severity of early and late insomnia were significantly greater for depressed than non-depressed women (39% versus 20%, p<0.05 for early insomnia; 43% versus 16%, p<0.01 for late insomnia). Approximately 90% of both depressed and non-depressed pregnant women endorsed experiencing middle insomnia but severity was significantly greater for women with MDD (p<0.01). Among women who reported any middle insomnia, there was no significant difference in the extent to which it was attributable to pregnancy (p=0.16). Although there was no statistically significant relationship between gestation week and the severity of middle insomnia, gestational week was significantly and negatively correlated with the severity of late insomnia (r(119)=-0.21, p<0.05). In contrast, among women who experienced early insomnia, late gestation week was significantly associated with higher ratings of the extent attributable to pregnancy (r(46)=0.30, p<0.05).

Conclusion: These data suggest that although sleep continuity disturbance is common during pregnancy, Major Depressive Disorder further exacerbates the problem. In contrast, sleep onset difficulties and early morning awakening appear to be caused primarily by depression.

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0907
Insomnia As A Risk For Increased Morbidity In Depressed Elderly Subjects Treated For Depression: The Impact Cohort
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Introduction: Chronic insomnia is associated with the increased incidence of new onset and recurrent depression (MDD). Less clear is whether chronic insomnia is a mediating or moderating factor for the clinical course of MDD. The present study examines the relationship of insomnia to the continuation of depression in the context of an intervention study.

Methods: Data were drawn from Project IMPACT, a multi-site intervention study for late-life depression. The study enrolled 1,801 patients with either MDD and/or dysthymia as assessed with the SCID and the SCL. Those with dysthymia only were excluded from the present analysis. The SCID was administered at baseline and at 6 months. The SCL was administered at baseline, 6, and 12 months. Insomnia was assessed using three items from the SCL; the SCL was then recalculated absent these items. Patients were classified as having, or not having, Persistent Insomnia (PI) based on whether complaints were evident at both baseline and at 6 months. The two groups (PI, N=73 and NO-PI, n=111) did not differ with respect to demographic variables or baseline depression severity. The two groups were assessed for MDD at 6 and 12 months using χ² analyses with both the SCID and the SCL.

Results: The two groups significantly differed for percent of subjects who remained ill at 6 and 12 months (all tests p<0.001). At 6 months, PI subjects were 4.7 times more likely to be ill (95% CI 2.49.1) based on the SCID and were 10.8 times more likely to be ill (95% CI 5.4,21.6) based on the SCL. At 12 months, PI subjects were 17 times more likely to be ill (95% CI 7.7,37.3) based on the SCL. Results did not differ by gender.

Conclusion: These findings suggest that persistent insomnia may be both a precipitating and perpetuating factor for MDD.

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0908
The Impact Of Acupuncture For Depression On Sleep During Pregnancy
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Introduction: Sleep disturbance is common among pregnant depressed women. Because alleviation of depression often leads to improved sleep, this study investigates the impact that acupuncture targeting depression during pregnancy has on sleep.

Methods: Eighty-eight pregnant women meeting diagnostic criteria for major depressive disorder scoring at least 14 on the Hamilton Rating Scale for Depression (HRSD) were randomized to receive either acupuncture specific for depression (SPEC, n=28), acupuncture not specific for depression (NSPEC, n=30), or massage (n=30). The HRSD interview was administered by a blinded interviewer at baseline, midpoint, and end of 8 weeks of treatment. Treatment response was defined by 50% or greater reduction in HRSD scores and a total HRSD score <14. The sleep subscale of the HRSD was defined as the average of its early, middle, and late insomnia items.

Results: Although there was a statistically significant difference in the proportion of women who responded to each of the three treatments (71.4% SPEC, 53.3% NSPEC, and 36.7% massage; chi-squared=6.95, p<0.01), there was no significant differential impact of the three treatments on either of the sleep measures (p>0.21). However, repeated measures ANOVA with response status as a between-subjects factor revealed that improvements in sleep subscale were significantly greater in responders than non-responders (F=7.60, p<0.01). The effect was most pronounced for late insomnia (F=4.23, p<0.05) with a trend in middle insomnia (F=3.750, p=0.056), but no significant difference in early insomnia (p=0.14).

Conclusion: The observed relationship between improvement in late and middle insomnia and response to treatment is noteworthy because the advancement of pregnancy is associated with increased sleep disturbance. Although acupuncture targeting depression had no differential impact on sleep, the acupuncture utilized in this study was designed to target depression, not insomnia. Nonetheless, this study underscores the relationship between depression and insomnia--as depression is alleviated, insomnia
improves regardless of the treatment received.

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**0909**
Sleep Hygiene Practices And Sleep Quality In Depressed And Anxious Outpatients
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**Introduction:** Sleep hygiene (SH) consists of a series of recommendations aimed at reducing behaviors that produce increased arousal and/or behaviors that are inconsistent with sleep organization. Rather than a primary cause of insomnia, poor sleep hygiene contributes to insomnia of other types, mainly that associated with mental disorders. However, as far as we know, specific SH rules, which may be contributing to poor sleep of patients with depressive and/or anxiety disorders, have not been described. Therefore, the aim of this retrospective study was the comparison of sleep quality between patients who practiced SH and those who did not.

**Methods:** Psychiatric outpatients with a primary diagnosis of Major Depression (n=31), Anxiety Disorder (n=15), and comorbid Major Depression and Anxiety Disorder (n=16) were included. Subjects with pharmacological and/or no pharmacological treatment in the last month, psychotic and substance related disorders were excluded. All patients filled two questionnaires: the Pittsburgh Sleep Quality Index (PSQI) and a self-rated instrument that assessed the practice of 22 SH rules during the previous month. PSQI scores were compared between subjects who practiced and those who did not practice each one of the SH rules.

**Results:** Sixty-two patients were studied (age 33.5, ± 14.4; female 77.5%). There were no significant differences in age, gender or PSQI scores between diagnostic groups. Significantly lower PSQI scores were observed just in patients who practiced one of the following SH rules: a) Regular arising time in the morning (10.1 ± 3.6 vs 12.6 ± 3.4, t 2.6); b) Morning exercise (9.2 ± 2.9 vs 12.1 ± 3.4, t 2.8); c) Avoid cocoa cola drinks (10.5 ± 4.2 vs 12.6 ± 2.9, t 2.2); d) Not going to bed with hunger or thirst (11.1 ± 3.5 vs 13.1 ± 3.9, t 1.9); e) Not staying in bed if not sleeping or sleepy (8.9 ± 3.3 vs 12.4 ± 3.5, t 3.3) (all p<0.05). Furthermore, the sum of the scores of these items showed a significant negative relation with PSQI scores (r=−.53, p<0.01).

**Conclusion:** These results support previous observations with respect to the participation of inadequate sleep hygiene in the poor sleep of patients with major depression or anxiety disorders. In addition, they suggest the existence of “active ingredients” in SH. The next step is testing the efficacy of the voluntary practice of these rules.

**0910**
Comparing Symptoms In Two Clinical Samples Of Hypersomnia And Adult Attention-Deficit/Hyperactivity Disorder
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**Introduction:** We aimed to explore the possibility of diagnostic confusion between hypersomnia (patients suffering from narcolepsy or idiopathic hypersomnia (IH)) and the adult form of Attention-Deficit/Hyperactivity Disorder (ADHD).

**Methods:** We used validated self-rating questionnaires, the Epworth Sleepiness Scale (ESS) and the ADHD-Rating Scale, to screen for the presence of excessive daytime sleepiness (EDS) and ADHD symptoms in hypersomnia patients and patients with the adult form of ADHD. A score ≥12 on the ESS was considered to reflect pathological daytime sleepiness. To qualify for the diagnosis ADHD, subjects were required to currently have at least 5 symptoms from 18 items on the ADHD-Rating Scale, while symptoms must have started during childhood, and been chronically present across the lifespan.

**Results:** We included 74 hypersomnia patients (67 narcolepsy, 7 IH) and 61 ADHD patients. Using the self-reported scores on the ADHD-rating scale, 18.9% of the hypersomnia patients fulfilled the criteria for ADHD in adulthood, compared to 77% of the ADHD patients. Regarding pathological daytime sleepiness, 53.6% of the ADHD patients had a score ≥12 on the ESS, compared to 95.9% of the hypersomnia patients. Of the narcoleptics, 16.4% fulfilled the ADHD criteria compared to 42.9% of the patients suffering from IH (p=0.03). In ADHD patients, the correlation between inattention and excessive daytime sleepiness was significant (r=0.339, p=0.008).

**Conclusion:** Our results show that one should be aware of possible diagnostic confusion between hypersomnias and the adult form of ADHD when using self-reporting rating scales. The high percentage of overlap found in our study, raises the question if the validation of the used scales is adequate. It remains unclear whether our findings point to a ‘real’ overlap between hypersomnias and ADHD, meaning that the disorders share a common pathophysiology.

**0911**
Sleep Disturbance And Depression Symptom Severity In Postpartum Women
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**Introduction:** Maternal sleep disturbance and transient low mood are common during the early postpartum months. This is often attributed to the burden of infant care, particularly during the night. This study explores the correlations between maternal depression symptoms, attending to an infant and maternal sleep at 10 weeks postpartum.

**Methods:** The sample included forty-seven women (mean age 34.3 ± 4.7). Depression severity was determined with the Hamilton Depression Rating Scale (mean score 8.6 ± 6.4). Mothers completed sleep diaries for a week from which the following sleep variables were derived: sleep latency, minutes awake after sleep onset, early morning awakening, overall sleep quality, and number of awakenings and total time awake to attend to the infant.

**Results:** Depression severity was significantly correlated with maternal sleep but not with measures of attending to the infant. In particular, depression severity was significantly correlated with early morning awakening (r=0.60, p=0.001), sleep latency (r=0.53, p=0.001), and sleep quality (r=−0.43, p=0.01), but not with minutes awake after sleep onset (p=0.6). As expected, the total time awake to attend an infant was significantly correlated with maternal sleep latency (minutes awake after sleep onset (r=0.76, p<0.001) and early morning awakening (r=0.75, p<0.01)). Additionally, the number of times awakened to attend infant was significantly correlated with subjective sleep quality (r=0.57, p=0.02).

**Conclusion:** These findings challenge the common assumption that infant sleep disruptions drive maternal depression during the postpartum period. Although at 10 weeks postpartum, the number of times and minutes spent attending to the infant were clearly associated with disruptions to maternal sleep continuity and poor subjective sleep quality, it was not associated with depression symptom severity. In contrast, sleep latency and early morning awakening were significantly correlated with depres-
Premenstrual Dysphoria Disorder (PMD) is characterized by depressed mood and lack of interest in activities during the luteal phase of the menstrual cycle. It is estimated that as many as 18% of women may suffer from this disorder (Cantor, 2000). PMD was recommended as a disorder for future study and research is being conducted to determine its eligibility for inclusion in DSM-V as a clinical disorder. Previous studies suggest that physiological (e.g., changes in hormones) and psychological factors (e.g., perceived stress, negative affect) maybe related to symptoms of PMD. The purpose of this study was to further explore these factors in an ethnically diverse sample of college women.

Methods: Participants in this study were 327 women, undergraduate college students (36% Caucasian, 20% Latina, 20% Asian, 13% Pacific Islander) with a mean age of 19.1 years. Participants were asked to complete a battery of questionnaires that included items from the proposed DSM-IV diagnostic criteria for PMD, the Arousability Predisposition Scale (APS; Coren, 1988), Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989), and the Dream Types Survey (DTS; Spadofora & Hunt, 1990).

Results: Independent sample t-tests were computed to compare participants who score in the high (n= 83) and low 25th quartiles (n= 63) on the PMD scale on APS, PSQI and DTS. The High-PMD group scored significantly higher than the Low-PMD group on the APS (p < .001), and the sleep disturbance (p < .004) and daytime dysfunction (p < .001) subscales of the PSQI. In addition, the High-PMD group scored significantly higher than the Low-PMD group on seven of the eight dream types on the DTS (i.e., Lucid Dreams, Fantastic Nightmares, PreLucid Dreams, Control Dreams, Post Traumatic Dreams, and Night Terrors). Ethnicity did not moderate the strength of these relationships.

Conclusion: These data suggest that women suffering from PMD are more physiologically aroused in stressful situations and experience greater nighttime sleep disturbances and disturbing dreams than women who do not suffer from this disorder. Interventions designed to treat women with PMD should consider arousal and sleep disturbances as targets of their interventions.

Introduction: Seasonal Affective Disorder (SAD) is characterized by depressed mood, increased sleepiness, energy loss, decreased social activity, increased appetite and weight gain occurring during a certain period of the year. Sleep disturbances are considered a central feature of the disorder. In this study we explore correlations between seasonality and sleep complaints.

Methods: All men (n=15051) and women (n=14349) aged 40-45 years in Hordaland county, Norway, were invited to join a health survey in 1997-99. Totally 8598 men (57%) and 9983 women (70%) met at the screening station. These women and half of the men completed a health questionnaire containing the Global Seasonality Score (GSS), evaluating seasonal changes in sleep, mood, weight, energy, social activity and appetite. In addition, 3531 of the men and 5329 of the women answered a questionnaire asking about sleep problems. Depending on their GSS, subjects were divided into groups: no/low seasonality (GSS below 8), moderate seasonality (GSS 8-10) and high seasonality (GSS above 11). ANOVA was used to compare means.

Results: Poor/very poor sleep quality was significantly more common among subjects with high seasonality (men 9.7%, women 11.2%) than among those with no/low seasonality (men 4.2%, women 4.1%). There was also a significant correlation between high seasonality and sleeplessness affecting work the last year (men 22.0% vs. 9.1%; women 23.9% vs. 9.6%). Difficulties falling asleep, difficulties maintaining sleep and early morning awakening were reported significantly more often among subjects with high seasonality. Additionally, they were sleepier during daily activities and more frequently napped during daytime.

Conclusion: According to the nature of seasonal affective disorder (SAD), increased daytime sleepiness with high seasonality was expected. However, also symptoms indicating insomnia were common among subjects with high seasonality.
Results: for sex and age. Cohen's d effect sizes were computed to assess the magnitude of differences compared to data collected in 7 archival healthy control subjects equated to characteristics of the emergency ward. This suggests that: A) The dream experience of drug-naive patients with schizophrenia may not be so different from that of the general population; B) Differences may essentially lie in the capacity to organize verbal accounts.

Canadian Institutes of Health Research

0915
An Ecological Valid Study Of Sleep In PTSD
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Introduction: Sleep disturbances are a core feature of Posttraumatic Stress Disorder (PTSD), but sleep laboratory-based findings do not consistently corroborate subjective complaints. The goal of this pilot study was to investigate sleep in PTSD by using in-home sleep recordings.

Methods: Ten victims of violent crime with PTSD (mean age: 34.6 years old, SD = 6.3 years n = 7 women) participated in this study. Five suffered from comorbid depression. All completed two consecutive nights of in-home sleep studies. Recordings were conducted using the VitaPort system (Temec Instruments, 2002). Sleep parameters recorded on night 2 were compared to data collected in 7 archival healthy control subjects equated for sex and age. Cohen's d effect sizes were computed to assess the magnitude of group differences.

Results: Compared to healthy subjects, PTSD subjects showed longer sleep latency (d = .57), increased number and duration of nocturnal awakening (d = 1.06 and d = .93, respectively), and reduced total sleep time (d = 1.42). Quantitative EEG analyses indicated that PTSD subjects had greater beta activity (d = .36) and reduced delta activity (d = 1.45) during NREM sleep compared to healthy subjects. Preliminary heart period analyses conducted in 4 PTSD and 4 healthy subjects suggest that parasympathetic tone is lower in PTSD than healthy subjects during both NREM and REM sleep (d = 3.14 and d = 2.20, respectively), where as sympathovagal tone appears higher during NREM sleep in PTSD compared to healthy participants (d = .92).

Conclusion: Medium to large effects sizes observed in this study suggest that PTSD is associated with objective sleep disruption as indexed by visually scored sleep, EEG power spectrum, and heart period analysis. These findings are consistent with subjective complaints of poor sleep quality in PTSD. In-home sleep studies enhance the ecological validity of sleep findings in PTSD.

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0916
Eszopiclone Co-Administered With Fluoxetine For Insomnia Associated With Major Depressive Disorder (MDD): An Analysis Of The Effects On Depression
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Introduction: Insomnia frequently co-exists with depression but currently no treatment standards exist addressing hypnotic administration during antidepressant therapy. This study evaluated the efficacy of eszopiclone in patients with newly diagnosed MDD and co-morbid insomnia during concurrent fluoxetine treatment.

Methods: Patients who met DSM-IV criteria for both new MDD and insomnia received 10 weeks of fluoxetine QAM and were randomized to nightly eszopiclone 3mg (n=270) or placebo (n=275) for 8 weeks. Antidepressant efficacy was assessed using HAMD17 (assessed baseline, weeks 4, 8); Clinical Global Impression Improvement (CGI-I) and Severity (CGI-S; both assessed weekly); Response=50% decrease from baseline HAMD17; and remission=HAMD17 ≤ 10.

Results: Completion rates were similar (PBO=66%; ESZ=69%). In addition to significantly improved sleep versus placebo (p<0.05), eszopiclone co-administration resulted in significant reductions in HAMD17 scores compared to placebo co-administration at Week 4 (-9.9 vs -8.5 placebo, p=0.02) with progressive improvement at Week 8 (-13.8 vs -11.8, p<0.001). After removing HAMD17 insomnia items, differences remained significant at Week 8 (p<0.03). HAMD17 differences were greater in patients with more severe depression (baseline HAMD17 ≥ 22). At Week 8, significantly more eszopiclone patients were responders (74% vs 61%, p<0.009) and remitters (54% vs 41%, p<0.02). CGI-I and CGI-S scores were significantly improved with eszopiclone co-administration (p<0.05). Fewer eszopiclone patients required fluoxetine dose increases (44% vs 54%; p<0.05). Treatment was well-tolerated, with similar AE and drop-out rates. One patient in each group experienced a suicidal ideation AE.

Conclusion: In this study, eszopiclone/fluoxetine co-administration significantly augmented the antidepressant response in patients with MDD and insomnia. The sleep response to eszopiclone occurred immediately, followed by an augmentation of the antidepressant response. These results provide evidence that co-existing insomnia may be successfully targeted in conjunction with antidepressant therapy, and suggest that the addition of eszopiclone may augment fluoxetine efficacy in MDD.

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0917
Eszopiclone Co-Administered With Fluoxetine For Insomnia Associated With Major Depressive Disorder (MDD): Sleep Effects
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Introduction: Insomnia and MDD commonly co-exist. However, clinicians hesitate to co-administer hypnotics with antidepressants for insomnia associated with MDD given the lack of efficacy and safety data for this combination. This study evaluated the efficacy of eszopiclone co-administered with fluoxetine in patients with newly diagnosed MDD and insomnia.
Methods: Patients (n=545) met DSM-IV criteria for MDD and insomnia, including sleep latency (SL) ≥30 minutes (median=74), wake time after sleep onset (WASO) ≥45 minutes (median=90), and total sleep time (TST) ≤390 minutes (median=294). All patients received fluoxetine QAM, and were randomized to nightly eszopiclone 3mg (n=270) or placebo (n=275) for 8 weeks. Subjective sleep and daytime function were assessed weekly by telephone; depression was assessed in the clinic with the HAMD17 every 4 weeks; and insomnia was assessed with the Insomnia Severity Index (ISI) bi-weekly.

Results: Completion rates were similar (placebo=67%; eszopiclone=69%). Compared with placebo, eszopiclone was associated with significantly decreased SL and greater TST at each treatment week (p<0.03); significantly less WASO at Weeks 1, 3, 5, and 7-8 (p<0.04); higher ratings across the treatment period in sleep quality and depth (p<0.005); and higher ratings of daytime alertness, ability to concentrate, and physical well-being (p≤0.02). At each assessment point, all three sleep-related items of the HAMD17 (early-, middle-, late-insomnia; p≤0.05) and all scales of the ISI (p≤0.0002) were significantly lower in eszopiclone versus placebo groups. Combined treatment was well-tolerated. Unpleasant taste was more common with eszopiclone.

Conclusion: In this study, co-administration of eszopiclone with fluoxetine was well-tolerated and associated with significant improvement in sleep and daytime symptoms in patients with MDD and insomnia. The significant improvement in sleep in patients treated with adjunctive eszopiclone may be a particularly important finding for clinical practice, given the relatively slow onset of antidepressant effects with SSRIs.

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0918
Eszopiclone Co-Administered With Fluoxetine For Insomnia Associated With Major Depressive Disorder (MDD): Effects Following Eszopiclone Discontinuation
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Introduction: Insomnia and MDD frequently co-exist. One of the concerns with concomitant insomnia/depression treatment is rebound insomnia upon hypnotic discontinuation. This study evaluated the discontinuation effect after concurrent eszopiclone/fluoxetine therapy.

Methods: Patients met DSM-IV criteria for MDD and insomnia, including sleep latency (SL) ≥30 minutes, wake time after sleep onset (WASO) ≥45 minutes, and total sleep time (TST) ≤390 minutes. All patients received fluoxetine for 8-weeks QAM, and were randomized to 8-weeks of nightly eszopiclone 3mg (n=270) or placebo (n=275), followed by 2 weeks of continued fluoxetine and single-blind placebo to evaluate discontinuation effects. During the discontinuation phase, subjective sleep was assessed daily; depression was assessed with the HAMD17 at the end of the phase (Week 10). Discontinuation effects were examined 2 ways: 1) change from baseline to Week 10; change from end of hypnotic treatment (EOT; Week 8) to Week 10.

Results: There was no evidence of rebound insomnia. Relative to baseline, patients discontinued from eszopiclone had significantly improved sleep (p<0.05) during the discontinuation phase at each daily assessment point for SL, WASO, and TST (average change -49.7, -52.4, and 100.5 minutes, respectively). Relative to EOT, the 2-week average change was not significantly different for SL, WASO, or TST (average change 4.0, -0.7, and -0.7 minutes, respectively) in patients discontinued from eszopiclone. The eszopiclone group maintained the significant sleep improvements from the first 8-weeks versus placebo (Week 8-10 average p<0.05). The improvements in HAMD17 scores versus placebo seen at EOT (-14.2 vs -12.2; p=0.0009) were maintained at Week 10 (-14.8 vs -12.2; p<0.0001).

Conclusion: In this study the sleep improvements associated with eszopiclone/fluoxetine co-administration were not followed by rebound insomnia after hypnotic discontinuation. Discontinuing eszopiclone did not appear to negatively impact the antidepressant effect, but additional studies are needed to investigate the optimal duration of combination therapy.

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0919
The Association Between Sleep Continuity And Depression: Evidence For Partial Mediation By Global Attributional Style
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Introduction: Individuals with depression often experience sleep continuity disturbances. Depressed individuals also use internal, stable, and global attributions for negative events (i.e., Seligman’s learned helplessness model of depression). To date, no research in depression has investigated the relationship between sleep continuity and attributional style. We hypothesized that a negative, stable and global attributional style would mediate the relationship between sleep continuity and depression.

Methods: Twenty-three depressed and 23 never depressed participants completed the Attributional Styles Questionnaire and wore an actigraph over the course of one week. Linear and logistic regression techniques were used to calculate path coefficients. The significance of the mediation effect by computing confidence limits that were based on the distribution of the product of two normal random variables (MacKinnon et al., 2004).

Results: Increased wake time after sleep onset (WASO) was directly associated with increased use of global attributions in negative situations (β = 0.08, SE β = 0.04, p < 0.05), and the use of global attributions increased the likelihood of depression (β = 0.16, SE β = 0.06, p = 0.01, Odds Ratio = 1.17). The mediation effect was statistically significant (ab = 0.01; SE = 0.008; CI95% = 0.01, 0.04) and partial, instead of full. When controlling for attributional style, WASO continued to predict an increased likelihood of depression. Similar effects were found for other sleep continuity indices. No mediation effects were found for stable or internal attributions.

Conclusion: This is the first study to date testing the relationship between attributional style and sleep in depression. These results suggest that sleep disruption in depression may contribute to the use of a global attributional style. They also provide data consistent with the hypothesis that disrupted sleep is associated with learned helplessness. Future studies are necessary to test the directionality of these relationships.

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0920
EEG Delta Activity Deficit During nonREM Sleep In Drug-Naive Patients With Schizophrenia
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Introduction: Visual scoring of sleep records show a slow wave sleep deficit in schizophrenia. Spectral analysis of sleep EEG using restricted montage have also shown a delta activity deficit during non-REM sleep in previously or actively treated patients. We used a full EEG montage to map non-REM sleep delta activity in drug-naive patients with schizophrenia.

Methods: Eight acute patients never exposed to neuroleptics (4 women, 4 men, 31.3 ± 17.0 years old) were brought from the emergency ward to the sleep laboratory for two consecutive nights during the first week of their hospitalization. The final diagnosis of schizophrenia was confirmed within six months. Controls were seven healthy participants (3 women, 4 men, 23.3 ± 8.5 years old). Participants were recorded with a 10-electrodes EEG montage (C3, C4, Fp1, Fp2, F7, F8, T3, T4, O1, O2) referenced to linked earlobes. Non-REM sleep (stages 2, 3, 4) EEG spectral power amplitude was computed for the first seven hours of the night. Delta 1 (0.75-2.25 Hz), Delta 2 (2.25-3.75 Hz) and Total Delta (0.75-3.75 Hz) was extracted. Groups were compared using t-tests.

Results: Delta 1, Delta 2 and Total Delta activity was significantly reduced (all p < .05) in patients on bilateral central (C3 and C4) and temporal recording sites (T3 and T4) except for T4 Delta 2. Frontal electrodes did not show significant differences whatsoever.

Conclusion: The present results suggest that centro-temporal areas best express EEG Delta activity differences between drug-naive patients with schizophrenia and healthy controls. The absence of differences at the frontal level may be due to a ceiling effect, since maximum Delta energy is normally spent anteriorly. Although both frontal and centro-temporal areas are involved in the physiopathology of schizophrenia, this seems not to be expressed at the frontal level during non-REM sleep in drug-naive patients.

Canadian Institutes of Health Research

0921
Decrease In Left Ventral Anterior Cingulate Perfusion Correlates With Antidepressant Response To Partial Sleep Deprivation
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Introduction: This study used functional MRI (fMRI) to investigate mechanisms of antidepressant effect of 1 night’s late-night (awake beginning at 3 am) partial sleep deprivation (PSD) in current major depression. We hypothesized that change in depressed patients’ ventral anterior cingulate perfusion would correlate with antidepressant response to PSD.

Methods: 17 unmedicated unipolar outpatients (baseline 17-item Hamilton Depression Rating Scale (HDRS17) ≥ 16, M/F 5/12, 42.8 ± 9.7 years) and 8 controls (M/F 4/4, 35.0±9.5 years) received 3 nights polysomnography (adaptation, baseline, and PSD) in the sleep laboratory. Approximately noon after the baseline and PSD nights, subjects received anatomical and perfusion magnetic resonance imaging (MRI) using pulsed arterial spin labeling, with baseline and PSD blocks in randomized counterbalanced order. Data were analyzed using Analysis of Functional NeuroImages (AFNI) 2.56b. Stripped brains were segmented by fitting a 3-compartment Gaussian mixture model to the intensity histogram. Resulting gray matter masks were transformed into Talairach space and merged with Talairach daemon-based region of interest (ROI) templates to create standardized yet individualized ROI templates, which were used to mask perfusion data.

Results: In patients, decrease in left ventral anterior cingulate perfusion from baseline to PSD scans correlated directly with the decrease in the modified HDRS17 (omitting sleep and weight loss items) between baseline and PSD conditions (1-tailed Pearson correlation coefficient .457, p < .033). No other ROIs showed correlations between change in modified HDRS17 and change in perfusion.

Conclusion: These preliminary data—the first using fMRI—are consistent with previous PET (positron emission tomography) and SPECT (single photon emission computed tomography) findings of sleep deprivation and depression in linking decreased brain activity in this area with clinical improvement.
0923

Those With Depression Report Different Beliefs About Sleep Than Those With Primary Insomnia Or Good Sleepers

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Introduction: Primary Insomnia (PI) is a risk factor for Major Depressive Disorder (MDD). Both MDD and PI are characterized by dysfunctional thought patterns that can maintain the disorder. In PI, the thought content focuses specifically on sleep and its consequences, rather than the globally negative thought content in MDD. This study assessed whether beliefs relating to sleep were different in those with PI versus those with MDD or good sleepers (GS).

Methods: The MDD group was comprised of a treatment-seeking sample meeting diagnostic criteria for MDD. The PI group met diagnostic criteria for PI only, and the GS group did not meet criteria for MDD or PI. All three groups (N = 240) completed the Dysfunctional Beliefs about Sleep scale (DBAS-16).

Results: Analyses of variance (ANOVAs) were conducted on the 16 items of the DBAS. There were group differences on 15 items. On follow-up comparisons: DEP>PI>GS on 4 items and total DBAS score; DEP>GS=PI on 6 items; PI>DEP=GS on 1 item; PI>DEP>GS on 2 items, and PI=DEP>GS on 2 items.

Conclusion: The DEP group had higher scores on most items of the DBAS than either group. The beliefs that discriminated MDD from GS and PI groups were related to having unrealistic expectations about sleep and using medication or avoidance as ways of coping with sleep problems. In contrast, those with PI were more likely to attribute poor functioning or negative mood to poor sleep and viewed their sleep as more unpredictable than MDD or GS groups. The findings do not support the idea that global negative thinking completely accounts for the relation between sleep and depression, given that MDD do not have uniformly higher negative beliefs (e.g., PI have more negative beliefs on some items, and MDD and GS do not differ on some beliefs). Future studies could evaluate what sleep-beliefs change with depressive remission, and whether modifying particular sleep-related beliefs could lead to reduced sleep complaints or decrease relapse risk.

0924

Polysomnographic And Symptomatological Analyses Of Major Depressive Disorder Patients Treated With Mirtazapine


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Introduction: Although slow wave sleep (SWS) re-distribution and REM sleep changes are important features of depression knowledge of mirtazapine effects on them is limited. We investigated the mirtazapine-induced changes in polysomnographic measures, particularly SWS and REM sleep, subjective sleep evaluation and depressive symptomatology in a group of major depressive disorder (MDD) patients longitudinally as they were treated with mirtazapine.

Methods: Sixteen (16) MDD patients were treated with mirtazapine 30 mg taken at bedtime. Polysomnographic and subjective sleep, as well as other clinical data were collected at baseline and on days/night 2, 9, 16, 30 and 58 while on treatment. Repeated measures ANOVA, including pairwise comparison, was used to analyze data statistically.

Results: Mirtazapine administration increased total SWS (F = 2.95, p = 0.017) and the SWS in the first sleep cycle (F = 2.43, p = 0.043), but not that in the second sleep cycle. The medication increased REM latency (F = 2.72, p = 0.026) and the duration of the first REM episode (F = 2.46, p = 0.040), and decreased the number of REM episodes (F = 4.14, p = 0.002). Simultaneously, mirtazapine significantly reduced wake after sleep onset (F = 2.49, p = 0.038) and lowered the scores on the Athens Insomnia Scale (F = 6.90, p = 0.000). After taking the medication, the scores of the Hamilton Rating Scale for Depression (HRSD-17) decreased rapidly and continuously (F = 48.75, p = 0.000). The changes on Beck Depression Inventory-II (F = 7.67, p = 0.000) were similar to those of HRSD-17. Mirtazapine was shown to have a significant tendency to increase weight (F = 3.75, p = 0.016)

Conclusion: Mirtazapine significantly improved the sleep quality, reversed the sleep markers of depression and concurrently reduced the depressive symptoms in this group of MDD patients.

0925

Insomnia In Generalized Anxiety Disorder: Symptom Or Comorbidity?

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Introduction: The relationship between insomnia and GAD remains equivocal. Our objective was to examine the evolution of insomnia and GAD in time and assess the risk associated with the presence of each condition on the later occurrence of the other condition.

Methods: Data are derived from an epidemiological study assessing the prevalence, incidence, and natural course of insomnia over a 2-year period. Two thousand randomly selected French-speaking adults from the province of Quebec took part in an initial telephone survey. Respondents were categorized into three sleep/insomnia subgroups using an algorithm devised according to DSM-IV and ICD-10 diagnostic criteria: 1) good sleepers; 2) presence of insomnia symptoms; 3) insomnia syndrome. From the initial pool, 997 individuals completed several self-report measures at four time points: 0, 6, 12 and 24 months. The assessment protocol also included the Worry and Anxiety Questionnaire (WAQ), a self-report GAD screening instrument.

Results: At baseline, 122/961 individuals met GAD criteria according to the WAQ. Of these, 13% (17/122) were good sleepers, 23.8% (29/122) presented insomnia symptoms, and 62.3% presented an insomnia syndrome. Multivariate logistic regression showed that when the presence of GAD was controlled for, individuals with insomnia symptoms at baseline were 3.2 times [1.4-7.3] more likely than good sleepers to meet GAD criteria at the following time-point (6-month), those with an insomnia syndrome were 5.8 times [2.7-12.9] more likely to do so. Conversely, when the presence of insomnia was controlled for, those with GAD at baseline were 1.6 [1.0-2.5] times more likely to have insomnia symptoms or syndrome at the following time-point than those with no GAD. The other time-points remain to be examined.

Conclusion: Results suggest a reciprocal relationship between GAD and insomnia, but also stress the importance of assessing sleep in GAD patients because several may meet the criteria for a full insomnia syndrome.

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Sleep Disturbances In A Nationally Representative Sample 2 Months And 6 Months Following The Terrorist Attacks Of September 11, 2001

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Introduction: The terrorist attacks of September 11, 2001, traumatized many who watched the events and their aftermath unfold on television. Their horrific nature had a psychological impact on people throughout the United States, with many reporting difficulties with their sleep in the weeks and months following the attacks. This study documents these 9/11-related sleep disturbances in a nationally representative sample.

Methods: Questionnaires were distributed via Knowledge Networks (KN), a Web-based survey company which collects data from a nationwide sample. KN works to match its sample to current US Census data on benchmarks such as age, sex, race, household income, and geographic region. A total of 869 participants (394 male, 391 female, 84 sex unreported) completed questionnaires both at 2 months post-9/11 (November 10 - December 3, 2001) and 6 months post-9/11 (March 16 - April 11, 2002). Participants were asked to report 9/11-related sleep disturbances they had experienced in the past week.

Results: At 2 months following September 11, 2001, 34% of the sample reported difficulty staying asleep associated with 9/11; 15% described this difficulty as moderate or greater. 29% reported difficulty falling asleep associated with 9/11; 13% reported this difficulty as moderate or greater. 18% reported experiencing dreams related to 9/11; 7% reported the amount as moderate or greater. At 6 months following September 11, the percentages of people reporting sleep disturbances dropped as followed: 17% difficulty staying asleep (6% moderate or greater), 16% difficulty falling asleep (6% moderate or greater), 9% dreams (3% moderate or greater). The change in percentage from 2 months post-9/11 to 6 months post-9/11 was significant (p<0.001) for all variables.

Conclusion: These data suggest that the terrorist attacks of September 11, 2001, had a profound effect on Americans' sleep. This effect was attenuated with the passage of time, although large numbers of people still reported difficulties.

Stability Of Executive Function Across The Binge-Abstinence Cycle In Cocaine Users

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Introduction: Abstinent chronic cocaine users show executive function (EF) deficits, however little is known about EF fluctuations during binge-abstinence cycles in which significant sleep disturbances occur.

Methods: Ten cocaine-dependent males and 2 females (mean age 39) completed a 23-day inpatient protocol: Washout (WA) -- Day (D) 1-3; Binge (BI) -- D4-6 (six "early bingers") or D18-20 (six "late bingers"); followed (early) or preceded (late) by 2 weeks Abstinence (AB). Each binge day, participants self-administered up to 384mg/70kg of IV cocaine via patient-controlled analgesia pumps. An EF battery was administered four times: at WA on D3; during BI (D6 early bingers, D20 late); early (AE) abstinence (D8 early, D22 late); and late (AL) abstinence (D22 early, D17 late). Tests assessed: attention-- Forward Digit (DSF) and Spatial (SSF) Span; processing speed-- Symbol-Digit Modalities (SDM); working memory-- Backward Digit (DSB) and Spatial (SSB) Span and 2-Back; inhibition-- GO/NO-GO and D-KEFS Color-Word (CW); initiation-- D-KEFS Fluency (FL); set shifting -- D-KEFS Sorting (SO); concept formation-- D-KEFS 20-Questions (20Q); decision making-- Iowa (IG) and Rogers (RD) Gambling; orbitofrontal areas-- Smell Identification (SIT). Identical CW, SDM and SIT were given at four testings; alternate versions of FL, SO and 2Q were given twice (BI and AL); with the remainder four times in counterbalanced versions. ANOVA analyzed phase (WA, BI, AE, AL) and order (presentations 1-4) effects.

Results: DSF, SSF, DSB, SSB, 2-Back (accuracy), GO/NO-GO, SIT and FL, SO and 2Q major variables showed no phase effects. DS, SS and 2-Back accuracy showed no order effect. SDM, 2-Back (RT), CW (interference-switch) and IG and RD major variables showed more significant order than phase effects indicating practice effects. CW (interference) showed more significant phase (p<.02, AE > WA, AL) than order (p<.05) effects.

Conclusion: Results suggest stability of EF over the binge abstinence cycle. CW (Stroop) interference effects appear less in AE than AL.

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Effect Of Anticipatory Anxiety On Sleep

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Introduction: Anxiety disorders, including PTSD, are accompanied by changes in sleep. Little is known about the impact of experimentally-induced anxiety in healthy subjects. Investigation of the effects of anxiety on sleep in individuals without psychopathology may shed light on the neurobiological mechanisms of anxiety disorders. This study examined the threat of a mild electric shock as a model for identifying how anticipatory anxiety affects sleep.

Methods: Thirteen healthy subjects (mean(SD) age= 24.3(3.7)) spent three nights in the sleep laboratory. After an habituation night, subjects underwent, in random order, a baseline night and an anticipatory anxiety (AA) night. Subjects rated their anxiety on the State-Trait Anxiety Inventory and had their sleep monitored. On the AA night, subjects received a mild electric shock (1.5 mA) to the wrist before retiring and were told that they would receive up to three additional shocks during the night, although no more shocks were actually administered. Differences between baseline and AA nights in subjective ratings of anxiety, sleep macroarchitecture, and REM sleep beta power were compared using paired-samples t-tests. In addition, correlations between change scores were computed.

Results: There was a significant increase in pre-sleep subjective anxiety on the AA night (28.6 vs. 34.7; t(13)= -2.51, p<0.05). There were no effects on sleep macroarchitecture and spectral power. Higher anxiety on the AA night compared to the baseline night was associated with lower beta power during the third REM period (r= -84, p<0.05).

Conclusion: There was considerable variability in response to the threat of electric shock, which obscured global effects of anxiety on sleep. Decreases in beta power during the third REM period in more anxious subjects may suggest lower cortical arousal in these subjects later in the night. The significance of beta power during REM remains unclear. There results suggesting a modulatory role for anxiety in the generation of REM beta activity may contribute to the development of new hypotheses.

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Introduction: Meditation has been found to improve subjectively reported sleep disturbance, as well as depression. The purpose of this study was to investigate the effects of meditation on objectively measured sleep, and depression, and to assess whether improvements in sleep are associated with improvements in depression.

Methods: Individuals with partially remitted depression (n=14) underwent overnight PSG sleep studies before and after an 8-week meditation-based depression relapse prevention program called Mindfulness-Based Cognitive Therapy (MBCT). All participants also completed weekly sleep diaries and depression inventories before and after the program.

Results: Sleep diaries (n=14) showed a significant increase in sleep efficiency (p<.004), a marginal decrease in WASO (p=.054), and a trend toward decreased sleep onset latency (p=.11) between baseline and week 7 of the meditation treatment. From PSG data of participants with baseline sleep efficiency below 90% (n=8), the number of microarousals decreased significantly (p<.05), stage 1 minutes decreased marginally (p=.07), and there was a trend toward decreased awakenings (p=.10) following treatment. Medicated participants (n=6) showed more improvement in their sleep disturbance after meditation compared to unmedicated participants (n=8). However, the medicated participants showed more disrupted sleep at baseline, as evidenced by significantly more microarousals (p=.001), minutes in stage 1 (p=.008), and a trend toward more wake after sleep onset (p=.17). REM latency increased in the medicated participants and decreased in the medicated subjects. Multiple regressions with sleep efficiency and arousals as predictors for REM latency were calculated for medicated and unmedicated participants separately. Sleep efficiency significantly predicted REM latency in the medicated participants (R-squared=.70, p<.05), but not in the unmedicated ones. Thus, decreases in REM latency in the medicated group were strongly associated with reductions in sleep disturbance, although increases in REM latency were unrelated to sleep disturbance. BDI scores decreased significantly from pre to post treatment, (p<.05), with no effect of medication on baseline or change in depressive symptoms. Changes in self-reported sleep efficiency predicted improvement in depression scores (R-squared=.46, p<.05).

Conclusion: Improvement in sleep disturbance, including REM abnormalities, appears to be a mechanism by which MBCT improves depressive symptoms.

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Driving Simulator Performance In Bipolar Patients And Controls

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Introduction: Recently the Virginia Department of Motor Vehicles has requested psychiatrists’ reports on their bipolar patients’ fitness to drive. There is no current scientific basis upon which to base these decisions. We are not aware of studies of bipolar patients’ ability to drive during episodes of mania, depression, mixed states, or during recovery. This study examined driver simulator (DS) performance of bipolar patients and controls. We hypothesized that bipolar patients would have greater lane position variability (LPV) and more crashes due, in part, to task inattention.

Methods: Eleven bipolar patients (4 males, 7 females) and 9 control participants (5 males, 4 females) completed the study. We recruited bipolar patients from psychiatric inpatients at Sentara Norfolk General Hospital and among outpatients undergoing treatment through the Eastern Virginia Medical School (EVMS) psychiatric service. Patients met DSM-IV criteria for diagnosis. We recruited healthy control participants with a Epworth Sleepiness Scale < 11 from the community.

Results: Bipolar patients demonstrated increased LPV (mean = 1.66, SD = 0.69) over control participants (mean = 1.16, SD = 0.13), F (1, 18) = 4.611, p = .046. Three bipolar patients crashed during the drive. No control patients crashed. Bipolar patients had a mean Epworth Sleepiness Scale (ESS) score of 10.5 +/-5.5 (SD) while controls had a mean ESS of 4.8 +/-10.5.

Conclusion: Increased LPV occurred in bipolar patients in simulated driving conditions. This increased LPV is similar to that of severe obstructive sleep apnea patients who have demonstrated a mean lane variability ranging from 1.3 to 2.6 ft (Risser et al, 2000). We plan to compare bipolar patients who are controlled with those uncontrolled in an attempt to differentiate between disease state effects and medication effects.

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Driving Simulator Performance In Bipolar Patients And Controls

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Introduction: Recently the Virginia Department of Motor Vehicles has requested psychiatrists’ reports on their bipolar patients’ fitness to drive. There is no current scientific basis upon which to base these decisions. We are not aware of studies of bipolar patients’ ability to drive during episodes of mania, depression, mixed states, or during recovery. This study examined driver simulator (DS) performance of bipolar patients and controls. We hypothesized that bipolar patients would have greater lane position variability (LPV) and more crashes due, in part, to task inattention.

Methods: Eleven bipolar patients (4 males, 7 females) and 9 control participants (5 males, 4 females) completed the study. We recruited bipolar patients from psychiatric inpatients at Sentara Norfolk General Hospital and among outpatients undergoing treatment through the Eastern Virginia Medical School (EVMS) psychiatric service. Patients met DSM-IV criteria for diagnosis. We recruited healthy control participants with a Epworth Sleepiness Scale < 11 from the community.

Results: Bipolar patients demonstrated increased LPV (mean = 1.66, SD = 0.69) over control participants (mean = 1.16, SD = 0.13), F (1, 18) = 4.611, p = .046. Three bipolar patients crashed during the drive. No control patients crashed. Bipolar patients had a mean Epworth Sleepiness Scale (ESS) score of 10.5 +/-5.5 (SD) while controls had a mean ESS of 4.8 +/-10.5.

Conclusion: Increased LPV occurred in bipolar patients in simulated driving conditions. This increased LPV is similar to that of severe obstructive sleep apnea patients who have demonstrated a mean lane variability ranging from 1.3 to 2.6 ft (Risser et al, 2000). We plan to compare bipolar patients who are controlled with those uncontrolled in an attempt to differentiate between disease state effects and medication effects.

This study was supported in part by the Norfolk Foundation

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with findings of previous research that habitual short sleep is associated with increased drive and energy during the day. One possible mechanism that may explain this relationship is the activating effect of REM deprivation that has been shown in previous studies to be associated with shorter sleep (Vogel, 1979). The mood and energy reinforcement associated with being a short sleeper may also explain why some people choose to sleep fewer hours each night despite the documented negative physical consequences associated with habitual short sleep.

0932
Sleep Paralysis, Psychiatric Symptoms And Disorders In An Adult African American Population Attending Primary Care Clinics
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Introduction: Sleep paralysis (SP) is a feature of narcolepsy but can be an isolated sleep disorder (ISP). Prior studies have suggested that ISP is common and is associated with panic disorder in African Americans (AA). As narcolepsy is a disorder of REM sleep intrusion, and PTSD and depression can feature altered REM sleep, we were also interested in relationships between ISP, trauma exposure, PTSD and depression.

Methods: Items probing SP and other sleep phenomena were added to a study of trauma exposure and psychiatric disorders in AA attending primary care clinics affiliated with Howard University, a historically black institution in Northwest Washington D.C. Participants filled out surveys that included assessments of lifetime trauma exposure, and recent mood and panic attack symptoms. The subset with trauma exposure later received in-depth interviews that included psychiatric diagnostic criteria.

The mean age of participants was 40 and 67 % were female.

Results: Forty four or 11.8% of the 372 participants of the initial survey indicated having episodes of SP during the previous 6 months with most not expressing other features of narcolepsy. There were strong associations of SP with trauma exposure (77% of those with SP vs. 59% without, chi square = 5.7, p<.02) and recent panic symptoms (38% vs. 7%).

Mean self-reported depression symptoms were twice as severe with SP (t=6.9, p<.001). From the interview phase that included 31 of 44 participants with SP, SP was not associated with significantly greater rates of lifetime PTSD (58 % versus 42%), panic disorder (7% versus 6%), and major depression (32% versus 30%).

Conclusion: These data indicate that recent episodes of SP are not uncommon in adult African Americans and are associated with elevated rates of trauma exposure and current mood and anxiety symptoms. Preliminary diagnostic information, however, does not support a relationship to specific psychiatric disorders.

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0933
Cognitive Behavioral Therapy Of Insomnia In People With Major Depressive Disorder
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Introduction: Insomnia is a risk factor for higher attrition rates, lower remission rates, and less stable response to depression treatment. Because cognitive behavioral therapy for depression (CBTd) does not address insomnia in validated way, cognitive behavioral therapy for insomnia (CBTi) represents a possible adjunctive treatment. Little research exists on using CBTi to treat insomnia in patients with major depressive disorder (MDD). The current study examined if (a) one could treat only insomnia with CBTi in people with MDD, and (b) would depression then improve.

Methods: All volunteers went through an extensive screening process (i.e., phone interview, structured clinical interview, questionnaires). We excluded those with secondary insomnia, other sleep disorders, taking sleep-active medication, receiving psychological treatment. We included those with current complaint of chronic insomnia for at least six months and current major depressive disorder as defined by the DSM-IV. CBTi consisted 6 weekly treatments with stimulus control, sleep hygiene, and progressive muscle relaxation.

Results: The results that follow are a preliminary analysis of baseline and post-treatment data of 9 volunteers. Follow-up data will be presented at the conference. A repeated measures MANOVA was performed, with time period (pre- vs. post-treatment) as the independent variable, and measures of insomnia (i.e., total sleep time, sleep efficiency, sleep quality) as dependent variables. Results revealed significant overall improvement (p < .05), with a 57-minute increase in total sleep time, a 12% increase in sleep efficiency, and a 17% improvement in sleep quality (all ps < .05). Next, a repeated measures ANOVA was performed, with time period as the independent variable and the Beck depression inventory as the dependent variable. Significant improvement was seen, with depression scores decreasing from 14 to 6 (sub-clinical) (p < .05).

Conclusion: Results indicate it is possible to effectively treat insomnia, with CBTi alone, in patients with insomnia and MDD, and depression also improves.

0934
Hypothalamic-Pituitary-Adrenal Axis Activity And Sleep In Posttraumatic Stress Disorder
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Introduction: Alterations of the hypothalamic-pituitary-adrenal (HPA) axis and sleep disturbances have been described separately in posttraumatic stress disorder (PTSD). It is not known if HPA alterations and sleep disturbances are associated in PTSD. This study examined sleep and HPA activity in 20 male medication-free subjects with PTSD and 16 matched healthy controls.

Methods: Two nights of polysomnography were obtained and 24-hour urinary cortisol was collected during day 2. Subjects self-administered a low-dose (0.5 mg) salivary dexamethasone test at home.

Results: Compared with controls, PTSD subjects had higher 24-hour urinary μg cortisol/g creatinine (mean ± SD 40 ± 17 vs 28 ± 12, p=.03) but not significantly higher 24-hour urinary cortisol (mean ± SD 52 ± 15 μg/d vs. 43 ± 23, p=.19). PTSD subjects showed a trend towards less cortisol suppression after dexamethasone (73% ± 18 vs. 83% ± 10, p=.06). In the combined sample, delta sleep was significantly and negatively correlated with 24-hour urinary cortisol (r=.36, p=.04) and with 24-hour urinary cortisol/g creatinine on a trend level (r=.34, p=.06).

Conclusion: Our results suggest that increased cortisol is negatively associated with delta sleep. This may contribute to sleep abnormalities in conditions associated with elevated cortisol, possibly including PTSD. Future studies should explore the temporal relationship between HPA activity, sleep disturbances, and psychopathology after a traumatic event.

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Pre-Sleep EEG In High Functioning Autistic Spectrum Disorders
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Introduction: Persons with autism often report symptoms of sleep-onset insomnia, a condition characterized by hyperarousal. Spectral analysis of the EEG in idiopathic psychophysiological insomnia patients have shown high values in fast frequencies (Beta activity) and/or low values in slow frequencies (alpha, theta, delta). We analyzed the EEG of adults with autism at bedtime to verify whether typical insomnia-type patterns would be found.

Methods: Six men with high functioning (normal IQ) autism (21.8 ± 3.9 years) and six male controls (22.7 ± 3.5 years) were recorded for two consecutive nights. On the evening of night 2, just before bedtime, we recorded five minutes of EEG with eyes closed using a 23-electrode montage. Spectral analysis was performed on 60 seconds of artefact-free EEG and spectral amplitude was extracted for Delta, Theta, Alpha, and Beta activity. These data were then compared using Mann-Whitney U-tests.

Results: Compared to controls, the clinical group showed more Delta activity for Fp1 (p < .02), F7 (p < .06), T3 (p < .05), and T5 (p < .05). No significant differences were found for the other frequency bands or recording sites.

Conclusion: These results are in the opposite direction to what would have been observed in typical insomnia since persons with autism showed more slow activity than controls. Persons with high functioning autism also do not spontaneously complain of insomnia and they do not show abnormal cortisol levels (Limoges et al., Brain, in press). We conclude that insomnia in high functioning autism is of an atypical type.
Pilot Study Of The Influence Of Subject Training On Portable Sleep Testing Success

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Introduction: Long patient wait-times for NPSG studies causing laboratory backlogs demonstrate that sleep disorders are a growing public health concern. To address these backlogs, discussions have included a potential role for the use of various portable sleep data recorders (PSDR). This pilot study sought to evaluate a PSDR prototype kit (Pro-Tech Services, Inc.) compliant with CPT codes 95806 and 95807—sleep studies that have simultaneous ventilation recording, respiratory effort, ECG or heart rate, oxygen saturation, and are unattended or attended by a technologist, respectively.

Methods: Twenty healthy adult subjects (7 males, 13 females) were randomly assigned into two groups and were tested with the PSDR prototype kit in unattended domiciliary environs. The control group (N=11) was trained by a registered polysomnograph technologist (RPSGT) on the installation of the PSDR prototype kit (respiratory effort, pressure airflow, pulse oximetry, dual PLM sensors, and vest) using a standardized script and visual demonstration. The experimental group (N=9) received no training on kit installation. Both groups were supplied with a one-page installation sheet split into halves—written instruction and a graphic of the completed kit installation. Likert scales were used for subject kit evaluation. Sleep data were independently reviewed by the RPSGT and investigators, blinded to subject and group.

Results: A Mann-Whitney U test was used to analyze the data and demonstrated no significant difference between the groups in kit evaluation (p = 0.94). Moreover, the sleep data revealed that both groups achieved a test success rate of 100%.

Conclusion: This pilot study evaluated the PSDR prototype kit in its instruction clarity, ease of installation, patient comfort, and sleep test success rate. This pilot study demonstrated that successful unattended domiciliary tests could be obtained with the PSDR prototype kit without requiring a training session, and that training did not impact subject evaluation of the kit.

Assessment Of The Reliability And Validity Of One Brand Of Actigraphy Device In Young Children

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Introduction: Polysomnography (PSG) is considered the “gold standard” for sleep analysis and has been used in a variety of ages. Although this technique is noninvasive, it is not un-intrusive. Subjects are often required to spend additional nights in a sleep lab to allow for “first night effects”. In recent years the use of actigraphy to estimate sleep-wake patterns has increased dramatically. Although actigraphy is an objective and cost-effective method for conducting sleep research in a naturalistic setting, the reliability and validity of the many existing products and the algorithms used to interpret the raw data have not been established for all age groups or in clinical populations. The purpose of this study was to evaluate the reliability and validity of one brand of actigraphy, the Actiwatch-64® (Mini-Mitter, Sunriver, OR), in young children by comparing the device to the “gold standard” of attended PSG.

Methods: This study used a descriptive, correlational design. The setting was a pediatric sleep lab at a university affiliated medical center in the southeastern United States. Parents of children (n=40) between the ages of 1 - 5 years who were scheduled for standard diagnostic PSG provided consent. Each subject wore the Actiwatch-64® devices on the non-dominant wrist during a standard sleep study. The first two subjects in each group wore two devices to assess interdevice reliability. Sleep start, sleep end, sleep efficiency, actual sleep time, actual wake time, sleep latency, and wake bouts (as calculated by the manufacturer provided sleep watch software) were correlated with PSG readings. Epoch-by-epoch sleep-wake scoring was correlated between the two actigraphy devices for the dual watch subjects to assess the interdevice variability in sensitivity.

Results: All sleep parameters significantly correlated between the Actiwatch-64® and PSG. Also, there was a significant correlation seen with the epoch-by-epoch sleep-wake scoring for the dual watch subjects.

Conclusion: It can be concluded by these findings that the Actiwatch-64® device is a reliable and valid measure of sleep parameters. Although other investigators have determined that actigraphy is less reliable in predicting the transitions from sleep to wakefulness or vice versa, it is shown here to be accurate for determining sleep-wake parameters for a continuous sleep period when compared to PSG. This research also reconfirms that actigraphy is a cost-effective and un-intrusive means of assessing sleep in young children.

Comparison Of Pleural Pressure And Transcutaneous Diaphragmatic Electromyogram In Obstructive Sleep Apnea Syndrome

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Introduction: Obstructive sleep apnea syndrome is associated with increased cardiovascular risk. Based on studies of the impact of esophageal pressure (Pes) on cardiovascular variables during sleep, Pes may be used to refine the severity level in the clinical diagnosis of obstructive sleep apnea syndrome. We hypothesized that relative changes in diaphragmatic EMG (EMGdi) can reflect short-term changes in Pes during obstructive apneas and hypopneas.

Methods: EMGdi waveform was sampled at 0.25 KHz. The signal was band-pass filtered, digitally converted, ECG artifact eliminated, using a gating procedure, fast fourier transformed, digitally rectified, and a moving average of 200 msec calculated. For each inspiratory effort during apnea / hypopnea we calculated maximum EMGdi and Pes. Data was normalized calculating the percentage difference between the first obstructed and each subsequent inspiratory effort during the respiratory event. Individual regression slopes for the relationship between Pes and EMGdi were calculated.

Results: Nine patients with moderate obstructive sleep apnea syndrome presenting apneas and hypopneas during sleep underwent standard polysomnography with measurement of Pes and EMGdi. 861 respiratory events were scored and the evolution between Pes and EMGdi compared. Normalized data showed a good correlation between the two measures during apneas and hypopneas. There was a significant difference between the percentage increase in Pes and EMGdi for apneas and hypopneas (Pes, apnea: 118.1±118.5%, hypopnea: 76.1±74.3%; P<0.000, EMGdi, 123.5±131.7%, hypopnea: 73.3±74.2%; P<0.000). No significant differences for apnea-hypopnea were noted between the two measures under investigation. Individual regression slopes varied, but the direction of Pes and EMGdi changes was consistent and comparable during the respiratory events.
**Conclusion:** EMGdi may be clinically useful to describe relative changes in respiratory effort under conditions of apnea and hypopnea during sleep and to reliably dissociate central from obstructive events where Pes monitoring is not readily available.

**0941**

**Does Zolpidem Enhance The Yield Of Polysomnography?**

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**Introduction:** An uncomfortable environment or CPAP intolerance may result in poor sleep efficiency during polysomnography. Unsatisfactory studies often must be repeated. Non-benzodiazepine hypnotics may improve sleep efficiency without disruption of sleep architecture. We hypothesized that premedication with zolpidem improves polysomnogram quality and decreases the need to restudy

**Methods:** We retrospectively reviewed 200 consecutive polysomnograms from our laboratory. Zolpidem premedication was not standardized and was prescribed at the discretion of the consulting sleep physicians who were unaware of this study. We compared patient demographics, sleep latency, sleep efficiency, polysomnogram quality, and need to restudy between patients receiving zolpidem 10mg and those who did not. A poor quality study had insufficient sleep time to allow for diagnosis, incomplete CPAP titration or CPAP intolerance.

**Results:** Of the 200 patients, 54 (27%) received zolpidem prior to polysomnography. Age and gender did not differ between the groups. Premedication with zolpidem resulted in a significant reduction in sleep latency (11.8 min ± 9.5 vs 26.0 ± 19.9, p=0.002) and improvement in sleep efficiency (89.5% ± 5.6 vs 78.8 ± 12.3, p<0.0001). The quality of the study and need to restudy were also significantly improved (poor quality 18.5% with zolpidem vs 47.9% without zolpidem, p=0.002; need to repeat 7.4% with zolpidem vs 33.6% without zolpidem, p=0.005). Among 49 studies needing to be repeated, 21 were repeated using zolpidem, showing significant improvements in sleep latency (10.8 min ± 7.1 vs 42.8 ± 30.5, p=0.0004) and sleep efficiency (89.5% ± 4.9 vs 61.8 ± 13.7, p<0.0001). Studies repeated with zolpidem showed improved study quality (poor quality 4.7% with zolpidem vs 100% without zolpidem) and no patients needed additional studies.

**Conclusion:** Pretreatment with zolpidem significantly improves polysomnogram quality and reduces need for repeat studies. These findings suggest that routine premedication with zolpidem may enhance the yield of polysomnography.

**0942**

**Sleep Fragmentation/Continuity Measured By Survival Curve Analysis**

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**Introduction:** Fragmentation of normally contiguous sleep causes daytime hypomnolence and cognitive impairment. Most analyses of sleep, such as total sleep time (TST), time (or percent) in each sleep stage, sleep efficiency (SE), sleep stage shifts and arousal indices (AI) only capture fragmentation incompletely. This abstract presents a novel analysis of sleep fragmentation based on parametric survival analysis techniques.

**Methods:** Existing sleep stage records from subjects were used: 10 normal, 10 severe sleep disordered breathing (SDB) (AHI>40) and 6 mild SDB (AHI 15-40). TST, SE and AI were calculated. For each subject, the sequence of sleep stages was converted to runs of contiguous sleep. First, survival curves were calculated from combined data within each group and compared using log rank tests. Second, for each subject a parametric power function model was fit to the individual’s survival curve. The power coefficient was used to characterize survival curve shape.

**Results:** Statistically significant differences between normal and severe SDB were found for SE (p=0.02) and AI (p<0.001) but not for TST. No significant differences between normal and mild SDB were found. In contrast, survival curves from the combined group data showed statistically significant differences between all 3 groups (p=0.001 for all pairs). When individual subject’s survival curves were analyzed, the power coefficients showed significant differences between all groups (p<0.05, Tukey’s HSD).

**Conclusion:** This study demonstrates that a novel analysis of sleep continuity using survival analysis techniques identifies differences between subjects with severe SDB, mild SDB and normal subjects that were not evident in conventional summary measures of sleep. This was true for both grouped continuity data and for continuity measures analyzed separately on each subject. These novel measures may improve the quantification of fragmentation.

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**0943**

**Comparison Of Sleep Assessment Devices Within Groups Of Sleep Disordered Patients**

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**Introduction:** There is a paucity of data comparing alternative sleep methodologies such as actigraphy (ACT), sleep log (SL), and REMView™ (RV; Respironics, Inc., Pittsburgh, PA) with the “gold standard” of polysomnography (PSG). We investigated the performance of these alternative devices against PSG for estimating common sleep parameters within distinctive sleep disorder groups.

**Methods:** Participants were 83 (76 male) VA primary care outpatients undergoing screening procedures for an insomnia treatment study. Participants underwent one night of unattended ambulatory PSG with Compumedics® recorders. They also wore an Actiwatch-64 actigraph (Mini-Mitter Co., Inc., Bend, OR) and the RV. They completed a sleep log the following morning. These devices 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:** Participants were divided into 3 groups based on their sleep diagnoses (31 sleep apnea, 32 primary insomnia, 20 insomnia comorbid with another active medical or psychiatric disorder). Group differences between PSG and the other devices were investigated using repeated-measures ANOVA with Dunnett’s adjustment. For all 3 groups, RV overestimated SOL, while RV and AW underestimated WASO. For the apnea and primary insomnia groups, AW overestimated SE and TST while underestimating TWT. SL overestimated SOL and underestimated SE in the primary insomnia group. In the apnea group, SL overestimated SOL while underestimating TIB and TST.

**Conclusion:** These data replicate and extend our previous findings. RV performed similarly within all 3 groups. AW and SL provided reasonably accurate estimates of sleep in the comorbid insomnia group. SL was the
only device that estimated WASO accurately for all groups. The accuracy of different sleep devices varies depending on the sleep parameter of interest and the sleep diagnosis.

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0944
Factor Structure And Validity Of The Modified St. Mary’s Hospital Sleep Questionnaire

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Introduction: The St. Mary’s Hospital Sleep Questionnaire (SMHSQ) was originally created to evaluate sleep in hospital inpatients. The purpose of this study was to assess the utility of a modified 12-question version of the SMHSQ for evaluating sleep quality and sleep symptoms in a population-based study.

Methods: Data were obtained from women participating in the Penn Ovarian Aging Study, an ongoing longitudinal cohort study of Caucasian and African-American women from Philadelphia County. Women participating in the study completed the modified SMHSQ at multiple visits. Exploratory factor analysis (Mplus 2.13) was performed on data from the initial assessment (N=422). An oblique promax rotation was used to identify correlated factors. A confirmatory analysis was performed on data from follow up after 8 years (N=269). Construct validity was assessed by Pearson correlation coefficients (PCC) between the factors and other sleep-related measures.

Results: Three factors were identified: Sleep Quality, Complaints and Latency. These factors appeared stable, as the confirmatory analysis gave similar results. The factors were correlated with one another (PCC 0.83 - 0.96). All 3 factors were moderately correlated with other sleep measures including the frequency (0.49 - 0.57) and severity (0.54 - 0.60) of self-reported difficulty sleeping and the Women’s Health Initiative Insomnia Rating Scale (0.58 - 0.68). The factors were also moderately correlated with 2 measures known to be related to sleep, including the Zung Anxiety Scale (0.41 - 0.46) and Center for Epidemiological Studies-Depression Scale (0.37 - 0.42). Modest correlations with the Quality of Life Enjoyment and Satisfaction Questionnaire (-0.32 - -0.38), Perceived Stress Scale (0.32 - 0.35), caffeine use (0.18 - 0.22) and hot flashes (0.18 - 0.20) were identified. Associations between the factors and age, marital status and race were negligible.

Conclusion: The modified version of the SMHSQ provides a brief assessment measure of 3 dimensions of sleep in a population-based cohort of women in the menopausal transition. Good correlations between these factors and other sleep-related measures support the construct validity of these factors and their utility for following changes in sleep over time.

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0945
Short-Term And Long-Term Variation In Sleep Characteristics In A Population-Based Study Of Early Middle-Aged Adults: The Cardia Study

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Introduction: The extent to which sleep varies from day to day and from year to year in healthy adults is unknown. The aim of this study is to describe the between-day and between-year variation in actigraphically measured sleep characteristics among early middle-aged adults.

Methods: As part of a larger study, Actiwatches (Mini Mitter, Inc) were distributed to 364 participants from the Chicago site of the Coronary Artery Risk Development in Young Adults (CARDIA) cohort study on two occasions 9-12 months apart. At each measurement, participants wore the Actiwatch for three sequential days, yielding measures of sleep duration, sleep latency and sleep efficiency. Time in bed is determined from a daily sleep log. Sleep efficiency is sleep duration divided by time in bed. For each sleep parameter, total variance was decomposed into between subject variance, within subject variance from day to day, and within subject variance from year to year. The standard deviation is calculated from the variance.

Results: For sleep duration, the within-subject daily standard deviation (SD) was 1.25 hours and the within-subject yearly SD was 0.31 hours. Daily SD was 0.49 hours and yearly SD was <0.01 hours for within-subject variability of sleep latency. Daily SD was 8.34% and yearly SD was 2.38% for within-subject variability of sleep efficiency. Finally, daily SD was 1.33 hours and yearly SD was 0.30 hours for within-subject variability of time in bed.

Conclusion: For each of the four sleep characteristics, night-to-night variability was much greater than year-to-year variability. This means sleep behavior changes little in one year in this cohort of adults in early middle age, despite large daily fluctuations. These results have important methodological implications, including that single day measures of sleep parameters only weakly reflect the multiple-day within-subject averages.

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0946
Stability Of The Pittsburgh Sleep Quality Index And The Epworth Sleepiness Questionnaires Over One Year In Early Middle-Aged Adults: The Cardia Study

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Introduction: The Pittsburgh Sleep Quality Index (PSQI) and the Epworth Sleepiness Scale (ESS) are widely used in clinical and non-clinical research. The aim of this study is to determine how stable these instruments are over a one-year period among a population-based sample of early middle-aged adults.

Methods: As part of a larger study, we distributed the PSQI and ESS to 370 participants from the Chicago site of the Coronary Artery Risk Development in Young Adults cohort study on two occasions 9-12 months apart. We calculated the seven PSQI component scores, the global PSQI score and the ESS score. Following the developer's recommendations, PSQI global scores >5 were classified as poor quality sleep, and ESS scores >10 were classified as high daytime sleepiness. Scores for each year were compared within subjects.

Results: Fifty-six percent of subjects had a follow-up PSQI score that was within one point of the first measurement, with approximately equal numbers increasing and decreasing, and 22% would be differently classified for sleep quality category. Of the 7 PSQI component scores, medication use had the greatest stability (81% had the same score). The least stable components were the sleep latency component (55% had the same...
Results: time matched with PSG epochs. high activity thresholds, summary statistics generated, and epochs were
generated. Subjective estimates were made 30-minutes after in-
neously with an Embla PSG recorder (Medcare, Iceland) and Actiwatch
East Asia. Sleep in the layover hotel and in flight was recorded simulta-
graphic and subjective estimates for measuring the sleep of flight crew.

The aim of this research was to determine the validity of acti-
ticipants to be studied and/or monitoring to occur over extended periods
simpler, cheaper, and less intrusive, thus allowing greater numbers of par-
ical to use in certain situations. Actigraphy and subjective reports are
technique for determining sleep duration and structure, it can be imprac-

Although polysomnography (PSG) is the gold standard
together with subjective reports. Actigraphy and subjective reports are simpler, cheaper, and less intrusive, thus allowing greater numbers of partic-
tchers, with a high inter-rater reliability if no specific consensus training has been undertaken. In this study we quantified the reliability between sleep centers in Germany on a voluntary basis.

Methods: A CD-ROM with 8 selected cardiorespiratory sleep studies
(3 healthy subjects, three sleep apnea patients, two PLMS patients) using the EDF data format together with a visual sleep scoring program was sent to all sleep centers accredited by the German Sleep Society (n=170). The sleep centers were asked to score the recordings with the visual scor-
program and send back the resulting hypnogram data file. Comparison was done using common measures such as SPT, TST, laten-
cies, percentages of sleep stages, sleep efficiency. In addition a compar-
son on single epochs was performed using the Fleiss kappa coefficient.

Results: Finally 9 sleep centers managed to send back visually scored
hypnogram data files for all 8 recordings. A very high variability was found for the common parameters which was even higher in patients com-
pared to healthy subjects. Best reliability was found for REM sleep and worst reliability for stage NREM1. The epoch by epoch comparison con-
firmed lower reliability in patients and lowest in sleep apnea. There the
Fleiss kappa coefficient was below 0.4 which is regarded a weak reliabil-
ity. Pooling NREM3 and NREM4 improved the reliability to a minor
degree.

Conclusion: Inter rater reliability of sleep scoring according to
Rechtschaffen and Kales between sleep centers is low. Reasonable and
good reliability is reported only if sleep scorers are trained together in
order to find agreements on all questions left open by the original scoring
manual. This additional agreement is extremely important in patients with
sleep apnea.

0949

The Feasibility Of Adding Fetal Heart Rate To The Nocturnal Polysonmogram
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Introduction: In investigating the effect of maternal sleep-disordered
breathing and hypoxia on fetal well being the study of fetal heart rate
(FHR) in real time would be ideal. However, daytime FHR monitoring is
fraught with repeated failures of capture, principally due to maternal
movement. This study examines the possibility of capturing fetal heart rate
during maternal sleep.

Methods: We examined FHR by continuous monitoring of ultrasound
sampling every second (Hewlett Packard Fetal Monitor 8040A entered
into Alice version 1.8.03) in five pregnant women in the third trimester.
The digital signal capture was examined with respect to brief fail
time (baby kicks 5 to 30 seconds), prolonged fail time (baby movements
60 to 300 seconds) and total fail time in a single nocturnal polysomnog-
gram.

Results: The five mothers ranged in age from 27 to 41 (average
36). Capture of fetal heart signal at setup took from 5 to 45 minutes. The
fetal hand had to be replaced between zero and three times/night. The
sleep efficiency on average was 59% (range 24 to 78%). The number of
brief fails was 26 events/night (range 10 to 29 events inferred as kicks).
The number of prolonged fails on average was 8 events/night (range of 4
to 14 events inferred as baby movements). Finally the total fail as a per-
centage of TIB is on average 5% of the night (range 2 to 7%).
Conclusion: The FHR band is well tolerated by the mother and once the signal is attained a good signal is maintained during most of the night, failing with fetal kicks and position changes but not for more than 7% of the time in bed in these subjects. This result suggests it is feasible to monitor fetal heart rate during the nocturnal polysomnogram in the third trimester to assess in real time the possible effects of other recorded maternal events on infant wellbeing.

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0950

Bed-Actigraphy: A New Tool For Bedtime Sleep-Wake Assessment
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Introduction: In order to provide a more user-friendly sleep-wake assessment, we introduce a new method by which non-intrusive acquisition of activity data without attaching any sensors on the subject’s body is made possible. The bed-actigraphy comprises of 4 load-sensing cells supporting the bed, an analog/digital converter, and a central processing unit with software. In the present study, the performance of the bed-actigraphy was validated against the standard polysomnographic recordings.

Methods: Ten normal volunteers (5 males, 27 ± 2.5 years and 5 females, 26 ± 2.5 years) underwent full overnight polysomnographic recordings and simultaneously studied with bed-actigraphy. One sleep specialist scored each 30-second epoch of bed-actigraphic recordings for Wake or Sleep, using the criterion of ‘one-third rule’ (If activity occupies more than one-third of the epoch, the epoch is scored as Wake). The polysomnography recordings were manually scored by another experienced scorer and then, scoring results were merged into two categories: Wake or Sleep (i.e. sleep stages 1-4 and REM sleep). Agreement between bed-actigraphy and polysomnography was tabulated for Wake or Sleep on an epoch-by-epoch basis for the 10 subjects. Regarding to the total sleep time, the degree of agreement was estimated in absolute difference and Kendall coefficient between them.

Results: The mean epoch-by-epoch agreement between bed-actigraphy and polysomnographic recordings for 10 subjects was 87.6% (or kappa = 0.74). For total sleep time, the mean of absolute difference was 13.0 minutes (ranges: 8.5 ~ 16.2 minutes) and Kendall coefficient was 0.83 (p < 0.01).

Conclusion: Bed-actigraphic differentiation of Wake and Sleep states proved to be robust enough, with bed-actigraphy providing polysomnography-comparable information. This finding supports the experimental and clinical value of bed-actigraphic monitoring during sleep. We propose that the bed-actigraphy might be considered and utilized as a new and useful instrument for sleep-wake assessment.

0952

Evaluation Of Usefulness Of The Sleepstriptm Compared With Nocturnal Polysomnography Contained The Nasal Transducer
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Introduction: Sleep apnea is a largely undiagnosed and prevalent disorder. It is associated with cardiovascular morbidity as well as excessive daytime sleepiness and poor quality of life. But it may be difficult to screen large groups of patients with polysomnography (PSG). The SleepStripTM has been proposed to screen sleep apneas in the general population. And there were a few reports that the SleepStripTM scores are correlated with apnea/hypopnea index (AHI). But in those studies, there was no application of nasal transducer that is more sensitive to detect hypopneas and flow limitation. So we studied the efficacy of the SleepStripTM compared to PSG equipped with the nasal transducer.

Methods: We evaluated the SleepStripTM compared to full night polysomnography in patients addressed our center for a suspicion of sleep apnea. PSG was performed with the SleepStripTM in same night. The PSG was equipped with nasal transducer. The PSG was manually analyzed according to the Reschtffen and Kales rules and the RDI (AHI + Flow limitation arousals) and the AHI were compared to the one automatically proposed by the SleepStripTM score. A non parametric test was used to compare the results of the two explorations.

Results: In total 17 subjects, four were excluded due to less than 300 minute of total sleep time. In including 13 cases, men are 9 and women...
are 4. Sensitivity and specificity values are 75% and 80%, respectively, in comparison to AHI. In RDI (AHI+Flow limitation arousals), 88.9% and 100% respectively.

**Conclusion:** The SleepStripTM score is more correlated with RDI (AHI+Flow limitation arousals) rather than AHI, and more specific and sensitive in RDI(AHI+Flow limitation arousals). But the SleepStripTM score is more correlated in moderate sleep apnea patient and is less correlated in mild sleep apnea patient. And if sleep efficacy is low, the SleepStripTM score may be underestimated. So if the SleepStripTM score is normal and sleep apnea is suspicious, the PSG is needed to detect sleep apnea and hypopnea.

**0953**

**Sleep Apeana Detection By Slope Analysis**

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**Introduction:** We developed a digital polysomnography system and this is one of the serial studies related to the development. For the detection of sleep apnea, the most frequent observation in sleep studies, various methods have been applied. In our study, we introduced an innovative algorithm for analyzing slope of nasal airflow signal in polysomnography and detecting the presence of sleep apnea event automatically.

**Methods:** In this study, the slope was obtained by absolute differentiation of a signal, with time window of 3.8 seconds, and segmentation of 1 second and moving average applied. Apnea threshold was determined by 10% of the slope of normal breathing. If segments having slope below apnea threshold appeared for 10 consecutive segments, those segments were marked as apnea. With the above-presented algorithm, we analyzed polysomnography recordings from 13 subjects. Performance of the algorithm was evaluated by comparing its results with the sleep specialist’s manual scoring on the same recordings.

**Results:** The overall level of agreement based on 2,468 manually-detected and 2,500 automatically-detected apnea events collected from 13 subjects was 95.36% (or κ=0.86). The distribution of κ for individual subject’s recording varied from 0.47 to 1.00. The mean agreement and κ of the 13 subjects were 95.52% and 0.69 (p<0.05), respectively.

**Conclusion:** Generally, the agreement rate about apnea scoring between two sleep specialists is about 87%. Compared to this rate, 95% agreement rate in this study is a meaningful one. Slope analysis algorithm is not only simple and easy to implement but also robust in the analysis of nasal airflow signal in sleep apnea patients.

**0954**

**Pupillary Unrest In Sleep Disordered Versus Non-Sleepy Healthy Subjects**

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**Introduction:** Pupillary unrest index (PUI), a measure of pupil size instability associated with daytime sleepiness, is relatively quick and non-invasive but requires further validation as a measure of alertness. In this study, we compared PUI with MSLT sleep latencies (SL) as a measure of daytime sleepiness in subjects with Narcolepsy off treatment (n=19), Obstructive sleep apnea (OSA) off treatment (n=10) and in non-sleepy healthy controls (n=37).

**Methods:** Subjects were assessed in an academic health center sleep laboratory and underwent comprehensive health pre-screening. Following overnight PSG, a MSLT was conducted at 1000, 1200, 1400, and 1600 hours while PUI testing was conducted at 900, 1100, 1300, and 1500 hours with the AMTech GmbH pupillometer. During PUI testing (duration = 11 min.), subjects were seated comfortably in a quiet, dark room with instructions to stay awake and keep their eyes open.

**Results:** MANOVA for the mean PUI and SL scores across the four testing periods showed a significant difference across the three groups (Wilks Lambda = .248, exact equivalent F2,124 = 31.258, p<0.001). Univariate Planned Contrast analyses were performed to test the specific hypotheses that the Narcolepsy and OSA groups differed from non-sleepy controls. These analyses found significant differences between the sleep disordered groups and the control group in both the mean SL (t=12.447, p<0.001) and PUI (t=43.5=5.084, p<0.001, adjusted for non-homogeneity of variances). The correlation between the SL and PUI across all 66 subjects was moderately high (r =-.549, p<0.001).

**Conclusion:** The PUI distinguishes between sleep disordered and non-sleepy healthy subjects. In contrast to the MSLT, a more time consuming although current standard measure of daytime sleepiness, the PUI offers a quicker determination of excessive drowsiness without the need for naps. This has implications for timely detection of excessive sleepiness, which may impair function in real-world situations.

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**0955**

**Initial Validation Of The Rochester Sleep Continuity Inventory (Rsci)**

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**Introduction:** There are few validated instruments which assess insomnia and sleep disturbance in general. The Pittsburgh Sleep Quality Index (PSQI) is perhaps the most widely used of the global measures of sleep quality. The Insomnia Severity Index (ISI) and the Pittsburgh Insomnia Scale are the only validated instruments dedicated to the assessment of insomnia. To date, no instruments evaluate insomnia in a comprehensive manner. The Rochester Sleep Continuity Inventory (RSCI) was developed to provide a multi-factorial assessment of insomnia which is accomplished via PC and provides automatic report and database functions. The instrument itself contains 50 items which yield several severity measures. The RSCI is perhaps the most widely used of the global measures of sleep quality. The Insomnia Severity Index (ISI) and the Pittsburgh Insomnia Scale are the only validated instruments dedicated to the assessment of insomnia. To date, no instruments evaluate insomnia in a comprehensive manner. The Rochester Sleep Continuity Inventory (RSCI) was developed to provide a multi-factorial assessment of insomnia which is accomplished via PC and provides automatic report and database functions. The instrument itself contains 50 items which yield several severity measures.
be 0.957 for the entire instrument and 0.951 for the Severity Subscale (21 items). The Global RSCI index's association with the ISI was rho = +.606 and with the PSQI was rho = +.608. A Spearman's rho of > 0.60 is considered to represent a strong correlation between scales. The RSCI Severity Subscale's associations with the ISI and PSQI were +.610 and +.652, respectively.

Conclusion: These findings suggest that the RSCI has high internal consistency and reliability with good convergent validity. Validity and reliability tests of other subscales will be assessed. For the present, the RSCI can be used to assess insomnia severity, while providing additional information regarding possible etiological or maintaining factors.

0956
Intra-Subject Comparison Of Polysomnography And A Type 3 Portable Monitor
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Introduction: Type 3 portable monitors (PM) that record respiratory signals and oxygen saturation, but no signals for sleep staging, are increasingly being used to evaluate patients with suspected sleep apnea. The purpose of this study was to test the performance of a Type 3 PM that records nasal pressure as the surrogate marker for airflow.

Methods: 39 adult males with suspected sleep apnea (mean age 54 ± 9.6 SD yr, mean BMI 35.8 ± 7.0 kg/m2) performed a home unattended PM recording (Stardust II®, Respironics) followed the next night by an in-lab diagnostic polysomnogram with simultaneous PM recording. The PM recorded the following signals: nasal pressure, rib cage movement, oxygen saturation, heart rate, body position, and snoring. All recordings were scored manually. The apnea-hypopnea index (AHI) on the PM recordings was calculated using recording time.

Results: The AHI was 40.6 ± 35.5 events/hr on in-lab polysomnogram, 36.4 ± 27.7 events/hr on simultaneous PM recording, and 32.1 ± 27.4 events/hr on home recording. Nine of the subjects had an AHI < 15 on the polysomnogram. The correlation coefficient for AHI was 0.92 when comparing polysomnogram with simultaneous PM recording, 0.75 comparing polysomnogram versus PM recording, and 0.80 comparing the two PM recordings. Using an AHI ≥15 to diagnose OSA on polysomograms and PM recordings, the PM had a sensitivity of 96.6% and a specificity of 100% on simultaneous in-lab testing, and a sensitivity of 86.7% and a specificity of 77.8% on home testing.

Conclusion: In patients with a high prevalence of sleep apnea, a Type 3 PM monitor using nasal pressure as the airflow signal can both detect and exclude diagnoses of sleep apnea. The greater differences observed between in-lab and home testing were likely due to differences in environment and the known night-to-night variability in AHI.

CHERP; equipment provided by Respironics, Inc.

0957
Comparison Of Two Oximeters On Polysomnography
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Introduction: Previous reports have suggested that oximeter brands can significantly affect the scoring of respiratory disturbances on polysomnography (PSG).

Methods: Twenty patients with mild-moderate sleep apnea were recorded on a standard PSG montage which included two simultaneous oximeter signals, one from the Masimo Radical (oximeter M) and the other from the Nellcor N-595 (oximeter N). Each record was scored twice by a Registered Polysomnographic Technologist who was blinded to the identity of the oximeter brands. Only one of the oximetry tracings was displayed at a time during scoring. Centers for Medicare and Medicaid Services (CMS) definitions were used to calculate the apnea-hypopnea index. Data were analyzed using the t-test for repeated measures. The independent variable was the oximeter brand. Dependent variables included the CMS-defined apnea+hypopnea index (AHICms) and hypopnea index (HICms).

Results: The AHICms for oximeters M and N were 15.2 and 17.7 (t=-1.76, p=0.10). The HICms for oximeters M and N were 14.2 and 16.7 (t=-1.77, p=0.09). The HI<4 for oximeters M and N were 8.6 and 5.7 (t=-2.41, p=0.03). Overall, there were no significant differences in the mean HICms or AHICms between oximeters. The HI<4 was significantly higher with oximeter M than with oximeter N but there was only a trend for oximeter N mean HICms being higher than oximeter M. A significantly greater number of patients (15 on oximeter N vs 10 on oximeter M) achieved one of the CMS thresholds for treatment coverage, AHICms>15 (z=2.02, p<0.05).

Conclusion: Conclusions: Two oximeters appear to demonstrate different analog signal morphology on PSG but the mean AHICms values are similar. One oximeter, however, does allow the AHICms 15 threshold to be reached more often than the other.

Support: Nellcor Puritan Bennett.

0958
Measuring Sleep Onset: Comparing The Standard Versus An Experimental Montage
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Introduction: Obtaining EEG sleep latency measures can be time consuming and impractical in operational settings (e.g., hospitals). The more rapidly a test can be administered, the higher the likelihood of subject recruitment and use in real work settings. The standard EEG sleep montage uses electrodes placed on the scalp that requires 10-15 minutes for application. This study compared sleep onset using a standard EEG montage with an experimental EEG montage that could be quickly placed on skin.

Methods: After IRB approval, 46 physicians and nurses (23 female, mean age 33.8 ± 8 years) participated in this study. All subjects were studied between 0630 and 0900 after sleep restriction the night before (usually after hospital duty). The two recorded montages were: 1) C3, O2 (standard), and 2) electrodes placed on the forehead at points 10% of the nasion-inion distance towards vertex and 5 cm perpendicular to the right and left (experimental). Subjects' EEG was recorded in a recumbent position for 12 minutes in a dark, sleep conducive environment. The test was terminated after 12 minutes whether they had slept or not. Time to sleep onset (NREM stage 1 and NREM stage 2 sleep) was scored by a registered sleep technologist blinded to the purpose of the study and electrode placement. Sleep onset was scored separately for each montage and compared using Bland-Altman plots and regression analysis. Sleep onset is presented as mean ± SD.
**Results:** Mean time to sleep onset and stage 2 sleep were: 7.1 ± 4.4 and 8.9 ± 3.5 minutes (standard) and 6.6 ± 4.5 and 8.7 ± 3.5 minutes (experimental). The bias (difference between the means) for sleep onset was 0.5 ± 1.7 minutes and time to Stage 2 was 0.2 ± 0.9 minutes. The two montages correlated well in both time to sleep onset (P < 0.0001, R2=0.86) and time to stage 2 (P < 0.0001, R2 =0.93).

**Conclusion:** Time to sleep onset, as measured by the two montages, was similar. Using the experimental montage decreases study time by 10-15 minutes and maintains valid physiologic measurements.

**0959**

**G.A.S.P.: A Self-Administered Screening Questionnaire For Obstructive Sleep Apnea**

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**Introduction:** Obstructive Sleep Apnea (OSA) is well suited to screening by questionnaire. Several questionnaires for OSA exist, however their use has been limited by complexity. We now present the validation of a simple self-administered questionnaire for OSA. The G.A.S.P. questionnaire consists of five questions assessing the presence of: 1) snoring, 2) witnessed apnea, 3) fatigue or sleepiness, 4) hypertension or reflux and 5) being overweight. Questions can be answered ‘Yes’, ‘No’ or ‘Not Sure’. ‘Yes’ and ‘Not Sure’ answers receive a score of 1. ‘No’ answers receive a score of 0. Possible scores range from 0 to 5.

**Methods:** 99 subjects were recruited, partly from a shopping mall, partly from our clinic (SMN). Inclusion/exclusion criteria were: 18 and older, not pregnant, not hospitalized within 30 days, not previously diagnosed with OSA. 39 subjects were male, 60 female. Median age was 46. After consent, all subjects completed the G.A.S.P questionnaire followed by either home sleep recording (HSR) or polysomnography (PSG). PSG apnea/hypopnoea index (AHI) values were corrected to HSR values by multiplying by sleep efficiency. The threshold for OSA was defined as an AHI of 5 or greater.

**Results:** Raw data by score bracket (OSA+/Total): Score=0: 0/17; Score=1: 5/20; Score=2: 11/18; Score=3: 13/16; Score=4: 11/13, Score=5: 15/15. Receiver-operator area under the curve was 0.90. A threshold of 2 yielded specificity of 77% and sensitivity of 91%. A threshold of 3 yielded specificity of 89% and sensitivity of 71%. Mean AHI for scores of 3 or higher was 24.3 (95% CI = 18.0 to 30.6), and for scores of 2 or lower was 6.3 (3.9 to 8.6), p < .0001.

**Conclusion:** The G.A.S.P. questionnaire is a simple tool well suited for screening for OSA in the primary care setting, with sensitivities and specificities equivalent to currently existing more complex instruments. Higher G.A.S.P. scores correlate with higher AHI values.

**0960**

**Self-Rating Of Weight Status Agrees Well With Classification Based On Body Mass Index**

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**Introduction:** Questionnaires for Obstructive Sleep Apnea (OSA) commonly classify weight status using a threshold of Body Mass Index (BMI) >= 26 for overweight. BMI is typically either calculated or read off a table. Determination of BMI adds a cumbersome step to the scoring of screening questionnaires and limits their use in many busy primary care practices. We therefore sought to determine how well self-rating of weight status (overweight vs not overweight) agrees with classification based on BMI values.

**Methods:** 99 subjects were recruited, partly from a mall, partly from our clinic (SMN), to participate in a validation of a new screening questionnaire for OSA. Inclusion/exclusion criteria were: age 18 and older, not pregnant, not hospitalized in the past 30 days, not previously diagnosed with OSA. 39 subjects were male, 60 female. Median age was 46. Self-rating of weight status and BMI were collected for each subject as part of the overall dataset.

**Results:** 50 subjects had a BMI < 26, 49 had a BMI >= 26. 51 subjects rated themselves as not overweight, 48 rated themselves as overweight. 46/51 subjects (90%) correctly rated themselves as not overweight. 45/48 subjects (94%) correctly rated themselves as overweight. Kappa = .83 (SE = .05). Gender did not have a significant effect on the direction of incorrect self-rating.

**Conclusion:** Self-rating of weight status has excellent agreement with classification based on BMI values. Use of self-rating of weight status can significantly simplify screening questionnaires for obesity and for OSA.

**0961**

**The MWT And MSLT Can Be Performed On The Same Day In Normal Controls And Patients With Narcolepsy / Cataplexy Without Confounding The MWT**

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**Introduction:** Excessive daytime sleepiness (EDS) is a complex behaviour that is a function of the drive to sleep and stay awake which can be measured by the MWT and MSLT. The MSLT measures the physiological sleep drive, and the MWT measures manifest sleepiness and the drive to stay awake. A more valid index of EDS would be elicited by a combination of the MSLT and MWT investigations, however both tests are time consuming if performed over 2 separate days. This study aims to validate a test protocol that involves performing a combined MWT and MSLT test protocol on the same day. The key factor was whether the MSLT trial confounded the following MWT trial.

**Methods:** A prospective study was performed on 20 patients diagnosed with narcolepsy / cataplexy (1) and 15 normal controls (2). Each subject underwent a 4 trial MSLT and a 4 trial 20 minute MWT protocol (sleep onset 1 epoch of any sleep stage). The protocol was started 2 hours after waking with a two-hour interval between trials. The protocol involved first performing the MWT trial immediately followed by the MSLT trial.

**Results:** Amount of normal MWT trials 1=2/80, 2.5%, 2=45/60, 75%. Mean MWT sleep latency 1=5.7mins, 2=17mins. Mean MSLT sleep latency 1=2.6mins, 2=13mins. Both the control and narcolepsy / cataplexy groups showed linear regression (1=0.6, 2=0.5) and correlation scores (1= rho-0.22, p=0.32, 2 = rho-0.52,p=0.44) between the MWT and MSLT that were comparable to those found by other authors (Sangal 1992).

**Conclusion:** It appears that the key factor as to whether sleep during the MSLT leads to a normalising of the following MWT score is not supported. The narcolepsy/cataplexy group still showed evidence of EDS on the MWT and MSLT leads to a normalising of the following MWT score is not supported. The narcolepsy/cataplexy group still showed evidence of EDS on the MWT and MSLT that were comparable to those found by other authors (Sangal 1992).

**0962**

**Determining A Stable Baseline For Assessing Oculomotor Functioning**

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Introduction: The Fitness Impairment Tester (FIT) has been used to detect impairments caused by sleep deprivation, drug and alcohol use, and stress. Impairment is determined by involuntary changes to the ocular system relative to the individual's stable baseline measurements. The exact number of trials necessary to obtain a stable baseline is unknown. The current study was conducted as part of a larger effort to assess oculomotor changes during sleep-deprivation, under various ambient light intensities.

Methods: Twenty-two military personnel (9 F/13 M; 21-38 yrs) served as volunteers. Well-rested volunteers were administered five FIT tests per day (M to F). The oculometric measurements obtained were initial pupil diameter (IPD), constriction latency (CL), constriction amplitude (CA) and saccadic velocity (SV). Differences over time between the first FIT trial administered and subsequent trials were tested individually by Paired t-tests with Bonferroni corrections.

Results: All significant differences reported were determined with the values (t>3.4729, p<0.0022, df=21). There were significant differences from the initial trial, in IPD, only for the first ten FIT trials, followed by no other significant differences. Significant differences for CL were found on the 3rd and 5th trial of each day, and on the 4th trial on days 1, 2, & 4. Pupil CA showed no significant changes. Three trials were found to be significant for SV, specifically, on day 4, 5th trial and on day 5, 4th & 5th trials.

Conclusion: Of the oculometric measures assessed, IPD appears to be the most vulnerable to variability, which stabilized by the 11th trial. The consistent variability found with CL after repeated testing suggests that this is not a good indicator of baseline stability. The lack of changes associated with CA and SV suggest that these measures are likely to be sensitive to external manipulation (i.e., drugs, sleep loss, etc.).

This research was supported by the Saccadic Fatigue Measurement Research Program.

Validity Of 24-Hour Recall Interview For Sleep Patterns
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Introduction: Due to the limitations of sleep questionnaires and sleep diaries (e.g., compliance issues, errors in estimation), this study examined the use of a 24-hour recall telephone interview to measure sleep patterns.

Methods: 65 participants completed a series of 24-hour recall interviews measuring sleep patterns (2 weekday and 2 weekend) over a two week period, the Pittsburgh Sleep Quality Index (PSQI) and a two-week sleep diary. Participants were 89% female and 94% Caucasian (mean age = 38.5 years; range 23-49.6). A subset of participants (n=41) also completed a follow-up interview regarding preference and feasibility of recalls versus diaries.

Results: The 24-hour recall interview was significantly correlated with the PSQI and diary for all sleep variables: bedtime (Recall/PSQI, r = 0.80, p < .001, Recall/Diary, r = 0.88, p < .001), wake time (Recall/PSQI, r = 0.71, p < .001, Recall/Diary, r = 0.77, p < .001), sleep onset latency (Recall/PSQI, r = 0.47, p < .001, Recall/Diary, r = 0.87, p < .001), total sleep time (Recall/PSQI, r = 0.61, p < .001, Recall/Diary, r = 0.68, p < .001), and sleep quality (Recall/PSQI, r = 0.64, p < .001, Recall/Diary, r = 0.76, p < .001). Only 51% of participants completed and returned sleep diaries. Of those who completed both the 24-hour recall interviews and sleep diaries, 67% preferred the interview and 66% felt that the interviews were a more accurate representation of their sleep patterns.

Conclusion: This study supports the use of a 24-hour recall telephone interview as a subjective measure of sleep patterns. Validity is indicated by the strong correlations with well-established measures and higher completion rate. Feasibility was also supported with participants' preference and belief that the recall approach was more accurate. Additional research is needed to validate this novel approach, using objective measures of sleep.

PVT During MRI
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Introduction: The Psychomotor Vigilance Test (PVT) is an established measure in fatigue and sleepiness assessment. Its effectiveness has led to its widespread use in research, including research protocols supporting development of Department of Defense fatigue performance prediction models. Here, we examined PVT performance in a functional magnetic resonance imaging (FMRI) environment relative to more typical sleep lab administration.

Methods: Eighteen people completed the PVT in each of 4 conditions: seated in a lab environment and supine during FMRI, both with and without 36 hours sleep deprivation. Four PVT response time variables, their reciprocals, and missed responses (i.e., lapses) were compared.

Results: As is typically seen, across PVT variables, subject responses were slower and lapses more frequent after sleep deprivation than when well rested. However, it was also the case that subject responses were slower and lapses more frequent during FMRI than lab environment testing. Interestingly, there was an interaction between sleep and test environment conditions, in that the slowing of PVT responses and increase in frequency of lapses with sleep deprivation occurred to a greater degree during FMRI than lab environment testing.

Conclusion: Generally, the PVT retains its value as a measure of the effects of sleep deprivation in the FMRI environment even though PVT performance during FMRI appears to be slower overall than in a lab environment. However, given the nature of the FMRI physical environment (e.g., supine posture, confinement, noise), effects of sleep deprivation may be magnified in FMRI relative to sleep lab, as we see in the more sensitive PVT measures of lapses and slowest 10% of responses. This finding has implications for fatigue research conducted with FMRI and for generalization of fatigue research to development of fatigue-performance prediction models, which, when applied, may be used to predict performance with variable posture and other immediate environmental parameters.

Sleep Apnea Monitoring Using Sleep Disordered Heart Rate In An Implanted Device
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Introduction: The potential cardiovascular consequences of untreated sleep apnea syndrome (SAS) are of concern in heart failure patients. Unlike traditional oronasal airflow devices to measure SAS, Medtronic
has developed several sleep apnea detection techniques using implantable device sensors. Heart rate (HR) oscillations have been observed during recurrent sleep disordered breathing (SDB) events. This prospective study investigated the correlation between the cyclic variation of HR (CVHR) and SDB in patients implanted with a Medtronic Insync cardiac resynchronization therapy (CRT) device.

**Methods:** Thirteen patients (67.0±9 yrs, 2 females) were studied. Patients implanted with a Medtronic CRT device who met study eligibility criteria completed an overnight polysomnogram according to standard clinical practice with airflow measured using a thermocouple. CRT device and electrocardiogram data was collected throughout the polysomnogram using device telemetry and a DR-190 Holter monitor. Respiratory events were scored following AASM criteria. Atrial sensed events were retrieved from the DR-190 Holter monitor, converted to instantaneous heart rate, and examined for CVHR. CVHR was considered present if there were 3 consecutive cycles of HR oscillations with peak-to-peak of at least 5 bpm and a cycle length between 25-100s. CVHR performance was compared to AHI.

**Results:** Three patients were excluded from CVHR analysis due to a high incidence of atrial pacing. Overall, AHI and TST were 21±22 and 355±115.2 minutes, respectively. Four patients were diagnosed with a sleep apnea (mean AHI 34.7±21.3). For the normal group AHI was 7±2. Overall CVHR was 19±24 and correlated with AHI (rs=0.8, p<.05). CVHR correctly identified 3 patients of the apnea group (Sensitivity 75%) and 5 patients of the normal group (Specificity 83%) for accuracy of 80%.

**Conclusion:** CVHR can be useful and accurate as a sleep apnea screening tool. This study also demonstrated that device-based CVHR detection is a feasible method in assessing sleep-disordered breathing.

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**0966**

**Skin Temperature Changes Around Sleep Onset**

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**Introduction:** The aim of the study was to establish the best body position(s) for measuring changes in skin temperature, and to determine whether typical temperature changes precede sleep onset.

**Methods:** Ten non-sleep deprived, subjects with reported normal sleep underwent altogether 17 recordings of 1) core body temperature (rectal probe) 2) skin surface temperature (thermistors) glued on cheeks, earlobe, finger, wrist, fossa supraclavicularis and sole of foot. These signals, EEG, EOG and chin EMG were recorded continuously. On two occasions, thermography of the upper body with a high-resolution camera was also performed.

**Results:** To ensure good temperature baseline conditions, the subject had to be in bed with all body parts covered by blanket for an hour before actually trying to go to sleep. Ten to 20 minutes before sleep onset, skin temperature started to rise in all subjects. Core body temperature started to fall almost simultaneously, but the rate of change was less marked (in average 0.1 oC/min). Brief decreases in skin temperature were seen in conjunction with turning out the light. All body surface signals were well correlated, and in the beginning of the night inversely correlated to core body temperature. The sole of the foot and the earlobe were most prone to artifacts due to movements and pressure of head against pillow, respectively. Changes were recorded with a slight time delay in the fingers compared to other locations, and were in some cases clearly lower in magnitude than in the other surface locations. The cheeks and the nose showed the most marked changes in temperature in conjunction with sleep onset; temperature increases at 0.2-1.5 oC/min were recorded.

**Conclusion:** Skin temperature increases 10 to 20 minutes before sleep onset in normal, non-sleep deprived subjects. Changes in body temperature in conjunction with sleep are best recorded in the face with thermistors glued to the skin surface.

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**0967**

**Modification Of Respiratory Effect Related Arousal (RERA) Application Towards Elimination Of False Positive RDI Results In Patients Presenting With Insomnia**

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**Introduction:** The application of current RERA interpretation can and does lead towards the possibility of a mislead diagnosis of an increased RDI in patients with high, non-respiratory related cortical arousal index (CAI). Particularly in patients presenting with insomnia, of which an increased cortical arousal index may be present. The purpose of this study is to submit an alternative interpretation for RERA application to provide a more accurate representation of sleep events in insomnia patients.

**Methods:** A randomized sample of 20 patients and accompanying PSG was selected from a time period beginning January of 2004 to current time. These patients were then screened for Initial Sleep Study, Complaint of Insomnia, BMI (mean; 24.5±3.81), Total Sleep Time (mean; 5.27±1.91), Age (mean; 50.3±11.43) and Gender (50% male, 50% female). A resulting sample size of ten was then analyzed with RERA being modified to apply to; Hypopnea, Apnea, Desaturation and Movement Arousal Phenomenon (MA). The 10% decrease in respiratory channels characteristic to RERA was altered to apply only to movement arousal, stage shift arousal and was removed from cortical arousal (CA) events.

**Results:** Pre-application of these new rules yielded a false positive Moderate-Severe RDI of 32.1+/−9.29. Utilization of this modified RERA application presented a significantly reduced RDI mean of 23.8+/−12.98 (t(9)=2.96,p=.016)

**Conclusion:** This data suggests that current RERA rules yield a false positive result of moderate-severe RDI leading to the possibility of mis-diagnosis of RDI related Insomnia and thus exists the potential of incorrect application of therapy targeting the RDI as a core morbidity of the Insomnia. The modified protocol allows for a more precise analysis of the primary disturbance of Insomnia.

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**0968**

**A Novel Minimally Invasive Approach To Study Vascular Endothelium In Patients With Obstructive Sleep Apnea**


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**Introduction:** Endothelium-dependent vasodilation as assessed by flow-mediated dilation is impaired in patients with obstructive sleep apnea (OSA). The cellular mechanisms of vascular endothelial dysfunction are not well characterized in these patients in part due to limited availability of endothelial tissue. We hypothesized that systemic downregulation of endothelial nitric oxide synthase (eNOS) may contribute to vascular endothelial dysfunction in patients with OSA. We measured eNOS expression in endothelial cells harvested from a superficial forearm vein using a novel minimally invasive biopsy technique.

**Methods:** Venous endothelial cells were scraped from the intima of a superficial forearm vein using 3 guidewires successively inserted through an 18-gauge angiocath. Immunofluorescence staining for vonWillebrand factor identified endothelial cells in the biopsy specimens. Quantitative immunofluorescence analysis was used to measure eNOS expression. The number of positive (bright) intracellular pixels was quantified using com-
commercially available software.

**Results:** We studied 3 patients with OSA (1 F, 2 M, aged 31-45 years, BMI 30.7±3 kg/m², AHI 35±9 events/h) and 2 age matched healthy subjects (1 F, 1 M, aged 36-42 years, BMI 27±7 kg/m², AHI 0 events/h). The number of harvested endothelial cells per biopsy was 3.08±8.03 (mean±SD). eNOS expression was lower in patients with OSA compared with control subjects (831 vs 1714 pixels/μm²).

**Conclusion:** 1) Minimally invasive venous endothelial biopsy coupled with quantitative immunofluorescence analysis provides a novel approach to study vascular endothelium in patients with OSA. 2) Downregulation of eNOS in venous endothelial cells may contribute to vascular endothelial dysfunction in patients with OSA.

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**0969**

**Level 3, Unattended Studies: In Lab Vs. At Home**

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**Introduction:** The volume of patients requiring evaluation and treatment for OSA overwhelms the resources for testing them. We assessed the feasibility of using Level 3, unattended sleep studies to determine treatment plans. If the study indicated obstructive sleep apnea the patient would be referred for autopap, if the study was not diagnostic for OSA, the patient would be referred for full polysomnography. This abstract describes the initial phase, assessing the use of portable equipment unattended at home vs. unattended in a lab setting.

**Methods:** All patients evaluated in a sleep clinic were referred for full PSG if they had EDS, snoring and/or witnessed apneas with no exclusion criteria: severe unstable COPD, unstable heart disease, psychiatric illness, or parasomnias. Patients were randomly assigned to be studied in the lab or at home. The lab patients were hooked up to the equipment by a Registered Respiratory Therapist but were then left unattended in a lab bed. The home patients received instruction on using the equipment, which they then took home. After the study night they mailed the equipment back. The Stardust I, Respironics Corp., recorded SpO2, HR, flow, effort, and body position on all patients. Studies were evaluated by a certified polysomnographer blinded to the study site. Channel failure was assessed for SpO2, flow and effort. The study was non diagnostic if less than two hours of recording was obtained on two or more channels. Comparison of lab vs. home recording was made.

**Results:** Of a total of 52 patients, 21 were lab (F:M=1:20), X Age 53 years (23-69) and BMI 33±2 kg/m² (25-39), while 31 were home (F:M=2:29) X Age 58 (32-80), X BMI 32±2 kg/m² (17-44). Non-diagnostic studies included 0 in lab and 1 in home. The individual channel recordings were non-diagnostic for effort in 0 lab and 1 (3.2%) home studies; flow in 1 lab (5%) and 6 (19%) home; SpO2 and HR in 4 (19%) lab vs., 8 (26%) home. There was no total data or equipment loss using the protocol.

**Conclusion:** This study suggests that unattended diagnostic studies can be done in the home though lab based studies are more reliable.

**0970**

‘Smart Box’ Sleep Apnea Monitoring For The Neurological Intensive Care Unit (NICU)

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**Introduction:** Sleep apnea is believed to be common after stroke. However, as traditional PSG to identify apneas is generally not available in NICU, sleep apnea after stroke is rarely recorded. This study examines pilot data from a ‘Smart Box,’ which identifies apneas and oxygen blood desaturation in real time and creates an immediate computer record of events. This equipment would give physicians immediate reports on apnea status in patients for whom apnea monitoring is difficult.

**Methods:** 3 subjects with sleep apnea were observed for 24 hours in the IM Systems, Inc. sleep laboratory. One subject had moderate sleep apnea (>15/hr) and two had severe sleep apnea (>30/hour). Standard EEG, EMG, respiratory, and oxygen were monitored with both PSG and the novel NICU Smart Box. Each time the Smart Box identified an apnea (50% reduction in breathing for 10 seconds or longer) or a change of 4% in blood oxygen saturation, a mark was recorded on PSG. A trained sleep technician scored the PSG data without the Smart Box deflections. The Smart Box marks were later compared against the PSG scored events.

**Results:** Out of 2116 total events, the Smart Box correctly identified 1568 (74%), missed 548 (26%), and falsely identified 243 (11%). The Smart Box more accurately identified desaturations (1103 total, 860/78% identified, 243/32% missed, 135/12% false positives) than apneas (1013 total, 708/70% identified, 305/30% missed, 108/12% false positives).

**Conclusion:** The Smart Box accurately identified both apneas and desaturations. This record could be useful in a NICU setting, where regular monitoring for sleep apnea is unavailable. Proper treatment for sleep apnea in vulnerable patients could enhance treatment.

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**0971**

Utility Of A Sleep Disorders Questionnaire For Primary Care Providers

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**Introduction:** Most primary care physicians received little training in sleep medicine in their medical school or subsequent training. As a result most practicing physicians have not been taught the pertinent questions to ask when trying to identify sleep disorders in their patients. The primary objective of this study was to test the hypothesis that a questionnaire directed at identifying sleep disorders would increase the ability of physicians to recognize sleep disorders. A secondary objective was to determine the items that patients associated with their perceived severity of their sleep problems. We used this approach to establish content validity based on patient judgment rather than expert opinion.

**Methods:** The study involved two hundred and ninety two patients at a follow-up appointment with primary care physicians in one of three urban primary care clinics. The patients were selected with a computer generated random number system. We administered a questionnaire designed to evaluate sleep disorders to determine if (i) previously unsuspected sleep disorders could be identified, (ii) clinical management was changed, and (iii) the extent to which the questionnaire was considered to be useful by primary care physicians. We defined an impact on clinical management as ordering a test, requesting consultation, changing medications due to a sleep disorder, or counseled patients about their sleep problems. Patients were administered a sleep history questionnaire of 36 primary items by a research assistant prior to visiting their primary care provider. After the visit, the primary care provider was given a form to complete to assess the utility of the sleep history questionnaire and any new or suspected diag-
noses identified.

**Results:** On a scale of 1 (low) and 10 (high), 41% of patients ranked their sleep problems as higher than 5. The questionnaire resulted in new diagnoses being made or suspected, tests ordered or consultations requested, changed medications or counseled patients on their sleep problems in 35% of patients. Primary care providers rated the questionnaire as being useful in 53% of patients. Twenty nine of 36 items listed on the questionnaire were validated as being consistent with the patients' perception of severity.

**Conclusion:** Primary care providers found the questionnaire useful and it had a substantial impact on clinical management. Nearly all the questions listed on the questionnaire were validated as being consistent with the patients' perception of severity.

**0972**

**Identification Of Sleep Symptom Complexes In Patients Attending Primary Care Clinics**

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**Introduction:** We developed a sleep history questionnaire to assist primary care physicians identify patients with sleep disorders. To enhance the use of the questionnaire, we tested two hypotheses. First, the questionnaire may be shortened without loss of information content. Second, there are symptom complexes with which patients present to primary care providers.

**Methods:** We conducted a cross-sectional study of 292 patients at a follow-up appointment with primary care physicians in one of three urban primary care clinics. We analyzed responses to 36 items in the sleep questionnaire using cluster analysis, principal components analysis and generalized association rules.

**Results:** Cluster analysis indicated that there was little grouping of the responses by partitioning. Principal components analysis suggested that two groupings: restless legs syndrome with and without refreshing sleep. There was strong evidence of hierarchical groupings. Classification trees were used to determine the hierarchical structure. Four groups were identified: infrequent sleep symptoms (44%), and symptomatology suggestive of insufficient sleep syndrome (21%), insomnia (15%) and sleep apnea (10%). All patients either could not sleep throughout the night or had non-refreshing sleep.

**Conclusion:** Only two questions are needed to determine whether a patient has significant sleep symptoms: ‘Do you awake up at night?’ and ‘Is your sleep refreshing?’ If the answers are never and yes respectively, then it is unlikely that there will be positive responses to other items in the questionnaire but a prospective study is needed to test this hypothesis. The symptom complexes with which general medical patients may present to their providers are predominantly restless legs syndrome, insufficient sleep syndrome, insomnia and sleep apnea.

**Division of Pulmonary, Critical Care and Sleep Medicine, UB.**

**0973**

**Correlation Between Epworth Sleepiness Scale And Drowsy Driving**

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**Introduction:** More than 100,000 motor vehicle accidents annually are sleep-related. An estimated 70 million adult Americans have clinically significant sleep problems. The annual indirect cost estimate of sleep-related problems is $50-$100 billion, due to accidents, litigation, property destruction, hospitalization, and death. More efforts need to be done to increase public awareness of the magnitude of this public health burden. This study investigated the agreement between this test and the standard objective clinical test of sleepiness, the Multiple Sleep latency Test as well.

**Methods:** We conducted a cross-sectional study of 292 patients at a follow-up appointment with primary care physicians in one of three urban primary care clinics. We analyzed responses to 36 items in the sleep questionnaire using cluster analysis, principal components analysis and generalized association rules.

**Results:** Cluster analysis indicated that there was little grouping of the responses by partitioning. Principal components analysis suggested that two groupings: restless legs syndrome with and without refreshing sleep. There was strong evidence of hierarchical groupings. Classification trees were used to determine the hierarchical structure. Four groups were identified: infrequent sleep symptoms (44%), and symptomatology suggestive of insufficient sleep syndrome (21%), insomnia (15%) and sleep apnea (10%). All patients either could not sleep throughout the night or had non-refreshing sleep.

**Conclusion:** Only two questions are needed to determine whether a patient has significant sleep symptoms: ‘Do you awake up at night?’ and ‘Is your sleep refreshing?’ If the answers are never and yes respectively, then it is unlikely that there will be positive responses to other items in the questionnaire but a prospective study is needed to test this hypothesis. The symptom complexes with which general medical patients may present to their providers are predominantly restless legs syndrome, insufficient sleep syndrome, insomnia and sleep apnea.

**Division of Pulmonary, Critical Care and Sleep Medicine, UB.**

**0974**

**Close Agreement Between An Ambulatory, Fast, EEG/Behavioral-Response Test Of Sleepiness And Clinical MSLT In Patients With EDS**

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**Introduction:** An ambulatory, quick-duration test of sleepiness, the NeuroCAP, has been reported previously and shown to be capable of providing a highly sensitive measure of sleepiness in mildly sleep-restricted (3 hours) normal individuals. This test can be administered in virtually any location and operates based on simultaneous acquisition/analysis of EEG and behavioral response (push-button pressed by the subject in response to certain types of auditory stimuli). We investigated the agreement between this test and the standard objective clinical test of sleepiness, the Multiple Sleep latency Test (MSLT), in patients with excessive daytime sleepiness.

**Methods:** Twelve patients undergoing their routine clinical evaluations were sleep-related problems. The annual indirect cost estimate of sleep-related problems is $50-$100 billion, due to accidents, litigation, property destruction, hospitalization, and death. More efforts need to be done to increase public awareness of the magnitude of this public health burden. This study investigated the agreement between this test and the standard objective clinical test of sleepiness, the Multiple Sleep latency Test as well.

**Results:** Our data showed that 30 patients (60%) scored over 9 in Epworth Sleepiness Scale, yet only 20 patients (40%) were complaining of being drowsy and/or falling asleep while driving. Of those 20 patients, 4 patients (10%) scored less than 9 in Epworth Sleepiness Scale. The mean age of those 20 patients was 49.05 year-old. Amongst them, 19 patients (95%) were diagnosed with Obstructive Sleep Apnea Syndrome, 6 patients (30%) with Psychophysiological Insomnia, 3 patients (15%) with Restless Legs Syndrome, 3 patients (15%) with Idiopathic Hypersomnia, 2 patients (10%) with REM Behavior Disorder, 2 patients (10%) with Non-REM Parasonnia, and one patient (5%) with Narcolepsy.

**Conclusion:** Epworth Sleepiness Scale may not be always an accurate indication for drowsy driving. Clinicians need to specifically ask their patients about drowsiness while driving. Federal regulations, similar to those for medical disorders such as epilepsy, need to be developed and implemented. Such a step is necessary in order to make our roads safer and prevent further loss of lives.
the presence of excessive sleepiness (mean=1.9; range: 1.26-2.36).

Conclusion: The results of this study support the validity of this ambulatory, integrated EEG/Behavioral-Response test of sleepiness by demonstrating a close agreement with the current standard objective clinical test of sleepiness, the MSLT.

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0975
Evaluating Nocturnal Events With Video Polysonomography-Electroencephalography Monitoring: A One-Year Clinical Experience
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Introduction: Nocturnal events can be challenging to diagnose clinically, especially when epileptic seizures are a consideration. This study aims to describe the diagnostic utility of Video Polysonomography Electroencephalography (VPSG-EEG) in evaluating nocturnal events.

Methods: A retrospective review of the Vanderbilt Sleep Disorders Center database from September 2003 to 2004 identified 28 patients (age 2-80 years, 46% women, 54% men) who had VPSG-EEG monitoring to evaluate nocturnal events. VPSG-EEG monitoring was performed for one night on 22 patients and for two nights on 6 patients. Based on VPSG-EEG results, clinical history, and response to treatment, three groups were formed: patients who either received a new diagnosis or confirmatory diagnosis for their nocturnal events (Group A); patients who received probable diagnoses, including those who required additional evaluation (Group B); and patients whose diagnosis remained unknown (Group C).

Results: Group A included 15 (54%) patients, 8 of whom were diagnosed with epilepsy. This was a new diagnosis for 3 of these 8 patients, as previous routine EEG was normal. Other diagnoses in Group A were: NREM arousal disorder (2), psychiatric medication side effects (2), pseudoseizures, (1), rhythmic movement disorder (1), and OSA (1). Group B included 6 (21%) patients with probable diagnoses of epilepsy (3), NREM arousal disorder (2), and excessive daytime sleepiness (EDS) due to a psychiatric condition (1). Group C had 7 (25%) patients. In Groups A and B, 5 (24%) patients were found to have co-existing sleep disorders including PLMS (3), OSA(1), and both OSA and PLMS (1). VPSG-EEG alone was diagnostic in 73% of patients in Group A and 50% of patients in Group B. In Group C, 5 (71%) patients were diagnosed with other sleep disorders including OSA (2), PLMS (2), and EDS of unclear etiology (1).

Conclusion: Video-PSG-EEG is diagnostically useful in patients with nocturnal events.

0976
The Screening Of Sleep Disordered Breathing (SDB): Comparison Between The SleepStrip And An 8-Channels Cardiorespiratory Monitoring Device
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Introduction: Sleep Disordered Breathing (SDB) is a common disorder affecting 2% of females and 4% of males in the adult population (1, 2). SDB is associated with increased cardiovascular morbidity; studies have shown increased mortality of SDB patients mainly from cardiovascular causes (3). Moreover, SDB patients with excessive daytime sleepiness are at higher risk for motor and work-related accidents. However, it is estimated that the vast majority of these patients remain undiagnosed. Aim of our study was to assess the accuracy of the SleepStrip (SLP, Israel) device, a low cost disposable sleep apnea screener versus a validated portable cardiorespiratory monitoring system the Polymesam (MAP, Germany) for the screening of patients with suspected SDB.

Methods: 33 consecutive adult patients (5 F and 28 M) referred to our Sleep Disorders Center for suspected SDB were included. All subjects underwent one night of simultaneous use of the SleepStrip (SS) and of the Polymesam (PM). Age ranged between 32 and 68, BMI between 22 and 34. Polymesam recordings were visually scored by two expert scorers who were blinded to the SS final score. Pearson correlation was computed between RDI (PM) and SS scores. RDI thresholds were defined as: 15-24: mild; 25-39: moderate and >=40: severe SDB.

Results: one subject was removed from the analysis due to insufficient total sleep time. Correlation between the two scorers was r=0.99 and between SS score and RDI was r=0.85, p<0.001 for both scorers. Measures of accuracy using the SS score thresholds (mild=1, moderate ≥2, severe=3) against RDI thresholds (mild ≥15, moderate ≥25, severe ≥40) were calculated. Sensitivity in the three thresholds categories was 0.93, 1.00 and 0.7; specificity 0.71, 0.64 and 1.00; positive predictive value 0.72, 0.56 and 1.00; negative predictive value 0.92, 1.00 and 0.93; overall accuracy 0.81, 0.75 and 0.94. Sensitivity values using the SS score threshold held constant at mild or above against three RDI thresholds (mild ≥15, moderate ≥25, severe ≥40) were respectively 0.93, 1.00 and 1.00.

Conclusion: Beyond the two blinded scorers and regardless of the cutoff method used, measures of accuracy were very high, particularly when the SS score threshold was held constant at mild and above. We conclude that the SS in its current version seems to be a useful tool that enables physicians to confirm or reject the suspicion of SDB, as well as to determine the severity of the condition.

0977
Comparison Of Actigraphy And Sleep Diaries In A Sample Of Pregnant And Nonpregnant Women
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Introduction: Actigraphy is often used in lieu of or as an adjunct to polysomnography to assess sleep-wake patterns. Methodological concerns regarding the use of actigraphy include difficulty detecting differences between movement and awakenings, or between sleep and inactivity (Lockley, 1999). Its accuracy declines as the quality and quantity of sleep diminishes (Kushida et al, 2001). Sleep diaries are self-reports of sleep patterns, and like actigraphy, are used for their ease of administration and minimal costs associated with its use. Likewise, their data utilization is confounded by poor recall and discrepancies on parameters, such as sleep onset latency. Few studies have compared sleep logs to actigraphy despite the common practice of using both measures in many research settings. This study provides such a comparison in pregnant vs non-pregnant women.

Methods: Actigraphy and sleep diary data were collected from 40 women (12 not pregnant and 28 pregnant women) between the ages of 21-40 in the Denver Metro area. Two weeks of actigraphy and sleep diary data were collected from each subject. A total of 46 data points are reported in the analysis. The sleep parameters of interest were SOL, WASO, TIB, TST, and SE.

Results: Correlations show significant relationships between WASO, TIB, TST reports. Paired samples t-tests indicate that there was no difference between the actigraphy and subjective reporting of SOL and TIB, although there were significant differences for WASO, TST and SE (all p < .000). Means for these parameters suggest that diaries underestimate WASO (20.3 ±19.1min vs 54.6
Introduction: We have implemented comprehensive interscorer and intrascorer agreement using random effects intraclass correlation coefficients.

Results: The use of sleep diaries in healthy, pregnant women is a more cost-effective and unobtrusive means of collecting sleep data, although variability in subjective reporting of sleep patterns has encouraged the use of more objective forms of data collection. Actigraphy is much less intrusive than PSG, but has its shortcomings. This study suggests that the use of both sleep diaries and actigraphy can complement one another in the estimation of sleep disruption for healthy, pregnant women; however, neither method appears suitable to be utilized on its own.

0978
The First Night Effect - Does Sleeping In A Hotel Make A Difference?
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Introduction: Hotel-based sleep laboratories are becoming increasingly popular. One potential advantage of a hotel-based laboratory is the increased familiarity and comfort provided by the hotel atmosphere. Sleep studies in hospital-based laboratories have been associated with a first-night effect (FNE), which includes increased NREM and REM latencies and decreased sleep efficiency. We tested the hypothesis that hotel and hospital-based sleep studies differ in these parameters.

Methods: We reviewed all adult sleep studies performed in our hospital-based laboratory since August 2003. We excluded patients assigned to the hospital-based laboratory because of serious medical conditions. All patients were studied to evaluate for obstructive sleep apnea. Hospital-based patients were matched with hotel-based patients for age and apnea-hypopnea index (AHI) using a single month of hotel-based data.

Results: Eighteen (hospital-based) and twenty (hotel-based) patients were included. Age was 43.1 ± 9.3 (mean ± standard deviation) in the hospital-based patients and 43.7 ± 13.6 in the hotel-based patients (p = 0.88; independent samples two-tailed t-test). The AHI was 7.6 ± 5.8 in the hospital-based patients and 7.5 ± 5.5 in the hotel-based patients (p = 1.0). The two groups did not differ in sleep efficiency (82.6 ± 9.6 and 87.3 ± 8.77, p = 0.12), sleep latency (16.4 ± 20 and 14.1 ± 9.0, p = 0.7), or REM latency (167.6 ± 104.2 and 167.2 ± 86.8, p = 1.0).

Conclusion: This pilot study did not show a significant difference in sleep parameters associated with the FNE in our hotel and hospital-based sleep laboratories. The FNE may be more associated with sleeping away from home or the testing procedure itself. One limitation of this study is the small sample size that may have resulted in no difference being detected. In future studies, we plan to examine a larger group of subjects and assess overall patient satisfaction and cost effectiveness.

0979
Comprehensive Assessment Of Intrascorer And Interscorer Agreement Using Random Effects Intraclass Correlation Coefficients
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Introduction: We have implemented comprehensive intrascorer and interscorer reliability assessments beyond the epoch-by-epoch comparisons of sleep staging required to meet AASM accreditation requirements. The clinical significance of a sleep study depends upon many continuous measures including sleep efficiency, percent of time in sleep stages, REM latency percent, respiratory events such as RDI and low O2 saturation and limb movement indices. It is important that clinicians are constantly informed that these overall measures are reliable as scored according to Rechtschaffen and Kales rules by the board certified technicians (RPSGT).

Methods: Previously scored polysomnograms are randomly selected from each of the technicians for reevaluation approximately 3 months after the initial assessments and then later assigned to another technologist working the opposite shift. Random effects intraclass correlation coefficients are calculated for the intrascorer and interscorer agreements. Results are presented as average measure correlations with 95% confidence intervals.

Results: After 5 rounds of randomly selected polysomnograms for 8 board certified technologists the average measure correlations were much better than expected. For sleep efficiency the average intrascorer correlation is 0.993 with 95% confidence interval (0.978, 0.998) and the average interscorer correlation is 0.994 with 95% confidence interval (0.983, 0.998). The lowest intrascorer correlation for sleep stage was for delta sleep 0.932 (0.786, 0.979) with an interscorer correlation 0.939 (0.841, 0.977). Among the respiratory events the RDI had an intrascorer correlation 0.993 (0.977, 0.998) and an interscorer correlation 0.985 (0.958, 0.994). The limb movement PLMS with micro index had the lowest interscorer correlation overall 0.739 (0.317, 0.902) with an intrascorer correlation 0.978 (0.932, 0.993).

Conclusion: Manual scoring in a clinical sleep disorder center with board certified technologists can be very reliable and an ongoing process can assure clinicians that sleep study results are accurate. With an ongoing review process when discrepancies are identified then workshops can be scheduled to target specific areas of scoring.

0980
Relationship Of Heart Rate Based Arousals And Scored Events During Overnight Polysomnography
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Introduction: Among patients with relatively intact autonomic nervous system functioning, autonomic arousals, whether due to respiratory or other events during sleep, are often associated with sharp increases in heart rate (HR). It has been suggested that HR arousals (HRAs) during sleep, identified from continuous ECG recordings, may be helpful in identifying patients who require further study. Also, HRAs might provide information about sleep disturbances beyond that provided by standard polysomnographic scoring.

Methods: N=59 digitized overnight polysomnograms were obtained in a study of depression and sleep-disordered breathing among patients with cardiovascular disease. Polysomnograms were scored using standard criteria. The extracted ECG was scanned on a MARS 8000 Holter analyzer using standard research Holter analysis techniques. Intervals between normal heart beats were converted to instantaneous HRs and plotted as HR tachograms using MatLab. Customized software identified the start, peak and end of each HRA, defined as a non-overlapping change in HR of ≥8 beats/min, lasting at least 10s. This was visually verified and edited as needed. In addition, the number of HRAs that occurred as part of a pattern of cyclic variation of HR (CVHR, at least 3 HRAs with ≤2 mins from peak to peak) was determined. The total number of scored events (combined respiratory and non-respiratory) was compared with the number of HRAs and also the number of HRAs in CVHR by paired t-tests.

Results: There were 270±169 scored events. There were significantly

SLEEP, Volume 28, Abstract Supplement, 2005
more HRAs than scored events (358±196, p<0.001). Limiting this to HRAs in CVHR reduced HR-based events to 297±211, and paired differences between HR-based and scored events were no longer significant. Correlations between the number of scored events and the number of HRAs, however, were modest (r=0.42 for all HRAs, r=0.40 for HRAs in CVHR, p<0.02).

Conclusion: Results support the use of CVHR patterns from continuous ECGs (e.g., Holter recordings) to identify patients who require polysomnography. The presence of a large number of HRAs not associated with scored events, and the lack of correlation between daytime sleepiness and scored events, suggest the potential validity of considering HR-based changes during sleep as a possible additional marker of sleep disturbances.

1-R01 HL65356

0981
Automated, Computerized System For Simultaneous Administration Of MSLT/MWT In Multiple Patients
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Introduction: The current standard objective clinical tests of assessing daytime sleepiness, multiple sleep latency test (MSLT), and maintenance of wakefulness test (MWT), are short-duration tests (~30 minutes each) that are repeated 4-5 times during the day in two-hour intervals and in some ways require more elaborate human technician involvement than overnight PSG. This is because the PSG technologist must perform live, real-time sleep staging (to determine sleep onset and duration of the test) which usually prohibits a technician to perform MSLT/MWT on more than 2 patients per day. This limits the accessibility and cost-effectiveness of these tests. The objective of this effort was to utilize our recently developed novel algorithms for real-time automatic sleep staging to develop systems that are capable of administering MSLT/MWT in multiple patients with minimal technicians involvement.

Methods: To facilitate the monitoring of up to 4 MSLT/MWT tests simultaneously, we developed a technician workstation, which is comprised of a computer system, 4 PSG monitoring units (CleveMed Crystal Monitor 16-S), and a software package that incorporates the real-time automatic sleep-wake tracking index. This system was then tested using a Patient Simulator, which is comprised of a PC whose output is a stream of analog signals converted from previously recorded data from actual patients during MSLT studies. The system was also evaluated in 8 normal volunteers who participated in one or two 30-minute naps during the daytime hours while being automatically monitored by the developed system.

Results: The EEG data from the subjects were processed in real-time by the developed system and compared with the sleep-staging of a PSG technologist who staged the data after the completion of the test. The detected sleep onset times of the two methods were within 30 seconds of each other in every subject with a very high correlation coefficient (0.998). Bland-Altman test of agreement also showed that the mean differences between the automatic and technologist-staged sleep onsets were within clinical acceptable range (<30 seconds).

Conclusion: The real-time sleep onset detection capability of the developed system performed very well in these limited sets of studies with normal volunteers. This system is currently being finalized to become fully automatic capable of guide a novice operator to easily perform up to 4 MSLT/MWT studies simultaneously.

0982
Determination Of Apnea-Hypopnea Index Using Nasal Pressure Versus Thermistor Recordings
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Introduction: During polysomnography (PSG), nasal pressure and oronasal thermistor signals are recorded, either singly or in combination, as surrogate markers of airflow. This study's purpose was to compare indices of sleep-disordered breathing scored using one or both of these airflow signals along with the other recorded signals.

Methods: Overnight home PSGs were performed on 60 adults participating in the Sleep AHEAD study, an ancillary study of Look AHEAD, a multicenter, randomized controlled trial of a weight loss intervention in obese adults with type 2 diabetes. The following signals were recorded (PS2, Compumedics): electroencephalogram (C3A2, C4A1), electrooculograms, pulse oximetry, chest and abdominal movement, nasal pressure, oronasal thermistor, and body position. Using standard guidelines, PSGs were separately scored by a registered technologist using: (1) oro-nasal thermistor only, (2) nasal pressure only, and (3) both signals. The technologist was blinded to the unexamined airflow signal on each scoring pass. On a separate set of 32 PSGs, the intraclass correlation coefficient assessing the technologist's intrascorer reliability for apnea-hypopnoea index (AHI) was 0.89.

Results: The mean ± SD AHI of 31.8 ± 15.7 events/hr scoring with nasal pressure was greater than the AHI scoring with thermistor (27.6 ± 15.5) or with nasal pressure + thermistor (28.7 ± 15.6) (p < 0.001). More hypopneas were scored using the thermistor signal (140 ± 75.7) compared to the nasal pressure (105.7 ± 52.2) or nasal pressure + thermistor (106.7 ± 59.7) signals (p < 0.05). The number of apneas scored using nasal pressure (94.1 ± 90.3), thermistor (33.5 ± 56.2), and nasal pressure + thermistor (69.5 ± 77.9) were all significantly different from each other (p < 0.001).

Conclusion: When scoring a PSG using a nasal pressure and oronasal thermistor signal, either separately or in combination, AHI and number of apneas is greatest when scoring with nasal pressure alone.

NHI HL 70301, DK57135, DK57002, DK57178, DK56992

0983
Relationship Of Heart Rate Arousal Patterns To Total, Respiratory And Non-Respiratory Events During Polysomnography
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Introduction: Sleep-disordered heart rate (HR) patterns can be quantified from plots of HR vs. time (HR tachograms). We tested whether heart rate arousal (HRA) patterns from tachograms would correlate with HRA patterns associated with specific types of scored events during polysomnography.

Methods: N=59 scored digitized polysomnograms were obtained from a study of patients with cardiovascular disease. ECGs from polysomnograms were extracted and scanned on a MARS 8000 Holter analyzer. HR tachograms were plotted using MatLab. Customized software identified the start, peak and end of each HRA, from tachograms (HRA-T) and, sep-
arately, for each scored (HRA-E), respiratory (HRA-R) or non-respiratory (HRA-NR) event. HRA-T and HRA-E, HRA-R and HRA-NR patterns were categorized by magnitude of HR change, duration of HR arousal and peak-to-peak time. Paired t-tests and correlation analyses compared categories of HRA-T and event-based HRA patterns.

Results: Respiratory and non-respiratory scored events (131±110 vs. 133±110) were roughly equal. HRA-T was > HRA-E for all categories. Correlations between HRA-E and each category of HRA-T (except HRA-peak to peak times of 90-120s) were significant (p<0.002). The strongest correlation of HRA-E and HRA-R was for HR changes of 15-20 (r=0.83) and >20 beats (r=0.95). Correlations between HRA-resp and HRA-T category were significant for all but HRA duration <20s, and HRA-HRA times of 60-90s and >90s. The strongest correlations between the HRA-T and HRA-resp were seen for 15-20 beats (r=0.84) and >20 beats (r=0.83).

The strongest correlations between the HRA-T and HRA-Nresp was also seen for 15-20 beats (r=0.64), but there was no relationship between HRA-Nresp and HRA-T for durations of >40s, or HRA-HRA times between 30 and 90s.

Conclusion: HR-based criteria, especially HR changes >15 beats/min, had a strong association with the total number of scored events. Different HRA patterns were associated with respiratory and non-respiratory events. Short HRAs (<20s duration) or HRAs >60s apart were not likely to be respiratory events and, conversely, HRAs >40s duration and between 30s and 90s apart were not likely to be non-respiratory events.

1-R01 HL65356

0984
Validation Of The Apnealink Device As A Screening Tool For Diagnosis Of Obstructive Sleep Apnea
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Introduction: Polysomnography is the accepted standard for diagnosis of obstructive sleep apnea, but is not practical for use in certain settings (acute hospital wards, nursing homes) or as a screening device to define which patients might benefit from full polysomnography. Apnealink (ResMed, Poway CA) is a sleep screening device that records and analyzes signals for breathing sound and respiratory flow, using a nasal cannula. Integrated software allows derivation of an Apnea/Hypopnea Index (AHI).

Methods: This study was designed to determine the sensitivity and specificity of the Apnealink (designated microMESAM in Europe) compared with polysomnography (PSG) in patients with Type 2 Diabetes. Eligible subjects who consented to study entry used Apnealink for one night at home and agreed to undergo confirmatory laboratory PSG evaluation. Validation was performed on data from 61 subjects, with simultaneous Apnealink and PSG recording. Flow reduction of greater than 10 seconds duration which was associated with an EEG arousal or a 2% desaturation (3% if baseline O2 saturation was below 93%) defined an AHI event. Sensitivity and specificity were calculated for the device in comparison to PSG derived AHI values of 5, 10, 15 and 20.

Results: The device demonstrated excellent reliability as a screening device for OSA in comparison to PSG derived AHI values. For AHI ≥25, sensitivity was 87.2% and specificity was 50.0%; for AHI ≥10, sensitivity was 82.1% and specificity was 85.2%; for AHI ≥15, sensitivity was 90.5% and specificity was 91.2%; for AHI ≥20, sensitivity was 82.4% and specificity was 89.5%.

Conclusion: The Apnealink demonstrated utility as a screening device for OSA in comparison to laboratory PSG. The device showed greatest sensitivity and specificity using an AHI value of ≥15, yielding a sensitivity value of 90.5% and a specificity value of 91.2%. These findings are similar to those previously established for the microMESAM device in comparison to PSG.

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0985
Effect Of Selective Serotonin Reuptake Inhibitors On Eye Movement Latencies In Sleep
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Introduction: Eye movements are an integral parameter for distinguishing sleep stages. Currently no polysomnographic definitions exist for defining what constitutes a rapid eye movement. Yet, many investigators have noted selective serotonin reuptake inhibitors (SSRI) influence eye movements in NREM sleep. We measured eye movements in each stage of sleep in patients with and without SSRIs to evaluate if standardized parameters could distinguish eye movements in each stage.

Methods: We measured ten eye movements in ten subjects (5 male) without antidepressant medication and ten subjects prescribed a SSRI (5 male). Standard polysomnographic lateral outer canthus electro-oculograms compared to ear reference were recorded during sleep. Eye movement latency was defined as the time from movement from the baseline to the initial peak deflection. A registered technologist independently measured eye movements using low frequency filters of 0.3 and 0.5 Hz. Eye movement latencies were averaged for each stage for each person and groups and were compared using dependent t-tests.

Results: Average eye movements for subjects without antidepressant medication demonstrated that REM related eye movement latencies were significantly shorter than all other stages of sleep (0.46 seconds, p<0.003) when a low frequency filter of 0.5Hz was used. Eye movements in Stage 1 and 2 sleep averaged (0.86 and 0.82 respectively) In subjects with SSRI medication, eye movements in REM sleep were also significantly shorter (0.52 second, p<0.05) than eye movements in stage 1 and 2 sleep (0.89 and 0.80). Sleep stage dependent eye movement latencies were more variable in patients with SSRIs.

Conclusion: This study shows in patients, without antidepressant medication, the majority eye movement latencies in REM sleep are less than 0.5 seconds (LFF 0.5Hz). This work also demonstrates subjects prescribed SSRIs have greater variability in eye movement latencies, but average eye movement latencies are not significantly different from subjects without antidepressant medication.

0986
Simultaneous Estimation Of Interscorer And Intrascorer Reliability Of Sleep Study Staging
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Introduction: As a portion of comprehensive interscorer and intrascorer reliability assessments, we have implemented epoch-by-epoch comparisons of sleep staging to meet AASM accreditation requirements. By chance alone scorers can sometimes have measures of agreement with each other and with a Gold Standard (interscorer reliability) greater than the measure of agreement with themselves alone (intrascorer reliability).
By restricting inter-scorer reliability above by intra-scorer reliability, estimates of reliability for 5x5 (Wake, S1, S2, Delta, REM) will be more accurate.

Methods: The design includes periodic random selection of starting points for board certified technologists (RPSGT) for 3 blocks of 50 epochs within larger sets of 75 epochs scored by the Ambassador (Gold Standard), the manager of the Sleep Disorder Center and the technologist with the highest volume. Using random starting points none of the scorers have the same staging distributions but still have comparable measures of agreement. Restricting generalized log-linear models so that each scorer is at least as likely to agree with himself or herself as they are with anyone else, maximum likelihood estimation is implemented for the measures of agreement. Since measures of agreement are non-directional for shifts in staging, cross-diagonal odds are estimated to determine if these are shifts tend to under or overestimate the stages of sleep.

Results: The order-restricted measures of agreement have a 10-fold reduction in error and yield results that more easily reproducible. The Kappa statistic continues to have problems in the extremes and for various distributions, but some of these problems are addressed with the proposed functions of the global and conditional global odds-ratios that are also bounded by -1 and 1. The accuracy and agreement can be excellent and yet there can be very significant shifts in the cross diagonal odds, for 8 technologists these odds varied from 0.31 to infinity as they tend to either underestimate or overestimate the stage of sleep when there is disagreement with the gold standard. In fact, accuracy and agreement can increase and the cross diagonal odds become more extreme.

Conclusion: These order restrictions along with estimates of accuracy, runs tests and cross diagonal odds models lead to a comprehensive picture that can maintain a reliable quality sleep disorder center. Criteria are also established to refine the Gold Standard when necessary.

An Inter-Laboratory Proficiency Testing Program In Australian Sleep Laboratories
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Introduction: Proficiency testing is an integral part of quality assurance programs. Within Sleep Laboratories periodic assessment of inter-observer variability in sleep scoring is recommended. While this may give confidence in the consistency or ‘precision’ within a laboratory it gives no information about agreement with other laboratories. The preponderance of Compumedics® software in Australian laboratories allows the possibility of inter-laboratory comparisons.

Methods: Studies were distributed on CD to laboratories in Adelaide and Perth, Australia. Participation was voluntary and anonymous. An in-house computer application was used to compare sleep scoring, arousals and respiratory events on an epoch by epoch basis with the ‘best’ estimate of each event or sleep stage being computed as the most commonly chosen one amongst all scorers. A composite hypnogram was constructed from individual best epoch scores. Kappa and Intra-Class Correlation coefficients were calculated to provide a measurement of concordance. Graphical depictions of sleep histograms and spreadsheets of epoch by epoch results were provided to participating laboratories to allow examination of discrepancies between scorers.

Results: Eleven, 32 and 27 scorers participated in Studies 1 to 3 respectively. The table shows agreement between individual scorers and composite hypogram and compares results with published data. Diagnosis % Agreement® Kappa® Intraclass C® (mean, range) (mean, range) Study 1 Narcolepsy 87.5 (69-93) 0.83 (0.60-0.91) 0.928 (0.83-0.97) Study 2 Mild OSA 82.7 (73-88) 0.75 (0.57-0.84) 0.925 (0.81-0.98) Study 3 Mild OSA 85.4 (67-94) 0.78 (0.54-0.91) 0.960 (0.90-0.99) Ref 1 Normal 76 (65-85) 0.65 (0.49-0.79) Ref 1 Sleep apnea 71 (66-78) 0.59 (0.54-0.70) Ref 2 All 76.8 0.68 Agreement on arousals and respiratory events was significantly poorer averaging 44.2% (range 26-63%) and 27.5% (range 5-51%) respectively.

Conclusion: The level of agreement on sleep scoring in the participating laboratories was better than that reported in two similar studies from the United States and Europe. However, in the important analysis of respiratory and arousal events agreement was poor. Examination of differences between scorers is possible from this exercise and should assist in achieving a greater consistency between and within laboratories. The program has been universally accepted by participating laboratories and is viewed as a valuable exercise.

Accuracy Of A Single Channel Nasal Pressure Recording Device For Repeated Ambulatory Use In Suspected Sleep Apnea
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Introduction: The high prevalence of obstructive sleep apnea (OSA) necessitates simpler methods for clinical or population screening. We investigated the diagnostic reliability of a single channel nasal pressure-recording device (FW, Flow Wizard®, DiagnoseIT, Australia) that uses an automated algorithm and is suitable for repeated home recordings.

Methods: We studied 34 consecutive patients (age 43±10 years, BMI 30.2±5.4 kg/m2, ESS 11.9±4.7) referred for sleep investigation (PSG). The PSG included a standard montage, including nasal pressure via nasal prongs. The PSG Apnea/Hypopnea Index (AHI) was scored according to the Chicago criteria (AHIPSG). The FW records a nasal pressure signal and uses a specific analysis algorithm to evaluate aspects of the flow/pressure curve including amplitude and stability to automatically determine apneas, hypopneas, flow limitation and snoring. Automated AHI calculations are based on the recording time minus the time with a poor quality signal (RT). All patients underwent automated FW analyses on four occasions; 3 consecutive nights in the home (AHIFW/HM 1-3) and during their PSG (AHIFW/LAB). 33 eligible recordings were obtained.

Results: Total PSG sleep time was 6.4±1.1h, total recording time 7.9±0.9h and the AHIPSG was 31.5±27.2 (range 0-100). Using an AHIPSG >=10, an OSA diagnosis was confirmed in 26/33. The FW/LAB recording time was 8.2±0.9h with a mean RT of 80±23% and AHIFW/LAB was 35.0±23.4 (range 6-95). Applying an AHIFW/LAB >=10, an OSA diagnosis was confirmed in 29/33. AHIFW/HM 1-3 was 28.0±17.0. A Bland-Altman plot demonstrated a slight underestimation of AHIFW/HM 1-3 in the high severity range. Sensitivity and specificity for the AHIFW/HM 1-3 analyses were 92 and 75% using an AHI>=10 cut-off. The area under the ROC curve for the AHIFW/HM 1-3 was 0.90.

Conclusion: OSA may be identified with high accuracy using a single nasal flow/pressure recording during repeated nights in the home in a clinical population. The utility of this approach in population screening is worthy of further research.

Supported by DiagnoseIT, Australia
Transduction Of Respiratory Movements Via Mattress Actigraphy

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Introduction: Laboratory polysomnography makes extraordinary demands upon subjects, is expensive, and substantially modifies the social context of sleep. As a result, we have almost no objective data continuously quantifying naturalistic sleep over durations of weeks or months. This presentation will describe the design and preliminary validation of an updated method of mattress actigraphy, extending the approach introduced by Alihanka and colleagues (Alihanka & Vaahtoranta, 1979). Our method involves locating small but highly-sensitive DC accelerometers in a foam mattress topper approximately one-inch deep that may be incorporated into virtually any sleep foundation. Like conventional limb actigraphy, mattress actigraphy records gross sleep behavior and large body movements. Mattress actigraphy is also uniquely sensitive to very brief low-amplitude limb and thorax movements, including the ballistocardiogram, and thoracic vibrations induced by snoring. Most importantly, mattress actigraphy can directly transduce the thoracic and abdominal motions associated with breathing.

Methods: Simultaneous recording of sleep with standard PSG and/or LifeShirt and mattress actigraphy. Subjects were twelve adult males, aged 35-55, diagnosed with posttraumatic stress disorder, apnea status variable.

Results: In non-apneics, respiratory effort signals derived from mattress-embedded DC accelerometers closely approximate those derived from conventional piezo-electric bands or the stabilized inductive plethysmographic coils in the LifeShirt. For typical 30 second epochs, signal cross-correlations between circumferential and mattress-embedded transducers exceeded 0.85. A limitation is that even small body movements degrade the respiratory signals provided by mattress-embedded accelerometers, impairing discrimination of mild, moderate, and severe levels of respiratory disturbance.

Conclusion: Though precise assessment of respiratory disturbance may not be achievable with this approach, it does provide nightly, zero-burden verification of non-apneic status, along with high-resolution recordings of movement, snoring and the ballistocardiogram.

This research has received technical and financial support from European Sleep Works (Berkeley, CA) and financial support from the Stanford University Office of Technology Licensing and the National Center for PTSD, Department of Veterans Affairs. Relevant patent (USPO 6,485,441) assigned to Department of Veterans Affairs and Stanford University. Not currently under commercial development.
**Category S—Sleep Education**

**0990**

**Curriculum And Composition Of Accredited Sleep Fellowship Programs**

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**Introduction:** An accredited sleep medicine fellowship should provide a thorough and well-rounded educational experience, but few studies have examined the curriculum and composition of existing accredited programs.

**Methods:** The American Academy of Sleep Medicine identifies 42 accredited sleep fellowship programs. We sent an email survey in May 2004 to the director of each program. The survey consisted of questions regarding number of fellows enrolled per year, length of training, primary department where the fellowship is “housed,” opportunities for research, teaching experiences, and long-term career plans of the fellows.

**Results:** Twenty-one surveys were returned (response rate = 50%). The majority of sleep fellowships are “housed” in pulmonary departments (43%) with 19% in neurology, 19% in psychiatry, 9.5% in freestanding centers, and 9.5% in combined programs. A similar trend was seen for the primary training a fellow had before entering a sleep fellowship: pulmonary 60%, neurology 27%, psychiatry 7%, and pediatrics 2%. Most programs trained one fellow per year (43%) (range = 1 to 4). The length of training was one year for 71% of the programs. All programs provided exposure to adult respiratory and behavioral sleep issues as well as pediatric sleep issues (81%), “alternatives to CPAP” (71%), and epilepsy (57%), plus a surgery rotation (ENT, dentistry, oral surgery) or cognitive-biofeedback groups. All programs had didactic options, including introductory lectures, sleep conferences, journal club, grand rounds, and “interesting case” files. All programs reported exposure to sleep research with 52% requiring the fellow to complete a research project. Sixty-two percent of the programs offered an additional optional year of training in sleep research. Funding for the research year included NIH or institutional grants. In regard to long-term outcomes, 37% of fellows accept an academic position vs 62% go into private practice.

**Conclusion:** Our data reveal that while most fellows in sleep medicine have previously trained in pulmonary medicine and proceed to pulmonary-based programs, the fellowship experience itself is heterogeneous. Our data reveal a multidisciplinary approach in teaching and clinical experience offered across the country in sleep fellowships. With the ongoing expansion of sleep medicine, these results illustrate the successful emergence of a multidisciplinary approach to sleep education regardless of prior training, institution, or trends in practice type.

**0991**

**Innovative Teaching Method Incorporating Sleep Medicine Education For Medicine Residents Improves Sleep Medicine Knowledge**

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**Introduction:** Sleep Disorders are as common as hypertension, yet most internal medicine residents have little to no formal or informal sleep medicine education. An innovative, required medical education course provided the opportunity to introduce sleep disorders as an important topic not formally integrated into residency education. This abstract describes our experience and learning outcomes associated with embedding sleep disorders into a new core curriculum format.

**Methods:** Internal Medicine 201, a 2-day required medical education course for second year internal medicine residents is an innovative educational format for incorporating common medical topics not routinely covered in detail in residency. All residents are required to attend and are excused from other duties during this structured learning experience, which began in 2004-5. Sleep medicine education was included as a 2.5-hour course unit delivered using a combination of formal lecture, hands-on workshop using CPAP equipment, and sleep disorder video clips from the sleep laboratory. The content of the instruction included normal sleep physiology, circadian rhythm disorders, restless legs syndrome, parasomnias, and sleep apnea. A multiple choice examination given pre and post the instructional unit was designed to assess basic principles reviewed during the course. Self-assessment tools were employed to measure effectiveness and learner satisfaction.

**Results:** 25 residents completed the course; 16 completed both the pre and posttest. The mean percent correct on the pretest was 46% (SD 12) and 64% (SD 11) on the post test. A paired t-test of pre-post scores revealed a significant improvement in sleep knowledge (p > 0.001). There was also significant learner satisfaction and subjective improvement in patient care, medical knowledge, practice-based learning, and systems based practice skills per self-assessment tools.

**Conclusion:** A short, 2.5-hour instructional unit within a new Internal Medicine 201 course significantly improves internal medicine residents’ knowledge of sleep disorders. In hectic residency training programs, this required education format provides relatively sleep naive residents the foundations for sleep disorders diagnosis and care.

**0992**

**What Do Young Australian Drivers Know About Sleep And Safe Driving — Focus Groups And The Role Of Education Programs**

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**Introduction:** Young drivers in NSW are over represented in fatigue related fatal motor accidents. Previous work suggests sleep and safe driving knowledge in pre-driver Australians and in 18 to 24 year drivers is poor. This study aimed to determine via focus groups, whether better sleep and driver safety knowledge would alter future driving behaviours.

**Methods:** 26 young drivers (12 males, 14 females), mean age 22.08 years, SD ± 1.77 years from a previous survey attended a 1.5 to 2 hour focus group. Participants underwent performance testing, a driver simulator task (AusEd), and kept a Karolinska sleep diary (KSD) for 4 nights. Actimetry [ACT(Mini-Mitter)] was used in 15 respondents for 4 days nights. A power point standardised presentation and an audio tape recorded discussions. Performance outcomes were used as ‘triggers’ for discussion.

**Results:** Most participants were good sleepers (7-8 hours). Subjective sleep efficiency (SE) varied between week and weekend nights, and was used to determine good and poor sleepers. More respondents (n=9) became poor sleepers on Friday night. Increased SE [(≥85%) ACT] on Sunday night (n=24), was associated with poorer maintenance of lane position [AusEd (rho = 0.55; p = 0.04)] on Monday morning, whereas subjectively increased SE (rho = -0.42; p=0.03) was associated with faster braking times.

**Conclusion:** We found most participants had little knowledge of the importance of sleep. They generally did not recognise signs of sleepiness (video of a sleepy driver), and attributed these to boredom, alcohol or drugs. Most sleepy female participants were unlikely to stop driving due to safety issues unless “their eyes started to close”, and would use their phones, or turn up the radio to stay awake. Such findings suggest that ‘sufficient sleep’ messages have to be targeted to the level at which young
drivers will respond in order to change driving behaviours.

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Introduction: A survey of major medical textbooks by Aldrich in 1999 revealed little coverage of topics such as insomnia and insufficient sleep. We performed a follow-up survey of previously reviewed textbooks to determine the pattern of sleep coverage five years later.

Methods: The following texts were reviewed and are listed as older followed by newer editions: Introductory Textbook of Psychiatry, 1995 (700 pp) and 2nd Ed, 2001 (798pp); Nelson Textbook of Pediatrics, 15th Ed, 1996 (2200 pp) and 17th Ed, 2004 (2505 pp); Cecil's Essentials of Medicine. 4th Ed, 1997 (949 pp) and 6th Ed, 2004 (1184 pp); Cecil's Textbook of Medicine, 20th Ed., 1996 (2222 pp) and 22th Ed., 2004 (2506 pp); Harrison's Principles of Internal Medicine, 14 th ed. 1998 (2569 pp) and 16th ed. 2005 (2608 pp); Merritt's Textbook of Neurology, 9th ed, 1995; (1058 pp) and 10th ed, 2000, (1002 pp); Office Practice of Neurology, 1996 (1236 pp) and 2003 (1464 pp); Pages devoted to sleep to the nearest 0.1 page were located using the following index terms: neurobiology of sleep; sleep-disordered breathing (SDB); sleepiness; insomnia; narcolepsy; idiopathic hypersomnia; epidemiology of sleep disorders; periodic limb movements; restless legs syndrome; sleep hygiene; insufficient sleep; drugs; circadian rhythms; parasomnias; psychiatric, neurological, and medical disorders.

Results: Seven books devoted between 0.2 to 3.2% of their total content to sleep topics. The mean number of pages devoted to sleep disorders was 11.9±4.6. With the exception of one book, the proportion of pages devoted to sleep have remained the same or decreased. Topics such as SDB and narcolepsy received the majority of discussion, while topics such as insomnia, sleepiness, and insufficient sleep continued to be underrepresented.

Conclusion: Sleep medicine continues to receive little attention in major medical textbooks. Textbook information about important topics in sleep medicine such as insomnia, insufficient sleep and sleepiness has not increased.

Survey Of Sleep Disorders Knowledge And Practice Among Pediatricians In Romania Before And After A Focused Educational Intervention

Introduction: Sleep disorders (SD) in general and OSA in particular, impose neurobehavioral, somatic and psychosocial complications. However, awareness of SD in developing countries is unknown.

Methods: Romanian pediatricians attending a 2-day symposium were administered anonymous questionnaires before and after a series of two 1-hour lectures on SD (day 1) and on OSA (day 2). Questions were presented in Likert scale format. Post-lecture questionnaires were requested from only those with documented attendance at both lectures. Questions addressed issues pertaining to estimated prevalence, clinical presentation and complications of SD, as well as familiarity with OSA and barriers to SD-specific patient assessment in clinical practice.

Results: 91 of 98(92.8%) pre-lecture and 54 of 83 (65%) of post-lecture questionnaires were returned. About 85% of the attendees were pediatricians and the rest were pediatric residents. Most responders reported seeing 20-40 new patients/week. Physicians estimated <10% patients as likely to either often or almost always volunteer complaints of SD and cited lack of time (37.4%) and lack of knowledge (62.6%) as the most important barriers preventing a sleep-directed history during patient encounters. In the post-lecture survey, significantly more doctors (53.8% vs. 7.1%; p<0.05) estimated SD prevalence to be >5% and recognized snoring as a hallmark of OSA (96.3% vs.72.5%; p<0.01). Similarly, more responders agreed as being likely to often or almost always ask their patients for a SD history in the future (94.4% vs. 30.3%; p<0.001), with lack of time (63%) becoming now the major obstacle.

Conclusion: Pediatricians in Romania are aware of the existence of SD and OSA in childhood, but are likely to underestimate the prevalence and clinical significance. Instructional efforts aiming to reverse these deficiencies along with institution of systematic epidemiological surveys and establishment of pediatric sleep centers may lead to earlier diagnosis and more favorable outcomes in children with SD.

Sleep Medicine Education-Medical College Of Wisconsin Experience

Introduction: Sleep disorders are common among all age groups but physician performance on sleep related knowledge from medical students through practicing primary care physicians is poor at its best. This has been attributed to less than optimal teaching for sleep medicine education in undergraduate medical training. We describe our experience of instruction of sleep medicine education at Medical College of Wisconsin (MCW)

Methods: A 1-month fourth year medical student selective in Sleep Medicine was created in 2002. Curriculum was developed incorporating four teaching modules to include core competencies of sleep medicine. The selective was co-taught by a multi-disciplinary team of physicians and sleep technicians. MCQ test was developed to assess core competencies in sleep medicine that included chronobiology, sleep disordered breathing, excessive daytime sleepiness and parasomnias. Two sources of data were used to evaluate the selective: learner rating of the rotation and learner performance on a pre-post rotation multiple-choice examination (MCQ).

Results: Twenty medical students (13 male; 7 female) completed the selective. Lack of exposure to sleep medicine during the first three years of medical school was the commonest reason for taking the elective. Using the institution's standard rotation evaluation form (e.g., objectives were clear, rate attending staff as educators), the overall rating was 1.5 on a 5-point scale (1=best). Examination scores increased significantly from pre-selective mean of 56% to 86% correct post selective (p <.05). Unanticipated but associated outcomes included a) an invitation to provide a one-hour required lecture to M3 students and pediatric residents b) 2-hour workshop for Internal Medicine residents on sleep medicine c) Grant funding from MCW Curriculum and Evaluation Committee to develop electronic teaching modules on sleep medicine

Conclusion: A well designed fourth year selective improves student knowledge in sleep medicine and provided an entree for inclusion of required sleep medicine instruction for various trainees

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Sleep Coverage In Multi-Specialty Texts Is Little And Non-Uniform
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Introduction: Sleep medicine is comprised of practitioners from multiple facets of medicine. We evaluated textbooks in four major specialties for sleep content.

Methods: Thirty-one textbooks written in four major specialties over the past five years were evaluated: Geriatrics (n=7), Neurology (n=7), Psychiatry (n=10), and Pulmonary Medicine (n=7). Pages devoted to sleep to the nearest 0.1 page were located using chapter headings and the following index terms: asleep, bruxism, cataplexy, Cheyne Stokes respiration, central sleep apnea, circadian, hypnagogic hallucinations, hypersomnia, hypventilation, hypersonmolemence, hypnotics, idiopathic hypersomnia, insomnia, melatonin, myoclonus, naps, narcolepsy, nocturia, nocturnal, obstructive sleep apnea (OSA), parasomnia, periodic limb movements, polysomnography (PSG), rapid eye movement sleep, REM sleep behavior disorder, restless legs syndrome, snoring, sleep, sleepiness, sleep paralysis, sleepwalking, sleep apnea, snoring, and somnambulism. We then determined the most commonly appearing subject in each subspecialty.

Results: Total content devoted to sleep was as follows: Geriatrics (1.3%), Neurology (1.9%), Psychiatry (1.6%), and Pulmonary Medicine (1.4%). The three most commonly discussed subjects in each specialty are as follows: Geriatrics: insomnia, hypnotics, and OSA; Neurology: sleepiness, insomnia and narcolepsy; Psychiatry: hypnotics, circadian rhythms, and parasomnia; and Pulmonary Medicine: sleep apnea, OSA and hypoversilation.

Conclusion: Despite the high prevalence of sleep disorders in areas such as geriatrics, neurology, psychiatry and pulmonary medicine, this study illustrates that sleep coverage in multi-specialty textbooks uniformly receives less than 2% of the text volume covered. Topics covered vary with specialty. Few textbooks seemed to provide a comprehensive overview of sleep medicine.

Are Epworth Sleepiness Scale Scores Related To Subsequent USMLE Step 1 Board Scores?
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Introduction: Snoring German medical students perform more poorly on exams. Sleepy residents interpret ECGs less accurately and work more slowly with more errors in simulated surgery. Physicians sleeping 5 hours or less have 1.7 times risk of medical errors and 2 fold increased risk of malpractice suits. We hypothesized that cohorts of sleepier medical students (MS) would perform more poorly on USMLE Step 1. 

Methods: In April each year 2000-2004, 46 to 71 second year MS from classes of 100-110 anonymously completed the Epworth Sleepiness Scale (ESS) before a lecture on sleepiness (total students completing the ESS = 295). Students took USMLE Step 1 in June or later. We compared mean USMLE class scores to corresponding mean ESS class scores.

Results: The five-class mean ESS score (+SD) was 9.0+0.58, ranging from 8.4 to 9.9. The five-class mean USMLE score was 219.6+3.78, ranging from 214 to 223. The Pearson correlation between ESS and USMLE scores was -.097, p=0.01.

Conclusion: Classes with the lower ESS performed better on the USMLE. The number of data points is small but these findings support the idea that sleepiness in medical school degrades academic performance. EVMS medical students demonstrate slightly lower subjective sleepiness when compared to data reported from other medical students and considerably less than medical residents. The mean EVMS USMLE scores are slightly higher than the national mean scores (around 215) for the years studied. The strength of this relationship over the five years of the study is surprising in part because the ESS scores were from only a subset of those taking USMLE Step 1 and the ESS was completed more than a month prior to the USMLE. Continuing research at EVMS and similar studies at other medical schools are needed to confirm this relationship.
Introduction: The gene lipocalin 2 (Lcn2) has high homology with prostaglandin D synthase (PGDS). PGDS, via its product prostaglandin D2, promotes sleep and suppresses wakefulness in rats and mice. Lcn2 protein is secreted by macrophages, suggesting involvement during inflammatory processes. To assess the potential role of Lcn2 and prostaglandin mechanisms in mediating changes in sleep during infectious disease, we assessed Lcn2 expression in basal forebrain of C57BL/6J and BALB/cByJ mice, which respectively develop dark phase sleep enhancement and light phase sleep fragmentation after influenza infection.

Methods: Adult male C57BL/6J and BALB/cByJ were inoculated intranasally with influenza virus or vehicle (n=4 per group) and were euthanized 30 hours later (mid-light phase). Basal forebrain was removed, and tissue was prepared for analysis of lcn2 expression by quantitative PCR.

Results: Quantitative PCR analysis of basal forebrain collected at 30 hours post-inoculation revealed significant differences in Lcn2 expression as a function of mouse strain (C57BL/6J vs. BALB/cByJ) and health status (healthy vs. influenza infected) (two-way ANOVA: mean effect of strain, F=45, p<0.001; mean effect of health status, F=167, p<0.001; strain/health interaction, F=45, p<0.001). Relative Lcn2 expression was: healthy vs. infected C57BL/6J mice 0.7±0.1 vs. 180 ± 50, p=0.012; healthy vs. infected BALB/cByJ, 0.3±0.1 vs. 56± 29, p<0.001). Lcn2 expression was significantly higher in infected BALB/cByJ mice as compared to infected C57BL/6J mice (p=0.001), but did not differ significantly between healthy C57BL/6J and BALB/cByJ mice.

Conclusion: These data indicate that the infection induced by influenza virus promotes expression of Lcn2 in basal forebrain, perhaps by glial cells. Because of the high homology between the genes Lcn2 and Pgds, we speculate that LCN2 may subserve some functions of PGDS in the sleep regulation during infection.

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1000

Molecular Correlates Of Long-Term Sleep Deprivation In Rats: A Genome-Wide Analysis

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Introduction: Rats subjected to total sleep deprivation (TSD) for several days develop a syndrome that includes extreme sleepiness, weight loss, increased food intake and metabolism, and death after 3-4 weeks. The decrease in daily sleep amount persists under constant darkness, and is mainly due to a decrease in the duration of sleep episodes rather than in their number. Like wild-type flies, ss flies show a significant increase in sleep duration and intensity after 24h of sleep deprivation (SD). Adult ss flies are homozygous viable, are not hyperactive, and perform well in several tasks. While wild-type flies, ss flies show impairments when sleep deprived, show sleep rebound and performance impairments. By screening 9000 mutant lines, we isolated ~10 lines with a reduced daily sleep amount. Here we characterize one of them, called short sleeper (ss), a line obtained through chemical mutagenesis with EMS.

Methods: Flies (1-2 week old) were cultured and tested at 21C, 68% humidity. Locomotor activity, sleep intensity, and performance were measured as previously in our laboratory (Huber et al., 2004). Each behavioral experiment was performed in at least 16 flies/line, > or = 3 independent experiments/line.

Results: ss flies sleep only 4-5 h/day, instead than 9-15h like wild-type flies. The decrease in daily sleep amount persists under constant darkness, and is mainly due to a decrease in the duration of sleep episodes rather than in their number. Like wild-type flies, ss flies show a significant increase in sleep duration and intensity after 24h of sleep deprivation (SD). Adult ss flies are homozygous viable, are not hyperactive, and perform well in several tasks. While wild-type flies show impairment after SD, ss flies do not. The ss phenotype maps to the X chromosome and is recessive. ss flies carry a point mutation in a conserved domain of the ss gene. After crossing out genetic modifiers accumulated over many generations, all the null alleles of the ss gene identified so far also become short sleepers.

Conclusion: The ss gene may regulate sleep need or efficiency.

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1002

Coding Polymorphisms In Human Circadian Rhythm Genes PER1, PER2, PER3, Clock, BMAL1, CRY1, CRY2, And Timeless

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Introduction: Most of us sleep 7-8 hours per night, and if we are deprived of sleep our performance suffers greatly. However, a few do well with just 3-4 hours of sleep - a trait that seems to run in families. Determining which genes underlie this phenotype could shed light on the mechanisms and functions of sleep. To do so, we performed mutagenesis in Drosophila melanogaster, since flies also sleep for many hours and, when sleep deprived, show sleep rebound and performance impairments. By screening 9000 mutant lines, we isolated ~10 lines with a reduced daily sleep amount. Here we characterize one of them, called short sleeper (ss), a line obtained through chemical mutagenesis with EMS.

Methods: Flies (1-2 week old) were cultured and tested at 21C, 68% humidity. Locomotor activity, sleep intensity, and performance were measured as previously in our laboratory (Huber et al., 2004). Each behavioral experiment was performed in at least 16 flies/line, > or = 3 independent experiments/line.

Results: ss flies sleep only 4-5 h/day, instead than 9-15h like wild-type flies. The decrease in daily sleep amount persists under constant darkness, and is mainly due to a decrease in the duration of sleep episodes rather than in their number. Like wild-type flies, ss flies show a significant increase in sleep duration and intensity after 24h of sleep deprivation (SD). Adult ss flies are homozygous viable, are not hyperactive, and perform well in several tasks. While wild-type flies show impairment after SD, ss flies do not. The ss phenotype maps to the X chromosome and is recessive. ss flies carry a point mutation in a conserved domain of the ss gene. After crossing out genetic modifiers accumulated over many generations, all the null alleles of the ss gene identified so far also become short sleepers.

Conclusion: The ss gene may regulate sleep need or efficiency.

Supported by a grant from the United States Defense Advanced Research Projects Agency.
Introduction: Sleep disorders, such as insomnia, sleep apnea, and narcolepsy are common in humans, affecting nearly 20% of the population. While many sleep disorders are sporadic, some are chronic and can have long-term affects neurological health. A number of studies have shown familial segregation of sleep disorders suggesting a link between phenotype and genotype. Thus detailed analysis of genes that regulate the sleep-wake cycle could yield information on the cause and eventual treatment of sleep disorders.

Methods: Circadian rhythm genes PER1, PER2, PER3, CLOCK, BMAL1, CRY1, CRY2, and TIMELESS were re-sequenced in a panel of 95 individuals varying in race, nationality, and ethnicity. All exons, the 3’ untranslated region (UTR), and approximately 1 kb of the putative promoter were re-sequenced for each gene. Populations represented were US Caucasian, African American, Japanese, Chinese, Mexican, Mexican Indian, Puerto Rican, South American, Northern European, and Ashkenazi Jewish.

Results: Coding polymorphisms found were: PER1: Pro37Ser, Thr45Thr, Thr167Thr, Thr267As, Pro351Ser, Gly749Gly, Thr787Thr, Pro962Ala, Gin988Pro, Ala948Thr PER2: Leu83Arg, Leu157Leu, Thr374Le, Phe400Phe, Ala664Ala, Ser665Ser, Ser782Ser, Pro822Pro, Ala828Thr, Ala861Val, Ser875Ser, Val883Met, Val903Ile, Ala923Pro PER3: Tyr65Tyr, Pro67Leu, Val90Ile, His369His, Val639Gly, Ala820Ala, Pro827Leu, Ser864Ser, Leu929Arg, His1159Arg BMAL1: Arg666Gln, Ser459Phe CLOCK: Ala34Ala, Ser208Cys, Phe233Phe, Leu395Ile, Asn584Asn, Ser632Thr, Ser816Ser, TIMELESS: Leu38Leu, Lys467Lys, His531Lys, Lys535Lys, Gin831Arg, Met875Ile, His355His No coding polymorphisms were identified in CRY1.

Conclusion: Considerable genetic variation occurs within the coding region of the genes regulating circadian rhythm. Many non-synonymous coding polymorphisms may cause function changes in proteins produced by genes and thus could cause defects in control of the sleep wake cycle. Some of these functional changes may be specific to race, nationality, or ethnicity.

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Rna Interference Induces Orexin Knockdown And Sleep Changes In Rats
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Introduction: RNA interference (RNAi) is a sequence-specific gene suppression mechanism induced by a double-stranded RNA (short interfering RNA, or siRNA). However, to date, there is no study on sleep using RNAi. The Orexin (Hypocretin) system is linked to sleep disorders, especially narcolepsy. Yet its role in regulating normal sleep-wakefulness is less clear. In this study, we examined the effect of siRNA targeting the prepro-orexin gene on orexin-A immunoreactivity and sleep-wakefulness in rats.

Methods: Adult male rats were housed under 12:12 h light-dark cycle. A pool of 3 siRNAs targeting rat proopanexin (siRNA-sense) was unilaterally injected (0.03nmol) into one side of the orexneric perifornical lateral hypothalamus (LH). A corresponding control, siRNAs with scrambled sequences and no homology to known rat gene (siRNA-scrambled) or ACSF was injected on the contralateral side. Rats were sacrificed either 1 or 2 days later and orexin-A immunoreactivity was examined. For sleep recording, guide cannulas, EEG and EMG electrodes were implanted. Following 24 hr of baseline sleep recording, the rats were bilaterally injected with either siRNA-sense or siRNA-scrambled. Sleep recording was continued for at least 5 more days.

Results: Orexin-A immunoreactivity was substantially reduced on the side of siRNA-sense administration as compared to the side that received either ACSF (n=4) or siRNA-scrambled (n=4). Rats treated with siRNA-sense (n=2) had a persistent increase (over 50%) in REM for over four days during the dark period as compared to the baseline. No such persistent effect existed in animals treated with siRNA -scrambled (n=4). The amount of REM during light period did not differ from the baseline in either group.

Conclusion: Our preliminary results indicate that RNAi is a convenient and powerful tool for studying sleep-related genes. Furthermore, our data suggest orexins may be involved in the circadian control of REM sleep.


1004
A Role For BIP/GRP78 In Recovery Sleep Of Drosophila
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Introduction: 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 sleep deprivation (SD). We have examined the expression of BiP protein in Drosophila heads following SD and recovery sleep in the clock mutant Cyco and in Canton-S. In addition, we have examined the effect of alterations in BiP protein levels on sleep recovery in Drosophila.

Methods: The HS Gal4-UAS system was used to generate the BiP over-expressor, (HS-Gal4-WTBiP) and mutant BiP line expressing dominant negative BiP (HS-Gal4-D231S). Flies were maintained at 25°C and 40% humidity in a 12:12 light:dark cycle. Flies were sleep deprived between ZT 16 - ZT 22, using random stimuli mechanically applied throughout the observation period. Time matched controls were also used. For behavioral studies flies were allowed to recover for 2-3 days following SD. Flies were also sacrificed at the end of the deprivation or rest period for protein analysis.

Results: BiP protein expression is increased following SD and returns to normal baseline levels following recovery sleep in CS and Cyco males. Flies over expressing BiP displayed an increase in recovery sleep over baseline, while flies expressing the dominant negative BiP displayed reduced recovery sleep.

Conclusion: Sleep deprivation elicits the unfolded protein response (UPR) in Drosophila resulting in the increased expression of the molecular chaperone BiP. Recovery sleep restores BiP expression to normal levels. Our data suggest that BiP expression levels and the UPR have an effect on the amount of recovery sleep.

1005
Strain Variation In Ccl3 Expression And Protein During Influenza Infection In Mice
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Introduction: Targeted mutation of the gene Ccl3 (previously called macrophage inflammatory protein 1r”, or MIP1”) converts the dark phase sleep enhancement that is characteristic of influenza-infected C57BL/6J mice into a BALB/cByJ-like response of reduced sleep. We therefore determined whether Ccl3 production changed differentially during influenza infection in these two strains.
Methods: Adult male C57BL/6J and BALB/cByJ (n=4 per strain) were inoculated intranasally with influenza virus or vehicle and were euthanized at 30 or 42 hours later (mid-light and dark phases, respectively). Lung and basal forebrain were removed and assayed for Ccl3 expression and protein by quantitative PCR and ELISA, respectively.

Results: After influenza infection, relative Ccl3 expression in lung increased from values of less than 10 to over 100 in both C57BL/6J and BALB/cByJ mice. However, expression was nearly twice as high in BALB/cByJ mice as in C57BL/6J mice at both post-inoculation time points (relative mRNA expression: 296±69 vs. 160±53 during the light phase; 168±48 vs. 93±13 during the dark phase). Ccl3 protein levels (pg/ml) in lung of infected C57BL/6J and BALB/cByJ mice were 712±140 vs. 1534±138 during the light phase and 450±58 vs. 1437±391 during the dark phase. In contrast to lung, Ccl3 expression in basal forebrain increased about 2 fold during the dark phase in infected C57BL/6J mice but did not change in BALB/cByJ mice.

Conclusion: Influenza-infected BALB/cByJ mice have more Ccl3 expression and protein in lung than do infected C57BL/6J mice. However, infected C57BL/6J mice have greater expression in basal forebrain. These differences, together with our report that Ccl3-KO mice develop a BALB/cByJ-like sleep pattern after infection, suggest that central, rather than peripheral, Ccl3 production generates the dark-phase increase in sleep that occurs in infected C57BL/6J mice.

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1006 Changes In Gene Expression With Sleep And Wakefulness In Drosophila Brain

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Introduction: Rest in Drosophila meets the criteria established for sleep. Many genetic pathways are conserved between flies and mammals. Therefore, the determination of transcriptional regulation in the brain of Drosophila could elucidate basic molecular mechanisms of sleep. The aim of this study is to identify wake and sleep dependent gene regulation in the brain of Drosophila melanogaster.

Methods: RNA: Total RNA was isolated from pooled brains of 5-day-old adult CS females. Sleep deprivation: Flies were sacrificed at ZT14 for the 0 hour control group and after sleep deprivation for 2, 4 or 6 hours (SD). Time matched controls were also sacrificed (CON). Mechanical stimulation control: Flies were sacrificed at ZT10 for the 0 hour active period control group and after stimulation for 4 hours during a normal active period (MS). Time matched controls were also sacrificed.

Microarray: Expression data was determined using the Affymetrix Drosophila Genome Arrays. Statistics: Intensity data was normalized using the robust multi-array average method. Differential expression between experimental groups was determined using the MAANOVA procedure and temporal gene expression was addressed through a linear multiple regression analysis (MR).

Results: 352 genes were identified as significant between SD and CON by MAANOVA and MR analysis identified 209 genes that show significant temporal regulation. 169 genes were found in both analyses and could be separated into 7 classes of expression patterns. These 7 classes distinguished 32 genes whose regulation is sleep dependent, 135 dependent on extended wakefulness and 2 circadian genes whose expression is modified by sleep deprivation. 25 of the 135 wake dependent genes were also differentially expressed in MS and most are part of the immune response of Drosophila.

Conclusion: We have identified genes in the Drosophila brain whose expression is dependent on the sleep state and others induced by stimulation independent of the sleep state.

1007 Zebrafish Genetic Screen Reveals Mutant Expression Of Hypocretin And Histamine

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Introduction: Hypocretin and histamine are key neurotransmitters in the control of sleep and wakefulness. Hypocretin is involved in narcolepsy, and regulates histaminergic transmission. The rate-limiting enzyme for the production of histamine is histidine decarboxylase (HDC). Zebrafish (Danio rerio) are ideally suited for developmental and genetics research. In this animal model, hypocretin and HDC mRNAs are expressed in a pattern and location similar to that observed in mammals. We are employing a forward genetic approach to discover novel functional regulators of these neurochemical systems.

Methods: A three-generation ENU mutagenesis screen is ongoing. For each family, progeny from 3-6 independent F2 breeding pairs are analyzed. F3 progeny (wholemount larval zebrafish; 3-7 days post-fertilization, n=>16 larvae/pair) are hybridized with riboprobes for zebrafish HDC and hypocretin. Larvae are examined for number and distribution of cells and intensity of expression. Wild-type fish serve as controls. Families with potential mutants undergo additional testing, including expression analysis at different developmental stages, outcrossing, and assessment of lethality.

Results: To date, 150-159 F2 families have been screened. Putative mutations have been identified in three families. In two (F2W487, F2W778), mutants display little or no HDC, and in one (F2W315), mutants show laterally displaced hypocretin cells and an additional/extended midline group of hypocretin cells. Carriers have been outbred to wild-type (Tü) to confirm monogenic transmission. The phenotype of one family (F2W487) has been confirmed through outcrossing.

Conclusion: Zebrafish can be used as a model to study hypocretin and histamine systems. We hope that mutations, once identified, will shed new light on the development and regulation of these wake-promoting systems, and will provide additional candidate genes for human sleep disorders.

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1008 The Genetics Of Sleep And Starvation Tolerance In Drosophila Melanogaster

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Introduction: Many hypotheses have been proposed for the purpose of sleep-tissue restoration, thermal and energy regulation, immune system function, and memory consolidation. A wide body of evidence indicates that sleep is influenced by nutritional status, supporting the idea that sleep has a role in tissue restoration and/or energy regulation. We are exploring this hypothesis using P-element insertional mutagenesis in Drosophila melanogaster.

Methods: We measured sleep in male and female virgins from 162 homozygous P-element insertion lines previously shown to affect survival
time under starvation conditions. These lines were derived from an isogenic Canton-S parental line and differ from the parental line only by the P-element insertion, enabling us to detect mutations affecting sleep without confounding genetic background effects. Lines were tested in blocks, and the mean insertional effect was calculated as a deviation from the contemporaneous parental line mean in each block. We computed the magnitude of mutational variance and estimated 99.9% confidence interval limits using an ANOVA model. Candidate insertions exceeding the 99.9% confidence interval limits were re-tested and verified using a three-way ANOVA that included genotype, experimental block, and sex effects.

**Results:** Thirty-two P-element insertional mutations had significant effects on sleep. Eight insertions reduced sleep by as much as 4.75 hours as compared to the parental line. The remaining twenty-four lines exhibited more sleep than the control, increasing sleep times as much as 7.61 hours. Twenty of these lines exhibited sex-specific effects, although the same trend (increasing or decreasing) was seen in both sexes for each line.

**Conclusion:** Thirty-two P-element insertions previously shown to affect starvation resistance also had highly significant and sex-specific effects on sleep. Further characterization of these insertions will identify candidate genes involved in both traits and will lead to the elucidation of the molecular basis of the interaction between sleep and nutritional status.

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### 1009

**Elevated Plasma Corticosterone And Decreased Hypothalamic IL1β, CHRH R2 And GHRH Receptor mRNAs Are Associated With Sleep Inhibition Induced By Influenza Virus In Lit/Lit Mice**

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**Introduction:** Mice with deficits in GHRH signaling (lit/lit mice) have less spontaneous sleep than their heterozygote controls. After influenza virus challenge, heterozygous mice increase their NREMS. In contrast, lit/lit mice decrease their NREMS after viral inoculation. We investigated the hypothesis that these differences are due to differential expression patterns of sleep regulatory substances.

**Methods:** Lit/lit or heterozygous mice were intranasally challenged with PR8 influenza virus or vehicle control; 38 h later hypothalami and plasma samples were collected. Plasma corticosterone levels were measured by RIA. Real-time PCR was used to measure mRNAs in hypothalamic samples for IL-1 β, ICE, TACE, TNF-α, GHRH, GHRH receptor, somatostatin, IGF-1, CRH, CRH R1, and CRH R2.

**Results:** Corticosterone increased in both groups in response to virus with a significantly higher rise in the lit/lit mice than in the heterozygous mice. In control mice, influenza challenge increased hypothalamic IL-1 β, TNF-α, CRH R2 and GHRH-R mRNAs. These mRNAs did not increase in the lit/lit mice. The other mRNAs measured were not affected by the virus challenge.

**Conclusion:** The up-regulation of the GHRH-R in infected heterozygous mice is consistent with previous findings that this receptor is important for sleep responses occurring during viral infection. Further, it is implicated in the sleep promoting activity of IL-1. Most hypothalamic GHRH-receptive neurons are also IL-1 receptive and are GABAergic. IL-1 activates NFkB pathways and enhances hypothalamic GHRH-R mRNA levels. In addition, the massive up-regulation of plasma corticosterone in lit/lit mice likely exerts an inhibitory effect on prosomnogenic cytokines in the brain. The suppression of NREMS in lit/lit mice during influenza infection may result from the down regulation of the somatotropin axis and of IL1 and TNF in these mice.

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### 1010

**Three Genes Showing Homology To The Histamine Receptors In The Zebrafish**

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**Introduction:** Hypocretin neurons in the hypothalamus and histaminergic cells of the tuberomammillary nucleus (TM) interact in the regulation of sleep. In mammals, the arousal effect of hypocretin is mediated in part downstream through the action of histamine on the H1 receptor. Anatomical correlates of hypocretin, histamine, as well as cognate genes (HCRT, HDC), have been identified in zebrafish and interconnect anatomically as in mammals. Unlike mammals, however, zebrafish histamine is present only in the brain, making it a model for the study of the central histaminergic systems. In mammals, three histamine receptors have been identified in the central nervous system. H1 and H2 are excitatory or potentiate excitatory inputs, whereas H3 is inhibitory on TM (autoreceptor) and other (heteroreceptor) neurons.

**Methods:** We used protein sequences of the human histamine H1, H2 and H3 receptors in BLAST searches against predicted peptides in the zebrafish genome (EXPASY, Ensembl Zv4). Resulting hits were analyzed further (Sequencher, FGENES, FEX, ClustalW), and clones were obtained by standard rPCR and RACE methods.

**Results:** We identified zebrafish homologs of three histamine receptors. The zH1 gene has high homology with the mammalian H1 gene (44% identity and 60% homology over 267 of 487 amino acids). The zH2 gene has high homology with the human H2 (58% identical 71% homologous over 279 of 338 amino acids). zH3 is highly homologous to the human H3 receptor (74% identical 88% homologous). Complete characterization of cDNAs, genomic organization and patterns of expression are ongoing.

**Conclusion:** The histaminergic system is highly conserved at the genetic level in zebrafish, despite an absence of known peripheral production of histamine. The study of this system in the regulation of activity in lower organisms may shed light on the function of this conserved system.

NIH NS23724 and HHMI

### 1011

**Rapid Eye Movement Sleep Deprivation By The Flower Pot Method Increases Cytokine MRNA Levels In The Rat Hypothalamus**

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**Introduction:** Interleukin-1β (IL-1β) and tumor necrosis factor α (TNFα) are key elements in the brain cytokine network involved in non-rapid eye movement sleep regulation. Total sleep deprivation by gentle handling for 8 h increases brain cytokine mRNA levels. The aim of the current experiments was to determine the cytokine and neurotrophin mRNA responses in the hypothalamus, as measured by real-time reverse transcription-polymerase chain reaction, to extended REM sleep deprivation using the flower pot method (REM-SD).

**Methods:** Male Sprague-Dawley rats (4 to 6 weeks old) were selectively REM-SD for 48 or 72 h by the flower pot method. Controls that were housed separately as well as separate controls placed on a larger diameter flower pot permitting REM sleep were used thus a total of five groups of...
8 rats were used. The hypothalamus (hyp), a brain region that is important in sleep regulation, was quickly dissected, stored in RNAlater and total RNA was extracted using Trizol reagent. cDNA was prepared and then analyzed for IL1β, TNFα, IL6, BDNF, GluR1 and GAD mRNAs.

**Results:** Hyp BDNF mRNA increased significantly after 48 h of REM-SD. IL1β, TNFα, GluR1 and GAD mRNAs increased significantly after 72 hours of REM-SD. IL6, arc, MMP9, and homer mRNA levels did not change significantly at either 48 or 72 h of REM-SD.

**Conclusion:** These results suggest that IL-1β, TNFα, GluR1, GAD and BDNF up-regulate after extended REM-SD in the hypothalamus. Results are consistent with the hypotheses that a central cytokine network is involved in sleep regulation.

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**1012**
**Sleep-Wake Dependent Changes In Clock-Gene Expression And Sleep Homeostasis: A Strain Comparison**

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**Introduction:** Increasing evidence suggests that in brain areas outside the SCN circadian clock-genes play a role in sleep homeostasis rather than in circadian rhythm generation. Normally, expression of clock-genes such as per1 and per2 exhibit circadian rhythms in both the SCN and forebrain. Under various environmental conditions, including sleep deprivation (SD), changes in forebrain per-expression can, however, dissociate from the rhythm generated in the SCN, and instead follow the sleep-wake distribution. Here, we investigate these sleep-wake dependent changes in more detail by following per-expression after SDs of varying duration and after recovery sleep and compare these dynamics in two inbred strains of mice that differ in their response to SD.

**Methods:** 11 week old C57BL/6J (B6) and DBA/2J (D2) male mice were examined after 1-, 3-, or 6h SD. A 4th group was allowed 2h of recovery sleep after 6h SD. For each experimental group a control group was used (n=4/group; total n=32/genotype). Brains were removed and dissected at each time-point and per1, per2, and dbp mRNAs were determined by real-time RT-PCR.

**Results:** As we showed previously, per1 and per2 mRNAs consistently increased with SD while dbp decreased in forebrain. per1 increased more rapidly and reached maximum values after 3h, while per2 after 6h-SD. The per2 increase after 6h-SD was 2-fold higher compared to the per1 increase. Levels of both transcripts reverted to baseline during recovery sleep except for per2 in D2 mice where per2 remained elevated. The results were consistent with additional in situ hybridization studies and Northern analyses.

**Conclusion:** The sleep-wake dependent changes in per1 and per2 expression are consistent with their hypothesized role in sleep homeostasis as suggested by reports on altered homeostatic regulation in clock-gene knock-outs. The lack of a decrease in per2 in D2 might relate to the lack of a rebound in EEG delta power in this strain.

**1013**
**A Quantitative Trait Locus On Chromosome 18 Confers A Novel Early-Runner Phenotype In Mice Derived From The Inbred Strains CAST/EiJ And C57BL/6J**

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**Introduction:** Approximately 20% of (CAST/EiJ x C57BL/6J) x CAST/EiJ backcross progeny mice begin wheel running activity four or more hours prior to dark onset in a 12:12 light:dark cycle. Crosses between two such early-runner mice produce similar early-runner progeny. These observations suggest that the phenotype is under strong genetic control.

**Methods:** To address the genetic aspects of this phenotype, we performed a genome-wide screen on >100 backcross progeny utilizing 83 well-characterized microsatellite markers that differ between C57BL/6J(B6) and CAST/EiJ(CE). In our initial analysis, we sought to identify polymorphisms that were present at a higher frequency in mice exhibiting early onset wheel running (>4h before lights-off) than in normal controls (<1h before lights-off). DNA samples from early runners were preferentially selected for analysis since extreme phenotypes offer greater power in this type of quantitative trait loci (QTL) approach.

**Results:** Backcross progeny displayed a 1:1 ratio of homozygous CE:heterozygous CE/B6 throughout most of the genome, as would be expected at loci unrelated to the phenotype. Only markers on distal chromosome 18 were significantly skewed from this expectation with 85% of early runner mice and 40% of normals homozygous for CE in this region. Specifically, D18Mit162 (50cM) and D18Mit184 (41cM from the centromere) had the highest estimated LOD scores (>4), while markers D18Mit152 (37cM) and D18Mit127 (54cM) had lower LOD estimates.

**Conclusion:** The above data demonstrate a large effect QTL between 41 and 50cM on mouse chromosome 18 that accounts for a high percentage of the variance in the phase-angle-of-entrainment of these backcross progeny. This region contains no previously documented clock-genes. Since neither parental strain consistently displays the early-runner phenotype, there are probably epistatic interactions with other genes at multiple loci that also contribute to this phenotype. Larger crosses will be needed to map these additional loci.
1014
Performance And Cardiovascular Measures In Normal Adults With Extreme MSLT And Subjective Sleepiness Levels
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Introduction: It is common for adults reporting normal alertness during the day to have an MSLT consistent with pathological sleepiness. This study evaluated performance and cardiovascular measures of arousal in adults with normal MSLT, with short MSLT reporting normal alertness, and short MSLT reporting situational subjective sleepiness.

Methods: Fifty adult normal sleepers spent 3 baseline nights and the following days in the laboratory. Standard polysomnographic recordings were made at night. Each day, Ss had an MSLT, performance testing, and heart rate observation periods. Ss with MSLT > 10 minutes following the adaptation night (Alert) were compared with two groups of Ss with MSLT < 7 minutes following the adaptation night: a) those who reported subjective sleepiness during the day (> 1 standard deviation above the group mean called Sleepy-Sleepy) and b) those who did not report subjective sleepiness (subjective sleepiness equal to the Alert group called Sleepy-Alert).

Results: The Alert group maintained longer MSLT latencies than the other groups and had improved performance on vigilance compared to the Sleepy-Sleepy group on all days and on some days compared to the Sleepy-Alert group. Vigilance was improved in the Sleepy-Alert group compared to Sleepy-Sleepy group on all days. The Alert group had higher heart rate and increased low/high spectral heart rate power compared to both sleep groups, and the Sleepy-Alert group had higher heart rate and increased low/high spectral heart rate power compared to the Sleepy-Sleepy group at some points.

Conclusion: Normal adults with short MSLT latencies can be divided into those claiming subjective sleepiness and those denying sleepiness. Those denying sleepiness have improved vigilance performance, greater heart rate, and higher low/high spectral heart rate power compared to those with subjective sleepiness. This implies that ability to maintain wakefulness and performance in sedentary situations is related to innate ability to maintain physiological arousal.

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1015
Faking Sleepiness, Faking Alertness: Response Bias On The MSLT And MWT Based On Motivation
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Introduction: The Multiple Sleep Latency Test (MSLT) and Maintenance of Wakefulness Test (MWT) are used in clinical populations where test results may result in job loss or diagnosis of medical conditions treated with drugs of potential abuse. Such outcomes may motivate patients to fake results. The current study examined the effect of motivation on these tests.

Methods: Twelve subjects spent three nights and the following days in the laboratory. On the day following the first laboratory night (screen), subjects performed an MSLT and 40-minute MWT with normal test instructions. On the next day, random Ss were told to be as Sleepy as possible (i.e., do whatever they could to fall asleep rapidly, short of pain or discomfort). On the other day, Ss were told to be as Wakeful as possible (without pain or using methods such as movement noticeable to the technician). The subject with the ‘best’ performance was paid a bonus of $200.

Results: ANOVA showed significant main effects for condition for both the MSLT (F = 6.42, p < .01) and MWT (F = 9.70, p < .01). Respective baseline, Sleepy, and Wakeful means for the MSLT were 10.9, 11.2, and 14.6 minutes and for the MWT were 26.6, 11.6, and 21.3 minutes. For the MSLT, Newman-Keuls comparisons showed that latency was significantly longer than baseline in the Wakeful condition. For the MWT, latency was significantly shorter than baseline in the Sleepy condition.

Conclusion: Subjects have the ability to increase but not decrease the latency on MSLT, and this implies that the MSLT is a better measure of sleepiness rather than alertness (as in evaluation for reinstatement of a driving license). Subjects have the ability to decrease but not increase the MWT, and this implies that the MWT is a better measure of alertness rather than sleepiness.

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1016
ICU Stress And Sleep Disturbance Among Chinese-American Parents
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Introduction: Studies focused on sleep problems or daytime fatigue in parents with a sick child are rare, although there is strong research evidence that the critical illness of a child can be a devastating experience for parents. The aim of this study was to describe Chinese-American parents’ sleep disturbances and fatigue during hospitalization of their child in the intensive care unit (ICU) and the relationship to parental stress.

Methods: Subjects included 30 families (30 mothers, 25 fathers) who had a child hospitalized in three San Francisco ICU settings. Three sets of data were collected: 1) child’s medical records and parent’s demographic data, 2) Parental Stress Scale, General Sleep Disturbance Scale, Lee Fatigue Scale, and 3) total sleep time (TST) and wake after sleep onset (WASO) averaged from two nights of wrist actigraphy monitoring.

Results: Most of the mothers (93%) and fathers (60%) experienced sleep problems after their child was admitted to the ICU. The average TST for mothers was 367 minutes (SEM= 15.3), and 395 minutes (SEM= 16.5) for fathers; this was less than they reported needing to feel refreshed (p< .001). The average WASO was 17% (SEM= 2.6) for mothers and 7% (SEM= 1.3) for fathers. Mothers reported more difficulty falling asleep (p= .001), and a higher frequency of awakening during sleep (p< .001) than fathers. Mothers perceived more severe fatigue evenings and mornings (p < .001) compared to fathers. Parental stress levels were negatively correlated with TST for both mothers (r= -.51, p=.02) and fathers (r= -.62, p< .01), and positively correlated with morning fatigue for mothers (r=.43, p=.02).

Conclusion: Results indicate that higher parental stress levels are associated with less TST for mothers and fathers and worse fatigue for mothers. Mothers reported greater sleep disturbances and more severe fatigue than fathers.

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1017
The Relationship Between Sleep Patterns And Alcohol Consumption In College Students
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Introduction: College students' sleep is inadequate and erratic, accompanied by significant alcohol use. Studies report that 1st year students have particularly disordered sleep (e.g., Ling-Ling Tsai, 2003.) Moreover, inadequate sleep and alcohol use have adverse consequences for young adults. A structured interview assessed the relationship between college students' sleep and alcohol behaviors.

Methods: A sleep and health interview survey was administered to a random sample of college students (112 males, 123 females, distributed across class years). Analyses focused on sleep and alcohol behaviors in the past 1-2 weeks. Variables included: (1) Sleep: weekday/end bedtime, rise time, total sleep time; (2) Alcohol: frequency, amount/weekend, binging.

Results: Twenty-five percent reported more than 8.4 hours (M = 7.54) of sleep on weeknights. 24% reported rising before 8:00 am (M = 8:38 am) and 65% going to bed after 1:00 am (M = 1:06) on weekdays. 3rd/4th year students reported about 30 minutes more sleep than undergraduates due to later rise times (1st/2nd M = 7.30 vs. 3rd/4th M = 7.80, p < .05). On weekends, bed/rise times were delayed by over 2 hours compared with weekdays; there were no significant differences across class years. 71% reported consuming alcohol within the last week. Males drank increasingly more alcohol/weekend than females over the four years (M = 7.28 vs. 4.19, p < .05). 1st year students drank less frequently and had fewer drinks versus upperclassmen, p < .01. Increased alcohol frequency, drinks/weekend, and binging behaviors were associated with later weekend (not weekday) bedtimes, rise times, and less total sleep (r = .18 to .48, p < .01).

Conclusion: Sleep is inadequate and erratic for college students. Increased and more frequent alcohol use was associated with insufficient and delayed weekend sleep patterns. Future studies will evaluate the impact of poor sleep and alcohol abuse on daytime functioning.

1018
The Relationship Of Driving Simulator Performance To Multiple Sleep Latency Test Results
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Introduction: Sleep apnea patients demonstrate greater lane position variability during a driving simulator (DS) task (LPV; 1.3 to 2.6 ft) and increased crashes compared to normal subjects (LPV 0.7 to 1.0 ft; Rissel et al., 2000). We compared DS and Multiple Sleep Latency Test (MSLT) results in Sleep Disorders Center (SDC) patients suspected of daytime sleepiness.

Methods: After informed consent, 82 patients completed a standard 4-5 nap MSLT and an hour-long early afternoon DS task. In addition to correlating LPV with MSLT mean sleep latency, we placed participants into MSLT sleep latency groups: 1) Pathological sleepiness (n=28): <5 minutes; 2) moderately sleepy (n=33): 5-10 minutes; 3) normal (n=21): >10 minutes. LPV was analyzed with analysis of variance. We also compared MSLT scores in those who crashed to those who did not crash.

Results: Overall, the mean Epworth Sleepiness Scale score was 13.9 (SD = 4.7) with a MSLT mean of 7.5 minutes (SD=4.5). Greater LPV occurred with shorter MSLT scores (r = -0.29, p = .01). The pathologically sleepy group had greater LPV (mean = 1.7 feet, SD=0.7) than normal groups (mean = 1.2 feet, SD=0.3; F (2, 79) = 3.32, p=0.04). The moderately sleepy group (mean = 1.5, SD=0.5) did not significantly differ from other groups. Participants who crashed during the drive (n=22) had a mean sleep latency of 5.3 minutes (SD=3.3) while those who did not crash (n=60) had a mean sleep latency of 8.3 (SD=4.6) minutes, t (80) = 2.79, p=0.007.

Conclusion: Sleepy patients on the MSLT also perform more poorly on the DS task than those who are less sleepy thus adding to the validity to the DS task. However, the significant but modest correlation between the MSLT and DS tasks suggests that these tests may measure somewhat different parameters.

1019
The Neural Correlates Of Sleep-Dependent Perceptual Learning And Deterioration: A Role For Attention?
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Introduction: We have previously shown that repeated within-day testing on a perceptual task produces performance deterioration. But, an inter-test sleep episode (e.g. daytime nap) containing both slow wave and rapid eye movement sleep leads to performance improvement. Both phenomena demonstrate specificity to retinotopnic position. Here, we investigated the neural correlates of nap-dependent, perceptual learning and deterioration, and the particular role attention plays in these performance changes using functional magnetic resonance imaging (fMRI).

Methods: 11 subjects (ages 18-35) were scanned with fMRI during performance of a texture discrimination task twice in one day (10AM & 5PM). Prior to each fMRI session, subjects trained outside the scanner for one hour. Half the subjects took a 1.5-hour, polysomnographically-recorded nap in between test sessions (1-3PM). Behavioral performance was measured as the threshold inter-stimulus-interval (ISI) between the target and masking stimulus. fMRI analyses focused on comparing BOLD response changes between session 1 and session 2 between nappers and non-nappers. Region of interest analyses were conducted in retinotopically defined visual areas (V1, V2, V3, V4). Additionally, attentional effects were measured.

Results: Our behavioral results replicate previous findings of nap-dependent performance improvement compared to deteriorated performance in non-nappers. fMRI showed an increase in brain response across the visual areas during session 2 in nappers while non-nappers did not increase in session 2. This was especially evident during attentional conditions.

Conclusion: These results demonstrate the neural correlates of performance changes due to task training and daytime sleep. Increased BOLD responses during session 2 in nappers manifested as learning while responses in non-nappers were associated with deteriorated performance. The fact that these differences appear in the attentional conditions suggest that improvement in the ability to engage top down attentional mechanisms underlies performance improvement after a nap.

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The Differential Rapid Eye Movement Sleep Response To Cued And Contextual Fear Conditioning Is Suppressed By A Shared Response To Fearful Conditioned Stimuli

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Introduction: Rapid eye movement sleep (REMS) alterations are commonly observed in studies of the effects of stress and anxiety on sleep. REMS can be divided into two types: sequential (seqREMS), separated from adjacent REMS by less than 3 minutes of intervening wake or non-REMS, and single (sinREMS), separated from adjacent REMS by 3 or more minutes.

Methods: Rats were implanted for recording EEG and EMG. Following recovery, habituation, and baseline polysomnograms, separate groups underwent auditory cued fear conditioning (CFC), consisting of five footshocks either explicitly paired or unpaired with a tone, and contextual fear conditioning (CtxFC), consisting of five footshocks presented in the absence of explicit cues. For both CFC and CtxFC, subgroups were studied in either the presence or absence of fearful conditioned stimuli (CS).

Results: In the absence of CS, REMS recorded on the day following training for the CtxFC group was increased due to an increase in sinREMS (4.7±0.7 to 6.4±0.8 min/hr, p<0.01), while REMS was increased in the CFC group due to an increase in time spent in seqREMS (3.8±0.7 to 5.2±1.9 min/hr, p<0.05). Time spent in seqREMS for the CtxFC group was unchanged (4.2±0.8 to 4.8±0.6 min/hr, NS), and sinREMS time was not changed for the CFC group (4.9±0.7 to 3.8±0.8 min/hr, NS). In the presence of CS, sinREMS for both groups was significantly decreased (CtxFC: 4.7±0.7 to 2.2±0.4 min/hr, p<0.05; CFC: 4.9±0.4 to 3.4±0.5 min/hr, p<0.05). Both groups also displayed non-significant decreases in seqREMS (CtxFC: 2.7±0.7 to 1.2±0.4 min/hr, NS; CFC: 3.2±0.5 to 2.1±0.5 min/hr, NS).

Conclusion: We suggest that the different ways in which REMS was upregulated with these two modes of fear conditioning may relate to the different neural mechanisms believed to underlie perception of CFC and CtxFC. Furthermore, we suggest that the similar REMS responses in the presence of conditioned fearful stimuli represent a common fear response.

Sleep Disturbance, Depression, And Fatigue In Korean Family Caregivers Of Gastric Cancer Patients

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Introduction: Family members often take on the active caregiver role, placing them in an unsettling and distressed situation. Caregivers of patients with cancer experience sleep disturbances, depression and fatigue due to the time, labor, and stress involved. However, this area of sleep problems and the symptom experience for family caregivers of Korean gastric cancer patients has been little explored.

Methods: This cross-sectional study included 68 Korean family caregivers. Demographic Questionnaire, Pittsburgh Sleep Quality Index (PSQI), Lee Fatigue Scale, CES-Depression Scale, and three-day Sleep Diary were used.

Results: Mean age of family caregivers was 48.4 (SD 11.44), and 81% were female. Fifty-eight percent of family caregivers were homemakers and one third worked full or part-time. Responsibility of caring for the ill family member was 83.7% (no responsibility-100 full responsibility). Two-thirds of caregivers considered themselves financially breaking even or well off. Family caregivers had moderate level of fatigue (mean=4.89, SD 1.3), mild pain (mean=1.8, SD=3.1), depressed (mean=18.2, SD=8.6), and poor sleep quality (mean=5.9, SD=2.3). There were statistically significant moderate correlations between all three days (range r=0.37-0.53, p<0.01) in sleep hours, sleep quality, and AM and PM fatigue levels. There was no significant effect for time on any day. The average total sleep hours across the three nights were 6.8±1.5 hrs. Thirty-two (47.8%) family caregivers took longer than 15 minutes to fall asleep the first night, then 51% and 44% on the next two nights. The average sleep quality of caregivers was rated as fair on a 5-point scale and approximately 32% of caregivers had a nap each of 3 days.

Conclusion: This study provides support for the presence of sleep problems in family caregivers of cancer patients. The demands of selfless caregiving lead to sleep problems in conjunction with other unpleasant symptoms.

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The Clinical Efficacy Of Cognitive Behavior Therapy For Psychophysiological Insomnia Outpatients

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Introduction: It is well known that CBT (cognitive behavior therapy) is effective for PPI (psychophysiological insomnia) patients. But there are few reports about CBT for PPI in Japan even in the present. The aim of this study is to investigate the clinical efficacy of CBT for PPI outpatients.

Methods: The subjects were twelve PPI outpatients (5 males, 7 females). The mean age was 56 years. The mean duration of insomnia was 9.4 years. The actigraph recordings were taken over seven days during the baseline and the post-treatment phase. The patients also completed the sleep log, sleep questionnaire and Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS). We analyzed these data by using Wilcoxon rank test. In the first 2 hour session, combined CBT (checking baseline actigraph data, sleep hygiene education, stimulus control, restriction of time in bed) was administered for each patient. Patients received CBT over a 4 week period. After the first session, sleep log and sleep hygiene were observed as follow up.

Results: After CBT we found that there were significant improvements as follows 1) SOL (sleep latency), awakening during sleep, sleep efficiency on actigraph data, 2) duration of SOL on sleep log, 3) depth of sleep, physical and mental condition upon awakening on the sleep questionnaire, 4) consequences of insomnia, control and predictability of sleep and sleep-promoting on DBAS, and 5) reduction of consequences of insomnia and sleep-promoting practices in DBAS correlated with improvement of subjective SOL.

Conclusion: We investigated the clinical efficacy of CBT for twelve PPI outpatients. After the CBT we found significant improvement in objective and subjective measurements. CBT patients could recognize their objective sleep by checking actigraph data. The effectiveness of CBT is in the decrease of anxiety about own sleep.
1023
Daytime Sleepiness Associated With Cognitive And Functional Impairments In Alzheimer’s Disease (AD)
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Introduction: Poorer nocturnal sleep and increased daytime sleep have been correlated with severity of cognitive impairment in demented nursing home patients. In this study we evaluated self-reported daytime sleepiness (as reported by patient and/or caregiver) in non-institutionalized AD patients in relation to cognition and functional impairment in instrumental activities of daily living (IADLs). We also compared the timing of the major sleep period in such patients by comparison with reference values (Middlekoop, J Gerontol: Psych Sci 1996; 51A: M108-115.)

Methods: Patients were 137 AD patients (X age = 75.3, SD = 9.7; male/female = 59:78) diagnosed according to NINDS-ADRDA criteria. Mean (SD) MMSE and ESS were 19.3 (6.0) and 7.8 (5.4), respectively. Caregivers also completed the Lawton/Brody IADL scale (X = 15.5, SD = 11.4), which collects data relevant to self-care ability (e.g., use of phone, food preparation, housekeeping, etc).

Results: ESS correlated negatively with MMSE (r = -.289, p <.01), indicating greater sleepiness associated with poorer mental function, and positively with IADL’s (r = .327, p < .01), indicating greater sleepiness associated with greater impairment in everyday tasks. AD patients went to bed earlier than the control population (2217 vs. 2306 [p < .001] for males; 2153 vs. 2244 [p < .001] for females), but also had later wake-up times (0725 vs. 0652 [p < .01] for males; 0731 vs. 0632 [p < .01] for females)

Conclusion: Our data suggest that, just as in institutionalized patients, EDS in AD outpatients is associated with impaired cognition. Perhaps more surprising was that EDS has apparent real-world consequences in impaired functional capacities. The earlier bedtimes in AD may be construed as a phase advance of the sleep/wake cycle, however, the later wake-up times imply that the alerting function of the biologic clock may also be impaired.

1024
Comparison Of Actigraphic Sleep Measures In Adolescents With And Without A Parental History Of Alcohol Abuse/Dependence
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Introduction: Although associations between sleep disturbance and alcohol use/abuse in adults are well known, gaps in understanding factors (biological, genetic, environmental) that contribute to the onset of these problems exist. Studying young people at-risk for alcohol-related problems is a useful methodology to begin to address these gaps. The purpose of this study was to examine differences in actigraphic sleep measures between adolescents with (PH+) and without (PH-) a parental history of alcohol abuse/dependence.

Methods: Participants were 36 non-drinking students (17 male; 22 Caucasian) aged 15-16 years (M=15.1, SD=.42). PH+ (n=14) and PH- (n=22) groups did not differ on age, sex, race, SES, Morningness/Eveningness, or Tanner stage (range: 3-5). Participants wore mini-motionlogger actigraphs (Ambulatory Monitoring, Inc.) on non-dominant wrists for at least 8 days on a self-selected schedule (regular school sleep/wake schedule with a 2-hour restriction on weekend bedtimes and rise times). Nights were scored for sleep/wake using standard laboratory procedures and a validated algorithm (Action-W2 software). Actigraphic data were aggregated across nights for the following variables: Sleep Start Time, Sleep End Time, Sleep Period, and Sleep Minutes.

Results: The present analysis includes a total of 306 scored nights (6-14 nights per participant). Differences in actigraphic variables between PH+ groups were examined with t-tests. Sleep End Times were significantly later in PH+ than PH- adolescents [PH+: M=6:57, SD=.23, PH-: M=6:35, SD=.26; t(34)=2.54, p<.05, d=.90]. To explore the difference in Sleep End Time further, actigraphic data were aggregated separately for school and non-school nights. No significant PH group differences on school night actigraphic measures were found. On non-school nights, however, PH+ adolescents had significantly later Sleep End Times than did PH-adolescents [PH+: M=8:10, SD=.23, PH-: M=7:35, SD=.46; t(34)=3.03, p<.01, d=.95].

Conclusion: These results suggest that sleep patterns in PH+ adolescents, specifically rise time on ‘free’ nights, differ from those in PH- adolescents. These differences may be due to familial tendencies for abnormal sleep and alcohol abuse/dependence, differences in circadian timing, or to parental/familial lifestyle structure. Further study with additional participants may reveal other actigraphic sleep differences. Examination of similar measures using PSG to analyze sleep architecture and micro-architecture are underway.

AA13252
1025
Performance On A Dual Driving Simulation And Subtraction Task On Late Nights With And Without Alcohol
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Introduction: We examined effects of alcohol on late-night driving simulation/subtraction task performance, predicting worst performance at the latest session after alcohol.

Methods: Twenty-four adults (males=7) ages 21 to 25 years (M=22, SD=1.1) spent one week on an at-home stabilization schedule of 8.5 to 9 hours followed by 3 nights in-lab: one Adaptation night and 2 non-consecutive Placebo-Wake and Alcohol-Wake nights (separated by 5 to 7 nights on stabilized schedule). Task practice occurred on 3 occasions. Alcohol (vodka; .54 g/kg for men; .49 g/kg for women) was consumed over 30 minutes ending 1 hour before stabilized bedtime; the same quantity of placebo beverage was given identically on Placebo-Wake. Driving simulation tests occurred 30 minutes before and 60 and 240 minutes after alcohol/placebo ingestion (3 tests). Breath alcohol concentration (BAC) readings were taken before the 2nd and 3rd test sessions.

Results: Mean BACs for Alcohol-Wake before the 2nd and 3rd sessions were .041 (SD=.009) and .007 (SD=.008). Driving variables (lane variability, speed variability, off-roads, and wind reaction time [wind RT]) were analyzed separately for driving only and dual task components using repeated-measures ANOVAs within session (first, second, or third) and condition (placebo or alcohol). Dual-task subtraction variables (RT, percentage no-responses, percentage correct) were analyzed with similar repeated-measures ANOVAs. Lane variability, speed variability, and wind RT significantly deteriorated across task sessions and lane variability and wind RT were worse with alcohol when driving only. With the dual task, performance for all driving variables as well as percentage correct and percentage no-responses worsened significantly across test sessions. An interaction of session and condition for lane variability, speed variability, and off-roads on the dual task demonstrated worst performance with alcohol at session two.
Conclusion: Driving performance worsened with time awake and with alcohol. Performance for certain dual tasks was worst at peak BAC versus placebo, contrary to our prediction.

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1026
Sleep-Dependent Consolidation Of Category Learning
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Introduction: The ‘weather prediction task’ is a probabilistic category learning paradigm that has been validated for studying the neural substrates of incrementally learned cognitive skills mediated by the striatum. Subjects are required to predict a weather outcome (“sun” or “clouds”) based on a combination of cards presented in one trial, and receive immediate feedback. Visual discrimination and motor skill learning tasks depend on specific stages of sleep for optimal learning. Similar improvement patterns were observed over three days in a study of the weather prediction task comparing Parkinson’s patients and controls, suggesting a sleep-dependent component to learning this task.

Methods: To test this hypothesis, we trained subjects on the weather prediction task and then retested them after varying intervals. Training and retest involved 200 trials. A Wake group was initially trained at 9AM and retested at 9PM, and a Sleep group was trained at 9PM and retested at 9AM the next morning. For the third Control group, half of the subjects were trained at 9AM and half at 9PM, and all were tested just 20 minutes after completing the training session. These protocols allowed us to distinguish the effects of continued rehearsal (Control group) and the simple passage of time (Wake group) from possible sleep-dependent effects (Sleep group).

Results: Significant improvement occurred over the first two training sessions for all groups. This improvement did not differ for subjects retrained after intervals of 20 minutes or 12 hours of wake. However subjects showed significantly more improvement when the sessions were separated by 12 hours that included a night of sleep.

Conclusion: Thus while practice- and sleep-dependent processes seem to contribute to learning this complex procedural task, sleep appears to confer an additional learning benefit beyond what may be achieved by practice alone.

1027
Sleep, Stress And Mood In University Students: A 1-Month Questionnaire Study
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Introduction: It has been suggested that insomnia and poor sleep quality increase the risk for developing clinical depression. University students show both an increased risk for depression and substantial sleep disruption. The present study evaluated the relationship among sleep, stress and mood in undergraduate men and women over one academic term.

Methods: Twenty undergraduate students (13 women, 7 men), ages 18 to 22 (19.7 ± 1.3 yrs), completed weekly Profile of Mood States (POMS), Perceived Stress Scale (PSS) and daily pre- and post-sleep questionnaires. The Pittsburgh Sleep Quality Index (PSQI) was also completed at Week 2 and Week 4.

Results: Men slept 6.8 hrs at the beginning of study and 7.1 in the last week. Women increased from 7.1 to 7.4 average hours of sleep. Overall, women had shorter sleep latency than men, but both groups showed a significant decrease in sleep latency over the study period (p<.03). Women had slightly better sleep quality throughout. POMS scores were higher in women than in men and negative mood increased in women over the academic term. The opposite effect was found in men. Perceived stress showed the same effects. PSQI scores improved in men but worsened in women. Significant gender differences were obtained for stress, POMS and the gender by time interactions for PSQI and total sleep approached significance. Worse sleep quality was associated with more negative mood and higher perceived stress in women (r >.65, p<.05), during the first week of measurement, but the strength of these correlations decreased over the study. Sleep, mood and stress measures were not significantly correlated in men until final exams approached.

Conclusion: The relationship between subjective sleep, stress and mood changes significantly over an academic term in university students. However, it is strongly influenced by gender.

Discrepancy Between Self-Report And Objective Measurements Of Sleepiness: Which People Do Not Realize They’re Sleepy?
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Introduction: There are often discrepancies between subjects’ ratings of sleepiness and their performances on sleepiness-sensitive neuropsychological tasks during sleep deprivation. This study evaluated personality correlates of this discrepancy.

Methods: Preliminary analyses were conducted on the first 20 subjects (9m; 11f; aged 22-43y) of N=45 who participated in a 5 night sleep restriction (4h TIB) protocol. Following 2 baseline nights (10h TIB) they completed the Millon Index of Personality Styles (MIPS) and an IQ test-The North American Adult Reading Task. They also completed the Stanford Sleepiness Scale (SSS) and the Psychomotor Vigilance Task (PVT) every 2h each day. An average discrepancy score (ADS) was calculated by subtracting each subject’s Z-score PVT total lapse time from the Z-score SSS score using test bouts during the final sleep-restriction day.

Results: MIPS scores did not correlate with SSS or PVT scores. ADS correlated with a number of MIPS factors: “outgoing” (r=-.665, p=0.001), “dutiful-conforming” (r=-.562, p=0.005), “externally focused” (r=-.504, p=0.012), and “actively modifying” (r=-.438, p=0.027). A conditional stepwise multiple regression was conducted with ADS as the dependent variable and age, sex, IQ and the significant MIPS scores as predictors. The model was significant with only the “outgoing” factor as a contributor (p=0.002), accounting for 40% of the variance.

Conclusion: More outgoing (extraverted) subjects were less accurate in their ratings of sleepiness relative to their PVT performance lapses, following 5 nights of chronic sleep restriction. Since MIPS outgoing scores were uncorrelated with absolute SSS and PVT values, their relationship to the SSS-PVT discrepancy suggests that subjects who seek social stimulation are more likely to underappreciate their neuropsychological deficits from sleep loss.

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**1029**

**Effect Of Chronic Sleep Restriction On Pre-Frontal Cortex Functioning And Its Relationship To IQ And Personality**  
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**Introduction:** Acute total sleep deprivation has been reported to produce decrements in performance mediated by the pre-frontal cortex (PFC). The aim of this study was to investigate PFC tests of planning, verbal fluency and flexibility after chronic partial sleep restriction. The relationship of personality and IQ to these tests was also examined.

**Methods:** Preliminary analysis was conducted on the first 25 subjects (12m; 13f; aged 22-45y) out of N=45, who participated in a 5 night sleep restriction (4h TIB) protocol following 2 baseline nights (10h TIB). Subjects completed the Millon Index of Personality Styles (MIPS), an IQ task (North American American Reading Task; NAART) and half of a verbal fluency task (Controlled Oral Word Association Task; COWAT) at baseline. On the day after the fifth night of 4h TIB subjects completed the second part of the COWAT, Haylings Sentence Completion task (HSC) and the Tower of London test (TOL).

**Results:** Sleep restriction significantly reduced HSC (p=0.005) and TOL performance (p=0.003) when compared to normative values (Burgess and Shallice, 1997 and Cubertion and Zillmer, 2001, respectively). In addition, TOL initiation time scores were positively correlated with IQ (r=0.405, p=0.022) and TOL execution time scores were positively correlated with extraversion (r=0.435, p=0.017). The HSC task showed no relation to IQ or personality traits. COWAT scores showed no significant changes from baseline (p=0.846). However, there was a significant correlation between COWAT scores and IQ both at baseline and after sleep restriction (r=0.63, p=0.003).

**Conclusion:** Chronic sleep restriction at 4h per night adversely affected cognitive flexibility (HSC) and planning ability (TOL). However, sleep restriction did not affect all aspects of PFC functioning in the same manner. Moreover, both before and after sleep restriction, subjects with higher IQ had greater verbal functioning. After sleep restriction, subjects with higher IQ had better ability to plan than subjects with lower IQ.

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**1030**

**Time Of Day Effects In Waking Cognitive Function During Chronic Sleep Restriction**  
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**Introduction:** Chronic nocturnal sleep restriction has been shown to result in dose-dependent, cumulative cognitive performance deficits over days. Here we investigated time-of-day variations in performance deficits across days of sleep restriction.

**Methods:** During a 20-day laboratory experiment, 35 subjects were assigned to 4h, 6h, or 8h time in bed (TIB) per night over 14 consecutive days, with daily awakening scheduled at 07:30. Neurobehavioral testing occurred every 2 hours during wakefulness. The test battery included the psychomotor vigilance task, digit symbol substitution task, probed-recall memory test, Karolinska Sleepiness Scale, and Stanford Sleepiness Scale. Data were analyzed by mixed-effects ANOVA for condition (4h, 6h, or 8h TIB), time of day (9 test bouts between 07:30 and 23:00, with an additional bout at 01:00 for 4h and 6h TIB), day of sleep restriction (1 to 14), and the two-way and three-way interactions. Only results related to time of day are reported here.

**Results:** None of the outcome variables showed a significant interaction of day by time of day (F[125,4490]<1.17, P=0.096) or a three-way interaction (F[237,4490]<0.68, P=0.99). These terms were therefore removed from the ANOVA model. In the reduced model, there were significant effects of time of day (F[9,4490]>11.17, P<0.001) and condition by time of day (F[17,4490]>4.49, P<0.001) on all cognitive tests.

**Conclusion:** There was little interaction of diurnal variation with the accumulation of cognitive deficits across days of sleep restriction, as indicated by the non-significant interaction of day by time of day. Within days, waking cognitive function showed little variation, except for the first test bout each day. Performance was worst in the test bout immediately after awakening, particularly in the 4h TIB condition. This was due to pronounced sleep inertia.

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**1031**

**Which Aspects Of Work Patterns Effect Junior Doctors Performance, Safety, And Well-Being?**  
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**Introduction:** Restricted hours of work for junior doctors in the USA and European Union have been introduced with little scientific evidence regarding those aspects of working patterns that increase risks to patient safety or practitioner health.

**Methods:** A survey of full-time junior doctors in New Zealand was conducted in 2003-2004 (63% response rate, n=1366). Questions addressed demographics, work patterns (previous fortnight), sleep, and support at work. Multiple logistic regression analyses examined relationships between demographics, work and sleep-related factors, and the following outcomes: excessive sleepiness (Epworth Sleepiness Score>10); sleepiness at the wheel (previous 12 months); fatigue-related clinical error (previous 6 months); and problems in personal life.

**Results:** Night shifts (≥3 in either/both weeks; reference=≤1/week) was associated with increased risk of ESS>10 (OR=1.5, 95%CI=1.1-2.1), clinical error (OR=1.4, 95%CI=1.1-1.9), sleepiness at the wheel (OR=1.5, 95%CI=1.1-2.1), and problems in personal life (social life: OR=2.1, 95%CI=1.6-2.9; home life: OR=1.4, 95%CI=1.0-1.9; personal relationships: OR=1.4, 95%CI=1.0-1.8; other commitments: OR=1.8, 95%CI=1.3-2.4). Roster change in both weeks (reference=no change) was associated with increased risk of excessive sleepiness (OR=1.8, 95%CI=1.3-2.5), sleepiness at the wheel (OR=1.7, 95%CI=1.3-2.4), and problems in personal life (social life: OR=1.8, 95%CI=1.3-2.5; home life: OR=1.5, 95%CI=1.1-2.0; personal relationships: OR=1.4, 95%CI=1.0-1.9; other commitments: OR=1.4, 95%CI=1.0-1.9). Breaks <10hrs between shifts (reference=none) was associated with increased risk of error (OR=1.4, 95%CI=1.0-2.0), problems in social life (OR=1.5, 95%CI=1.0-2.2), and other commitments (OR=1.4, 95%CI=1.0-2.1). Working >70hrs in both weeks (reference=<120hrs total for both weeks) was associated with increased risk of excessive sleepiness (OR=1.5, 95%CI=1.0-2.3) and problems in personal life (social life OR=1.9, 95%CI=1.0-2.3).
95% CI = 1.3-3.0; home life OR = 2.8; 95% CI = 1.8-4.3; personal relationships OR = 1.6; 95% CI = 1.1-2.3; other commitments OR = 1.9; 95% CI = 1.3-2.8.

**Conclusion:** Total work hours were less consistently related to adverse outcomes than the frequency of night work, unstable rosters, or short breaks between shifts. Reforms of junior doctors working patterns should consider more than total work hours.

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**1032**

**Caffeine And Sleep Deprivation: Effects On Random Number Generation**

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**Introduction:** Sleep deprivation (SD) has a detrimental impact on frontal regions of the brain and is associated with deficits in performance of complex cognitive tasks that assess frontal executive function. Although caffeine helps to maintain simple types of performance during sleep deprivation, few studies have investigated its effects on complex cognitive functions. Random number generation (RNG) is thought to provide a sensitive index of executive function. The present study tested the hypothesis that SD would impair RNG and that caffeine would mitigate this impairment.

**Methods:** Healthy young men (n = 21) participated in two 40-hour SD periods one week apart. During each SD period, subjects received caffeine or placebo according to a randomized, double-blind crossover design, and they completed an oral RNG task at three hour intervals. The task required generation of 225 numbers (response alternatives: integers from 0-9) at fast and slow speeds. Dependent measures included deviations in the number of responses generated (number of permissible responses ~ 225), the number of rule breaks (responses that were not permissible), redundancy (deviation from ideal information generation), adjacency (a measure of counting tendency), and the null score quotient (stereotypy of adjacent response pairs). To permit comparison of results derived from number sequences of different lengths, the latter three variables were normalized with respect to values derived from computer-generated random sequences.

**Results:** Comparison of test sessions at analogous times of day revealed that SD was associated with significant drops in the number of permissible responses, a 3-fold increase in the percentage of rule violations, 59% greater response redundancy and a 20% increase in stereotypy of adjacent response pairs. There were no consistent effects of sleep deprivation on counting tendency. Caffeine ameliorated the decrease in the number of responses, but did not mitigate other deficits in RNG that arose during SD.

**Conclusion:** These findings concur with prior reports of diminished vigilance and increased perseveration during extended wakefulness. They support the conclusion that caffeine attenuates decrements in simple aspects of cognitive performance during SD, whereas caffeine may not prevent detrimental effects of SD on some complex cognitive functions.

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evaluated the relationship between driving accidents and a variety of demographic and functional variables, including the ESS score.

Methods: All patients who attend our Sleep Clinic complete a standard questionnaire which includes sleep habits and complaints, the ESS, questions regarding accidents/near-accidents related to sleepiness and medical, surgical, medication and social history. We randomly chose 150 patients who attended the Sleep Clinic in 2004 as subjects for this study. We assessed associations using logistic and ordinal regression.

Results: Fifty-five subjects (37%) reported at least one event (accident or near-accident), yielding a mean of 0.52 events per person (range 0-4). No association between the number of events and age, gender, body mass index, shift worker status, history of snoring or AHI was found. The mean (SD) ESS score of subjects reporting an event were 16 (4) vs 8 (4), for those denying events (P< 0.001). An increase of one point in ESS was associated with an increase of 1.6 (95% CI 1.4, 1.9) in the odds of having an event (P<0.001). An ESS > 12 had a sensitivity and specificity for the reported occurrence of an event of 85% and 86%, respectively.

Conclusion: The ESS score is strongly correlated with the incidence of driving accidents and near-accidents in a sleep center population. Prospective assessment is needed to confirm these results and decrease potential recall bias. Multiple regression analysis found excessive daytime sleepiness and ESS score as the most powerful predictors of the events studied.

1035
Good Supervision Moderates The Impact Of Work Patterns On Junior Doctors
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Introduction: Extended and irregular work hours among junior doctors have been linked to poorer patient care, and negative effects on the safety, well-being, and ability to learn of the doctors themselves. Internationally, awareness of these issues has resulted in restrictions on work hours, aimed at improving patient safety and practitioner health. However, such restrictions have raised concerns about both the quality and duration of trainee education.

Methods: An anonymous national survey of full-time junior doctors working in New Zealand was conducted in 2003-2004 (63% response rate, n=1366). Questions addressed demographics, work patterns (previous fortnight), sleep, and support at work. Aspects of work were classified according to the Australian Medical Association’s code of practice for hospital doctors. Participants were also asked how often they received adequate supervision at work (choices were: never, rarely, sometimes, often, always). Multiple logistic regression analyses examined relationships between demographics, work or sleep-related factors and the following outcomes: excessive sleepiness (Epworth Sleepiness Score >10); feeling close to falling asleep at the wheel (previous 12 months); recall of fatigue-related clinical error (previous 6 months); and problems in personal life.

Results: Most participants (72%) reported receiving adequate supervision often or always. Adequate supervision often/always (reference=never/rarely/sometimes) was found to be independently associated with a decreased risk of excessive sleepiness (OR=0.7, 95%CI=0.5-0.9), fatigue-related clinical error (OR=0.7, 95%CI=0.5-0.9), sleepiness at the wheel (OR=0.5, 95%CI=0.4-0.7) and problems in personal life (home life: OR=0.8, 95%CI=0.6-1.0; personal relationships: OR=0.6, 95%CI=0.4-0.8; other commitments: OR=0.8, 95%CI=0.6-1.0).

Conclusion: Adequate supervision at work may moderate the effects of work patterns on junior doctors’ perceived sleepiness, fatigue-related error, and life outside of work. This link is hitherto unreported, and highlights the complexity of the relationships between work demands and their effects on individuals. More detailed research is recommended into different aspects of supervision.

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1036
Efficiency Of Temporal Selective Attention Is Modulated By Circadian Phase And Duration Of Wakefulness
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Introduction: Selective attention, the ability to restrict processing to relevant information, is a critical aspect of performance. The influence of the circadian system and that of sleepiness on selective attention are poorly understood. We examined the effect of circadian phase and time awake on temporal selective attention.

Methods: Five healthy subjects participated in a 7 day forced desynchrony (FD) protocol. The sleep-wake cycle was adjusted from 24 h to 28 h (18 h 40 min wakefulness; 9 h 20 min sleep opportunity). Core body temperature was used as a marker of endogenous circadian phase (temperature minimum occurs during the circadian night and was assigned 0 degrees). A selective attention task was administered every 4 hours. We presented an 80 ms/item alphanumeric stream at fixation. Target items were digits 3 and 5, non-targets were letters. Subjects were asked to report the presence or absence of one or both digits. In the experimental condition, the independent variable was the lag between the first (T1) and second (T2) targets. Dependent variables were T1 accuracy and T2 accuracy (given correct T1 report). In the control condition, only T1 was presented. The signature of temporal selective attention is an impairment in reporting T2 at lags of < 500 ms; at longer lags, accuracy returns to control levels. We conceive of temporal selection as an attentional filter centered on T1. A narrow, efficient filter will allow only T1 access, while a broader, inefficient filter will include more items around T1, leading to a reduction in the T2 impairment. We hypothesize that adverse circadian phase and time awake will lead to a broader attentional filter, with more items perceived after T1, leading to a reduction in T2 impairment.

Results: Results showed that T2 impairment was minimal near 0 degrees (night) and maximal around 180 degrees (day) (0.08 ± 0.05 vs. 0.21 ± .03, p = .05). Time awake modulated the phase effect; the decrease in T2 impairment with time awake was greater at a phase of 180 degrees than at 120 degrees (F (1, 4) = 7.4, p < .05).

Conclusion: We conclude that adverse circadian phase and time awake impair the efficiency of temporal selection. Such considerations are important in our 24 hour society, where shift work and jet lag result in sleepy individuals performing at unusual phases of the circadian system.

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1037
Nocturnal Reverberations Of Adversity: The Effect Of Social Class, Ethnicity, And Stress On Nocturnal Blood Pressure (BP) And Sleep Architecture
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Introduction: Psychosocial adversity profoundly affects health, but few studies have examined how adversity affects sleep. This study examined the effect of adversity on nocturnal BP and sleep architecture.

Methods: 69 African-Americans (AA) and 84 Euro-Americans (EA) were studied. All were either healthy normotensives or else hypertensives tapered off antihypertensive medications before study enrollment. Individuals with current axis I psychiatric disorder, those taking psychotropic medications or medications known to affect sleep were excluded. Participants completed psychosocial inventories, 24 hours of outpatient ambulatory BP recording and were admitted for overnight polysomnography.

Results: Individuals who reported more discrimination also reported more physical fatigue (p<0.025), depressive symptoms (p<0.05), and less deep sleep (p<0.01). AAs did not decrease (or “dip”) their nocturnal BP as much as EAs; lower social class subjects manifested less nocturnal dipping, even after controlling for ethnicity, BMI, age, and RDI (p<0.005). High hostility and anger were also associated with less nocturnal BP dipping (p<0.005). AAs had half as much deep sleep as EAs (p<0.001), had lower sleep efficiency (p<0.02) and more Wake Time after Sleep Onset (WASO) (p<0.05). People of lower social class backgrounds had lower oxygen saturations during sleep (p<0.025), lower sleep efficiency (p<0.01), more arousals during sleep (p<0.05), shorter total sleep time (p<0.05), and more WASO (p<0.002). Numerous measures of distress were related to worsened sleep and more spontaneous arousals during sleep. This finding persisted whether distress was operationalized via Brief Symptom Inventory scores, Cook-Medley Stress scores, or POMS scores.

Conclusion: Psychoanalysts used to speak of “day remnants,” events of the day, which “leached” into the dream content at night. This study suggests that events of the day profoundly affect nocturnal BP regulation and sleep architecture. Consideration of the effects of deprivation and adversity are important in epidemiological studies of sleep.

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1038
Impact Of Fatigue Related Scheduling Factors On Sleepiness In Aviators
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Introduction: Pilot fatigue associated with circadian rhythm disruptions (light/dark cycle) and disturbances of sleep/wake cycle is of concern in aviation operations. Crew members are often required to work irregular schedules, regardless of their geographical location. As a result, flight crew can experience sleep loss and alertness decrements. The present study investigated potential fatigue factors experienced by domestic and international pilots, as driven by operational demands.

Methods: A 44-item survey that included questions focusing on duty information, layover activity, and scheduling factors was completed by 448 pilots (n = 120 US-based; n = 325 non-US-based).

Results: Ninety-five percent of the pilots were male, with an average age of 43 (SD = 8.56). Fifty-one percent of the pilots reported their current position as captain; 45% as first officer; and 4% as engineers or second officer. A multifrequency analysis indicated that the duration of duty hours and duration of overnight resting, for both US and non-US-based pilots affected alertness levels (as reported by pilots). One-way MANOVA revealed a significant difference between the two groups on five factors related to fatigue and duty time, F(5,433) = 2.27, Wilks Lambda = .974, p < .05. A main effect was seen for the amount of overnight rest time (F(1,437) = 10.49, p<.001) with the US-based pilots being more affected than the non-US-based pilots.

Conclusion: Preliminary results suggest that US-based pilots report being sleepier than non-US-based pilots, which may be due to less time off between scheduled trips, not allowing for sufficient recovery sleep. Additional analyses will investigate these differences to determine what scheduling factors and operational demands are affecting overnight recovery sleep.

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1039
Declarative And Non-Declarative Memory: Effects Of Slow Wave Sleep Following A Daytime Nap
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Introduction: Recent studies examining the relationship between sleep and memory demonstrate enhancement of declarative and procedural memory storage following early SWS-dominated, and late REM-dominated sleep, respectively. Two potential problems in this research are that the effect of SWS cannot be assessed independently from REM sleep, and differences between normal sleep and subjects deprived of sleep during the retention interval may reflect the influence of sleep deprivation on memory. The present study addresses these issues by examining the effect of sleep on memory following a short daytime nap rich in SWS.

Methods: Twenty-three undergraduates (10 males, 13 females), ages 18-48 (mean=25) participated in the study. At 11am after sleep monitoring electrodes were applied, Ss were trained on two memory tasks: paired associates (declarative), and reverse mirror tracing (procedural). At noon Ss in the sleep group napped for one hour (without REM sleep); Ss in the wake group sat quietly for 10 minutes to mimic the period of sleep onset for the sleep group. After the nap or 10-minute wake period, all Ss remained awake until 6 pm for restesting on the two tasks.

Results: An independent samples t-test for the paired associates revealed a near significant difference between subjects in the sleep group and wake subjects (mean improvement over baseline: 8.64 and 6.50, respectively), t(21)=1.85, p=.079. The difference between the sleep and wake group on the mirror tracing task was not significant, p=.36.

Conclusion: Given the shortness of the sleep period and small sample size, these findings provide further evidence that SWS enhances declarative memory formation, but that it has little impact on performance of a procedural task. A larger sample size will be necessary to assess the contribution of specific stages of sleep (ie SWS v. stage 2) to memory formation.

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1040
Positive Sleep State Misperception And Excessive Daytime Sleepiness
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Introduction: The aim of the study was to introduce the concept of positive sleep state misperception (PSSM), defined as subjective feeling of sleeping better than objectively measured, and to assess if the PSSM is associated with excessive daytime sleepiness.

Methods: A retrospective study involved a chart review of 300 patients who had an overnight polysomnography with MSLT, and who had completed a set of morning questionnaires including the Stanford Sleepiness Scale (SSS) and a question asking how much sleep they believe they had the night prior. Three subgroups covered the range of sleep state misperception: a first group of patients who had negative sleep state misperception (NSSM, n=33), underestimating their sleep duration with an error of >20%; a control group who estimated correctly their sleep duration (+/-10%, n=40); and a third group of patients with positive sleep state misperception (n=31), overestimating their sleep duration for more than 20%.

Results: The patients with PSSM were objectively sleepier, as judged by the MSLT, than patients from the other two subgroups, receiving less sleep and achieving poorer sleep efficiency. At the same time, they also reported the same level of sleepiness as patients from the other two groups on the SSS, indicating their inability to accurately estimate not only their overnight sleep, but also their level of acute sleepiness. When the cutoff value for sleep state misperception was raised from +/- 20% to +/- 2 hours, the difference in level of daytime sleepiness between the NSSM (MSLT of 12.08 minutes) and normal (MSLT of 12.06 minutes) groups on one side, and the PSSM group on other (MSLT of 8.38 minutes) was statistically significant (p<0.05).

Conclusion: Some patients may overestimate the adequacy of their sleep and at the same time underestimate their subsequent daytime sleepiness.

1041
Subjective Sleep Measures Predict Sustained Attention But Not Performance On Other Cognitive Tasks
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Introduction: Significantly restricting or extending sleep (e.g., 4-5hrs or 10-12hrs TIB) can influence cognitive performance. It is unclear if variations within a normal TIB range can influence performance. Here we examined whether subjective sleep parameters predicted performance on several cognitive tasks.

Methods: Fifty-five normal control subjects (30M, age=26.6±5.8, education=15.6±1.7) completed sleep diaries for 7 days prior to a night of sleep in the lab. Partial correlation analysis, controlling for education, was used to assess the relationship between averaged diary variables (TIB, TST, SL, SE, WASO and a 7-point Likert scale asking about how refreshed subjects felt upon awakening) and cognitive performance on three tasks: the PVT, arithmetic working memory, and verbal learning. Tasks were performed 12 hours after awakening.

Results: There were no significant relationships between subjective sleep measures and arithmetic or verbal learning performance. Subjective reports of how refreshed a person felt predicted some PVT performance variables. Specifically, how refreshed a person felt was associated with faster mean reaction time (RT), faster slowed 10% RT, and lower standard deviation of RT (p<0.02, p<0.003, and p<0.002, respectively). The number of awakenings during the night was also negatively correlated with the same PVT variables, plus lapses. No other subjective sleep parameters predicted PVT performance.

Conclusion: Subjective sleep measures can predict sustained attention. Overall, the more refreshed a person felt upon awakening, the faster the RTs and the more ability to consistently sustain attention. It is unclear why a greater number of reported awakenings would also predict better PVT performance. Interestingly, none of the subjective sleep measures predicted performance on more complex cognitive tasks. This suggests that while variations within a relatively normal range of sleep times can influence attention, the effect is not strong enough to influence other cognitive processes that do not rely exclusively on sustained attention.

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1042
Effects On Sleep And Fatigue Of Long Work Hours
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Introduction: Previous studies of 12h workdays and their effects on stress, sleep and health show inconclusive results. This may be partly due to methodological problems such as the use of between group designs, or before-after reorganizations. In addition, stress is usually a confounder. The present study examined the effects of working 8 or 12 hour shifts during a 5 day workweek using a within subject design and without any external stress.

Methods: In an experimental field study16 white-collar workers (10 women and 6 men, mean age 44.7±15 years) undertook one workweek with normal work hours (8h) and one week of 12h shifts (4 extra hours of the regular work tasks). Subjects wore actigraphs, rated sleepiness (Karolinska Sleepiness Scale, 1-very alert, 9-very sleepy) and stress (1=no stress, 9=extreme stress) 8 times a day and also workload (1-5 very low) and how exhausted they felt (1-5 very much). Eight samples of saliva for cortisol analysis were collected on Mondays and Thursdays.

Results: The week with 12h workdays was associated with higher levels of exhaustion (8h=4.8 std=0.1, 12h=4.6 std=0.1; p<0.01). Sleepiness showed a significant interaction (p<0.05) between conditions, with higher levels at the end of the workweek in the 12h condition. Sleep efficiency was lower (8h=92.3 std=0.8%, 12h=91.4 std=1.1%; p=0.05) and there was a trend towards shorter sleep (8h=6h40min std=6min, 12h=6h29min std=7min; p=0.09) during the 12h workweek. There were no significant differences in ratings of stress or workload. Cortisol showed a circadian variation but did not differ between conditions.

Conclusion: A week with 12h workdays was associated with greater exhaustion and lowered sleep quality. Despite low work/family conflict among the current participants, a week of 12h workdays resulted in negative effects on sleep and sleepiness. Groups with greater commitments outside work may possibly be more negatively effected by longer work hours.

1043
Effect Of Partial Sleep Deprivation And Recovery Sleep Dose On The Spaceflight Cognitive Assessment Tool (WinSCAT)
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Introduction: WinSCAT (Spaceflight Cognitive Assessment Tool for Windows) was developed to detect neurocognitive insult in astronauts. It is currently used on the International Space Station. The battery consists of four tasks: code substitution, running memory, match to sample, and a
Introduction: Growing evidence supports a relation between consolidation-based enhancement of motor learning tasks and stage 2 sleep or sleep spindles. Studies, however, did not consider the possibility that these sleep parameters may simply be related to motor activity associated with the task and not to the learning process per se. We investigated spectral power in sigma frequencies in stage 2 sleep, by comparing sleep following training on a motor sequence task for which significant overnight gains were anticipated and sleep after training on a control task where no such consolidation was expected.

Methods: After an adaptation/screening night in our laboratory, eight healthy participants (20-30 years old, right-handed) were submitted to two polysomnographic sleep recordings, separated by one week. Before each recording night, subjects were trained in the evening on either a specific motor sequence (SEQ), or on a control task consisting of pressing, as quickly and accurately as possible, the response key according to the displayed number (1 to 4) appearing in a random order (CTRL). Twelve hours later, subjects were retested on the task in the morning. The two tasks were counterbalanced across the two nights. For five of these subjects, spectral analysis was performed on 4-sec artefact-free sections in sigma frequency bands (12-16 Hz). Spectral power was averaged in stage 2 sleep for the first 4 non-REM periods.

Results: Significant improvements in the number of sequences (16%, p<0.01) and errors made (61%, p=0.03) were observed at retest in the morning for the SEQ task, but not for the CTRL task. Interactions Cycle X Task were found at sites C3 (p=0.02), C4 (p=0.04), CZ (p=0.001), F3 (p=0.03), FZ (p=0.01) and PZ (p=0.03). Post-hoc paired t-tests revealed higher sigma spectral power (12-16 Hz) within cycles 1 and 3 of stage 2 sleep in post-training nights associated to the SEQ compared to the CTRL tasks. No difference was observed in polysomnographic sleep parameters between the SEQ and CTRL nights including sleep efficiency, total sleep, and amount of stages.

Conclusion: These preliminary results demonstrate that sigma activity in post-training sleep is not simply related to the motor activity generated by the task. More interestingly, they suggest that consolidation-based enhancement effects are associated with enhanced sigma power during the night, especially on derivations situated near motor cortical areas known to be implicated in this task.

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1045
Neurocognitive Function Related With Sleep Factors In Questionable Dementia Patients And Normal Elderly Subjects
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Introduction: It has been known that nocturnal sleep disturbance or daytime napping could predict the mortality and nursing home placement in the elderly. This can be explained by clinical pictures related with dementia. However, cognitive dysfunction related with daytime sleepiness or sleep disturbance in early stage of dementia has not been studied yet. We aimed to examine this in non-demented elderly subjects including questionable dementia (QD).patients

Methods: Epworth Sleepiness Scale (ESS) and sleep questionnaire were administered to randomly selected 699 elderly subjects (X Age: 70.8, SD=7.4) in an urban community of Korea. Using CERAD-K (Lee, J Gerontol: Psych Sci 2002; 57B: P47-53), 115 normal control subjects (X Age: 67.8, SD=5.2) and 36 QD patients (X Age: 70.6, SD=6.1) with the CDR score 0.5 were defined. The subjects with the history of cerebrovascular-disease were excluded. CERAD neuropsychological battery and Stroop test were done for these 151 elderly subjects (X Age: 68.4, SD=5.5).

Results: In non-demented elderly subjects including normal controls and QD patients, the ESS scores was negatively correlated with the Color-Word score and Interference score of Stroop test (r=-0.171 and -0.202 respectively, p<0.05), and the sleep time was negatively correlated with the score of Constructional Praxis test (r=-0.166). The subjects with daytime napping showed lower scores of Word Recall test and Stroop test (Color-Word score and Interference score) than those of subjects without napping (p<0.05). The presence of insomnia made no difference in the scores of any neuropsychological tests.

Conclusion: In non-demented elderly, daytime sleepiness and napping was associated with decreased executive function and/or decreased verbal memory function. And increased amount of sleep was associated with decreased visuospatial function. Our data suggest that daytime sleepiness or napping could be a significant correlate of lower executive function in non-demented elderly including normal controls and QD patients.

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1046

Differences In Time-And Sleep-Dependent Learning And Memory Consolidation Of Motor Sequence And Visuo-Motor Adaptation Skills

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Introduction: Recent investigations have shown that consolidation-based enhancement of a motor sequence task occurs exclusively after sleep. Nevertheless, it is still unclear if sleep is necessary to induce consolidation in other motor learning tasks. We suggest that time alone may be sufficient to induce consolidation of another type of motor skill known to elicit different neural correlates, i.e., visuo-motor adaptation. We thus compared the effects of sleep and simple passage of time on consolidation of both motor sequence (SEQ) and visuo-motor adaptation (VMA) learning.

Methods: Forty young right-handed healthy participants (25 women) aged between 20 and 30 years old were trained on either the SEQ task (n=20), which required to repeat a sequence of finger movements as quickly and accurately as possible using the left, non-dominant hand, or the VMA (n=20) task, which necessitated to reach a target with a joystick following an elliptical trajectory, but where the relation between movements of the joystick and cursor had been inverted. Nine subjects of the SEQ group and 7 of the VMA group learned their respective task in the evening and were retested 12 hours later following a night of sleep (NIGHT group), while the others subjects were trained in the morning and retested 12 hours later, without intervening sleep (DAY group).

Results: Repeated measures ANOVA did not reveal any difference in the learning curve of the SEQ (p=0.43) or VMA (p=0.96) tasks between subjects trained in the morning and in the evening. Consolidation was measured by comparing average performance on the three last trials of the training session with the three trials of the retest session. In the SEQ task, as predicted, significant improvements were observed in the number of sequences (16%, p<0.01) and in the number of errors made relative to the number of correct sequences in 30-sec trial (61%, p=0.03) for the NIGHT group only. In the VMA task, however, both DAY and NIGHT groups showed similar significant delayed gains at retest as measured using speed (respectively 3.1%-2.4%, p=0.03), precision of the trajectory (2.6%-3.3%, p=0.02) and speed and precision (2.7%-2.5%, p=0.001) as indexes.

Conclusion: Our findings suggest that sleep effects on motor memory consolidation are task-dependent. Processivity changes underlying consolidation of a visuo-motor adaptation task are triggered by simple passage of time, while those involved in motor sequence learning depends on sleep.

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1047

Effects Of Acgme Duty Hour Regulations On Pediatric Residents’ Self-Reported Mood, Attention And Fatigue

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Introduction: Medical residents’ schedules consist of long duty hours on-call which often result in insufficient sleep. These schedules have been controversial as they can affect patient care, quality of life, and the efficiency of learning. The Accreditation Council for Graduate Medical Education (ACGME) created duty hour limitations, which went into effect July 2003, permitting residents to work no more than 80 hours a week averaged over a four-week period, and no more than 30 consecutive hours. This study investigated residents’ subjective reports of mood, attention, and tiredness before and after the new ACGME duty hour limitations went into effect.

Methods: Subjects were 17 medical residents from a children’s hospital in a large US city (14 females and 3 males, age 26-34 years). The subjects completed questionnaires for up to 40 days on which they logged daily sleep and work hours, and recorded subjective ratings of mood and attention. They marked their responses on four visual analog scales, with the anchors sad-happy, tired-rested, calm-tense, and inattentive-focused.

Results: Residents’ mean total sleep time was 7.03 in 2003, and 7.09 in 2004. In 2003, they slept for an average of 7.55 hours when working but not on-call, and 4.32 hours when they were on-call, and in 2004, 7.51 hours, and 5.04 hours, respectively. Subjects’ mean work hours per day were 11.80 hours in 2003, and 11.45 hours in 2004. In 2003, they worked for an average of 9.14 hours when not on-call, and 20.49 hours when on-call, and in 2004, 9.10 hours, and 17.73 hours, respectively. Being on-call had a significant negative effect on all mood variables (p<0.001) including calm/tense, sad/happy, tired/rested, and inattentive/focused. There was a trend towards improvements in sad/happy (p=.08), tired/rested (p=.06), and inattentive/focused (p=.09) for 2004 as compared to 2003.

Conclusion: Residents tended to work for consistently fewer hours on all workdays, and significantly less on on-call workdays in 2004, after the ACGME duty hour regulations went into effect. As a result they attained greater amounts of sleep on most nights in 2004, specifically for nights on-call. Residents’ self-reported happiness, restedness, and attention appeared to improve in 2004, suggesting that the ACGME change in work hour regulations may have had a positive effect on the residents’ quality of life.

1048

Gender Differences In Sigma EEG Spectral Amplitude During Stage 2 Sleep

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Introduction: Sleep spindle density during non-REM sleep is reported to be higher in women compared to men, particularly at the frontotopolar level (Huupponen et al., 2002). Studies of gender differences for Sigma activity (11-15 Hz) have mainly been restricted to central electrodes and total nonREM sleep, yielding inconsistent results. We investigated whether Sigma EEG activity during Stage 2 was sensitive to a gender effect using a full electrode montage.

Methods: Thirty-three right-handed healthy participants (18 women, age: 21.9 ± 2.7 years; 15 men, age: 22.8 ± 3.6 years) were recorded for two full nights of sleep. Thirty-three right-handed healthy participants (18 women, age: 21.9 ± 2.7 years; 15 men, age: 22.8 ± 3.6 years) were recorded for two full nights of sleep. Thirty-three right-handed healthy participants (18 women, age: 21.9 ± 2.7 years; 15 men, age: 22.8 ± 3.6 years) were recorded for two full nights of sleep.

Results: Women showed a greater Sigma activity compared to men. This was significant (p < .05) almost exclusively in the frontal areas (Fp1, Fp2, F8) and during the third and fourth cycles of the night.
Conclusion: These results are in the same direction as those reported for Stage 2 sleep spindle density and cover the same recording area. We find that this effect is more prominent during the later cycles of the night, together with increased proportions of Stage 2 sleep. We are now investigating whether these observations are compatible with the slow (frontal) vs. fast (centroparietal) Sigma activity dichotomy recently described.

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1049
Sleep Habits At The United States Air Force Academy
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Introduction: Numerous studies have identified traditional college age students as particularly susceptible to the effects of chronic sleep restriction. It is well established that academic performance is negatively impacted by decreased sleep and earlier wake times. However, there have been no comprehensive assessments of sleep habits at any of the college level military institutions. At the United States Air Force Academy, cadet life is vigorous with emphases on excellling in academics, physical fitness, and military positions and duties. As a result, cadets are often stretched for time to keep up with extensive responsibilities. This study was conducted to evaluate the sleep habits of cadets at the U.S. Air Force Academy and how sleep impacts academic and military performance as well as a standardized physical fitness assessment.

Methods: Three hundred cadets between ages 18-23 in all four classes were utilized. Participants were enrolled in Introduction to Psychology and Introduction to Leadership courses at the U.S. Air Force Academy during the 2004-2005 academic year. These participants were administered the Brown University Collegiate Sleep Habits Survey, a comprehensive 58 item questionnaire. We examined sleep across cadet performance in academic, military, and physical fitness as rated by the Academy.

Results: Overall, cadets sleep just over 6 hours during the week and just under 9 hours on weekends. Freshmen cadets received the least amount of sleep during the week and have the lowest GPA compared to upperclassmen (p < .05). Freshmen also significantly oversleep on weekends compared to upperclassmen (p < .01). Additionally, we found a significant difference on amount of sleep obtained and performance across all grades (p < .05).

Conclusion: These data demonstrate the effects of sleep restriction on military students at a highly selective military college. Comparisons with civilian cohorts are forthcoming.

1050
Transitioning From A Mars Day To An Earth Day: Effects On Psychomotor Vigilance Performance
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Introduction: Mars Exploration Rovers (MER) Surface Operations personnel were required to complete mission critical tasks on work schedules coinciding with a Mars sol (day) of 24h and 39m for a minimum of 3 months, while being exposed to 24h Earth-based exogenous cues. Once operations extended beyond 3 months, personnel were required to revert back to an Earth-day schedule. Performance data were collected during the transitionary periods to document associated performance changes.

Methods: Ten MER Surface Operations personnel (age 27-54y) performed a 10-min Psychomotor Vigilance Task (PVT) before major sleep periods preceding and following the schedule transition. The participants each completed 7 to 31 PVT trials during the course of 1 month.

Results: There was wide variability in PVT performance changes among participants, with 4 participants showing degradations over the protocol period reaching levels of >4 lapses (RT>500ms) per trial. In two of these participants, the changes in performance over time were progressive (t(21)=4.7, p<.01; t(9)=3.4, <p<.01). A mixed effects ANOVA suggested that age and recency of work did not contribute significantly to performance impairment.

Conclusion: These preliminary results indicated wide variability in performance changes across participants transitioning from a Mars sol to an Earth day. Home time zone and number of consecutive work days are being investigated as potentially relevant factors in this impairment. Results of this study will provide a more complete understanding of how psychomotor vigilance performance is affected by a 39-min daily shift while being exposed to an Earth-based environment, and while transitioning back to a 24h Earth-day schedule.

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1051
Parental History Of Alcohol Abuse/Dependence And Sleep Stages In 9- And 10-Year-Old Boys
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Introduction: A positive parental history of alcoholism is an important risk factor for development of the disorder. Associations between sleep (disrupted sleep) and alcohol use and abuse exist in adults but have not been examined in children. We present here a preliminary assessment of parental history of alcohol abuse/dependence and sleep of 9- and 10-year-old boys.

Methods: Fourteen healthy Tanner stage 1 (n=12) and Tanner stage 2 boys (mean age=9.2, SD = 6y) were classified with a positive (n=5) or negative (n=9) parental history of alcohol abuse/dependence according to DSM-IV criteria applied to structured interviews (CDIS -IV). All participants slept on a fixed 10- to 10.25-h schedule for at least 8 nights at home, confirmed by actigraphy, phone logs, and diary. Sleep was recorded for two nights within a 3-day period (adaptation and baseline) on fixed sleep schedules. Sleep stages on the baseline night were visually scored in 30-second epochs using Rechtschaffen/Kales (1968) criteria.

Results: No significant differences were found between parental history positive and negative groups for age, total sleep time, wake time after sleep onset, NREM sleep, REM sleep, total wake time, movement time, sleep onset latency, or REM latency. The mean NREM-REM sleep cycle lengths were longer (t=2.3; p=.04) on average in the parental history positive group (mean=121.6 min, SD=7.9) compared to the parental history negative group (mean=103.3 min, SD=4.1).

Conclusion: These preliminary findings point to a modest difference of sleep cycle length in boys with a positive parental history of alcohol abuse/dependence compared to boys with a negative parental history. Additional participants--including girls and older adolescents--are enrolled, and we also plan to examine sleep microarchitecture with all-night EEG frequency spectra to determine whether an influence of parental alcohol history emerges.

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**1052**

**Actigraphy Measures Vs. Cognitive Performance In Normal Sleepers**

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**Introduction:** Previous studies have shown that either a restricted or extended amount of sleep can influence cognitive performance. However, it is unclear whether variability within a "normal sleepers" population can also influence performance. Here we examined whether actigraphy measures of prior sleep in a sample of “normal sleepers” predicted cognitive performance.

**Methods:** A total of 17 (11F, 6M) normal control subjects with a mean age of 24.4±4.2 years and a mean education of 15.8±1.7 years participated in this study. Subjects wore actigraph watches continuously for 4-13 days (10.2±3.0 days) and nights while maintaining their normal sleep and wake times. After the last night of sleep, we administered the Psychomotor Vigilance Task (PVT), an arithmetic working memory task (MATH), and a verbal learning task (VL) at both 2 and 12 hours post awakening. Correlation analyses were used to assess the relationship between actigraphy measures (TIB, TST, SE, SL, and WASO) and performance variables at each time point.

**Results:** Subjects obtained a mean of 402.7±40.4 min TST (range 331.0min - 482.5min) and had a mean SE of 87.7±7.5% (range 75.9% - 99.0%). No significant relationship was found between any of the actigraphy measures and performance variables at either testing session.

**Conclusion:** Overall, actigraphy measures from individuals sleeping what is typically considered a "normal" amount could not predict performance on the PVT, MATH, or VL. Results suggest that these variations within a normal range of sleep, as measured with actigraphy, were not extreme enough to influence cognitive performance. Given that there was still considerable variation among individuals' cognitive performance scores, however, it is likely that factors other than sleep amount and continuity contributed to the differences in individual performance among these normal control subjects.

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**1053**

**Name Stimulus Discrimination From Stage 2 & REM Sleep**

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**Introduction:** It has been suggested that arousal of pre-attentive processes during REM sleep may explain enhanced dream recall upon waking from REM sleep. The aim of this investigation was to test whether such attention mechanisms are more functional during REM sleep than in Stage two NREM sleep. This was done by comparing arousal thresholds to OWN verses OTHER names from these sleep stages.

**Methods:** Twelve participants were polysomnographically monitored for microarousal and arousal latencies to their OWN name and OTHER syllable-matched names presented during REM sleep and Stage two NREM sleep from pre-made tape recordings. Each name was presented at increasing sound levels to a logarithmic scale (63, 65, 68, 72, 77, 83, 89, 98 and 105 dB +/- 2 dB) increasing every 30 seconds until arousal was observed. Names were presented in a counterbalanced order across subjects.

**Results:** For both ASDA microarousal and Rechtshaffen & Kales (R&K) arousal latencies, OWN NAME had significantly shorter arousal latencies than OTHER NAME from REM sleep (ASDA: REM-OWN M=34.0, SD=52.2, REM-OTHER M= 102.1, SD=88.9; t (16) = 4.01, p<0.01; R&K: REM-OWN M=44.9, SD=54.4, REM-OTHER M= 109.2, SD=85.7; t (16) = 3.44, p<0.01). However, no differences between name conditions were found from Stage two sleep.(ASDA: NREM-OWN M=53.7, SD=78.6, NREM-OTHER M= 55.8, SD=70.1; t (16) = 0.11, p>0.05; R&K: NREM-OWN M=70.1, SD=91.9, NREM-OTHER M= 72.9, SD=81.2; t (16) = 0.13, p>0.05)

**Conclusion:** These results are consistent with the proposal that REM sleep is a state demonstrating enhanced pre-attentive processing from sleep. This result is consistent with electrophysiological data showing P300 responses during REM but not during NREM sleep. It is also consistent with attention-based explanations for enhanced dream recall from REM sleep.

**1054**

**Personality Characteristics Related To The Decision To Drive When Fatigued**

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**Introduction:** Researchers have begun to investigate how personality factors influence driving behaviour and accident involvement. Personality characteristics found to have an association with risky driving are Extraversion, Sensation Seeking, Aggression and Optimism Bias. Therefore, these characteristics could play an important role in the decision making process when drivers decide whether to rest or continue driving when sleepy.

**Methods:** Eleven male and nine female subjects completed a Sensation Seeking Scale; Optimism Bias Questionnaire; Locus of Control Scale and State Driver Aggression Questionnaire before arriving at the laboratory to start a driving simulator task at midnight. The task involved a computer attached to an arcade-style steering wheel and pedals. Subjects had to complete the equivalent of 350 kilometers on a monotonous oval track in order to end the experiment. Participants were informed that they would have to start the task again if they drove off the road or crashed. They were allowed to take as many breaks as they wished.

**Results:** Eleven subjects had at least one break in completing the task and nine subjects had no breaks. The no break group were significant higher in sensation seeking ( t (2, 18) = 17.95, p = .002), optimism bias ( t (2, 18) = 7.06, p < .001), aggression ( t (2, 18) = 4.57, p = .003) and extraversion ( t (2, 18) = - 4.42, p < .001). Males scored significantly higher in sensation seeking ( t (2, 18) = 17.95, p = .002), optimism bias ( t (2, 18) = 7.06, p < .001), aggression ( t (2, 18) = 4.57, p = .003) and extraversion ( t (2, 18) = - 4.42, p < .001). Males scored significantly higher than females on aggression ( t (2, 18) = 2.74, p = .016), sensation seeking ( t (2, 18) = 2.27, p = .044) and took less rest-breaks ( t (2, 18) = 2.36, p = .028).

**Conclusion:** Traditional considerations of driving when fatigued have focused on the physiological characteristics of sleepiness. However, driving when sleepy involves a decision-making process, where psychological characteristics such as personality and attitudes play an important role that warrant further investigation.

**1055**

**The Electrical 'Brainscape' Reveals The Dynamics Of Brain States**

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**Introduction:** The periodic alternation of brain states during the wake-sleep cycle occurs in all Vertebrates. However, its consequences on the dynamic of large-scale neural ensembles and the mechanisms underlying...
state transitions remain poorly understood.

Methods: Using multi-electrodes, we performed long-term simultaneous recordings of local field potentials (LFPs) and single-unit activity (SUA) in cortical, thalamic, hippocampal, and striatal neural ensembles in behaving rats. Spectral analyses, correlation and coherence measurements were done on LFPs and SUA to objectively classify brain states and quantitatively investigate the dynamics of the forebrain ensembles during the wake-sleep cycle with particular attention to the transitions between states.

Results: All brain states could be consistently and unambiguously identified as distinct clusters in a three-dimensional state-space combining LFPs spectral composition and a coherence measurement. In this state-space, referred to as ‘brainscape’, subtle distinctions could be found within the major states, such as the graded difference between light and deep slow wave sleep. Spontaneous transitions between brain states followed trajectories with characteristic duration, spectral path, and striking changes in coherence spectra with synchronization peaks that coincide with the dominant frequencies of the underlying LFP oscillations. State transitions involving LFP oscillations of similar frequencies further presented distinct proportions of simultaneously active neurons suggesting a differential recruitment of neuronal populations.

Conclusion: The brainscape successfully captured the dynamics of forebrain neural ensembles and revealed very distinct regimes of neural activity. The distributed and highly coherent patterns of LFP oscillations at the boundaries of global brain states presumably reflect transient synchronizations of synaptic inputs. These transient episodes of oscillatory synchronization might be critical for information transfer within and across forebrain areas and for successful transitions between states. Distant forebrain areas thus appear to tightly coordinate the processing of neural information during and between global brain states, indicating a very high degree of functional integration across the entire wake-sleep cycle.

INSERM to DG, Pew Lat. Amer. Fellw., to SR, NIH 5 R01 DE11451 and 5 R01 DE13810 and DARPA N66001-01-C-8062 to MALN.
Key Word Index

<table>
<thead>
<tr>
<th>Term</th>
<th>Abstract Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
</tr>
<tr>
<td>5</td>
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<tr>
<td>6</td>
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<td>7</td>
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<td>8</td>
<td></td>
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<tr>
<td>9</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td></td>
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<tr>
<td>C</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td></td>
</tr>
<tr>
<td>E</td>
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<tr>
<td>F</td>
<td></td>
</tr>
<tr>
<td>G</td>
<td></td>
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<tr>
<td>H</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td></td>
</tr>
<tr>
<td>J</td>
<td></td>
</tr>
<tr>
<td>K</td>
<td></td>
</tr>
<tr>
<td>L</td>
<td></td>
</tr>
<tr>
<td>M</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td></td>
</tr>
<tr>
<td>O</td>
<td></td>
</tr>
<tr>
<td>P</td>
<td></td>
</tr>
<tr>
<td>Q</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td></td>
</tr>
<tr>
<td>S</td>
<td></td>
</tr>
<tr>
<td>T</td>
<td></td>
</tr>
<tr>
<td>U</td>
<td></td>
</tr>
</tbody>
</table>

A

Abstinence ........................................ 927
abuse potential ................................... 132, 133, 134, 135
academic performance ............................ 247
acetylcholine .................................... 25, 80, 171
acetylcholinesterase inhibitor ................. 335
ACGME ............................................ 1047
acromegaly ....................................... 885
Actigraph ......................................... 237, 352, 759
Actigraphy .......................... 140, 173, 186, 232, 243, 310, 313, 324, 336, 360,
413, 760, 816, 834, 939, 945, 947, 950, 977, 1024, 1052
Active Sleep ..................................... 412
activity ......................................... 83, 206, 869
activity levels .................................. 714
Acupuncture ..................................... 604, 908
acute phase response ........................... 123
ad / hd ........................................... 217
adenosine ........................................ 11, 434
Adenosine Receptor ............................... 6, 33
adenosine receptor antagonist .................. 41
ADHD .............................................. 276, 285, 292, 310, 910
adherence ........................................ 470, 503, 580
adiponectin ...................................... 537
adolescence ..................................... 209, 242, 244
adolescent ........................................ 188, 291, 301
adolescents ....................................... 189, 261, 263, 293, 310, 903
affect ............................................ 152
Afro American .................................. 311
After-effect of entrainment ...................... 212
Afternoon Sleepiness ............................. 118
Age ............................................... 603
age of onset ..................................... 661
age-of-onset ..................................... 827
aged people ..................................... 139
Aging ............................................. 7, 88, 148, 318, 323, 328, 329, 330, 334, 337, 343,
346, 347, 349, 350, 406, 672, 681, 696, 738
AHI ................................................. 603
AHI vs REI ....................................... 567
airway ............................................ 252
alcohol .......................................... 93, 111, 141, 355, 513, 1024, 1025, 1051
alcohol use ....................................... 513, 732, 1017
Alcoholism ........................................ 740
aldosterone ....................................... 493
Alertness ........................................ 974
Alertness and vigilance .......................... 432
Alpha ............................................ 891
Alpha activity .................................... 154
Alpha Attenuation Test ........................... 368
Alpha ECG ......................................... 726
ALTE ............................................. 303
alternating hemiplegia ......................... 227
alternating leg muscle activation ............ 784
Altitude ........................................... 467
Alzheimer ........................................ 164, 335, 1023
Alzheimer's disease .............................. 322, 767
<table>
<thead>
<tr>
<th>term</th>
<th>page(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>cerebellum</td>
<td>853</td>
</tr>
<tr>
<td>cerebral blood flow</td>
<td>577</td>
</tr>
<tr>
<td>cessation</td>
<td>867</td>
</tr>
<tr>
<td>Chagas Disease</td>
<td>893</td>
</tr>
<tr>
<td>chaperones</td>
<td>1004</td>
</tr>
<tr>
<td>chemotherapy</td>
<td>865, 870</td>
</tr>
<tr>
<td>child</td>
<td>251, 301, 315</td>
</tr>
<tr>
<td>Childhood</td>
<td>245, 282, 283</td>
</tr>
<tr>
<td>Childhood Depression</td>
<td>263</td>
</tr>
<tr>
<td>children's sleep</td>
<td>314</td>
</tr>
<tr>
<td>Chinese children</td>
<td>297</td>
</tr>
<tr>
<td>chloridiazepoxide</td>
<td>120</td>
</tr>
<tr>
<td>cholecystokinin</td>
<td>449, 654</td>
</tr>
<tr>
<td>cholinergic</td>
<td>75, 100</td>
</tr>
<tr>
<td>cholinergic basal forebrain</td>
<td>448</td>
</tr>
<tr>
<td>cholinomimetics</td>
<td>145</td>
</tr>
<tr>
<td>chronic administration</td>
<td>86</td>
</tr>
<tr>
<td>Chronic Fatigue Syndrome</td>
<td>856</td>
</tr>
<tr>
<td>Chronic insomnia</td>
<td>484</td>
</tr>
<tr>
<td>chronic renal failure</td>
<td>866</td>
</tr>
<tr>
<td>chronic sleep loss</td>
<td>392</td>
</tr>
<tr>
<td>chronic sleep restriction</td>
<td>383, 400, 407, 1030</td>
</tr>
<tr>
<td>circadian</td>
<td>23, 171, 186, 191, 192, 204, 210, 1012</td>
</tr>
<tr>
<td>circadian period</td>
<td>209, 212</td>
</tr>
<tr>
<td>circadian phase</td>
<td>24, 187</td>
</tr>
<tr>
<td>circadian rhythm</td>
<td>88, 178, 214, 215, 280, 785, 818</td>
</tr>
<tr>
<td>Circadian rhythm disorders</td>
<td>208</td>
</tr>
<tr>
<td>circadian rhythm genes</td>
<td>1002</td>
</tr>
<tr>
<td>circadian rhythms</td>
<td>165, 173, 174, 175, 176, 182, 183, 184, 187, 189, 190, 196, 199, 200, 211, 213, 423, 674, 857, 1036</td>
</tr>
<tr>
<td>circadian rhythms</td>
<td>205</td>
</tr>
<tr>
<td>classical conditioning</td>
<td>688</td>
</tr>
<tr>
<td>cleft palate</td>
<td>289, 290</td>
</tr>
<tr>
<td>Clinical Predictors</td>
<td>464</td>
</tr>
<tr>
<td>clinical evaluation</td>
<td>303</td>
</tr>
<tr>
<td>clock genes</td>
<td>178, 1012</td>
</tr>
<tr>
<td>cluster analysis</td>
<td>972</td>
</tr>
<tr>
<td>Cluster Headache</td>
<td>854</td>
</tr>
<tr>
<td>CME</td>
<td>998</td>
</tr>
<tr>
<td>co-existing headache</td>
<td>916, 917, 918</td>
</tr>
<tr>
<td>co-sleeping</td>
<td>222</td>
</tr>
<tr>
<td>CO2</td>
<td>578</td>
</tr>
<tr>
<td>COCAINE</td>
<td>927</td>
</tr>
<tr>
<td>cognition</td>
<td>105, 321, 409, 501, 633, 1023</td>
</tr>
<tr>
<td>cognitive behavior therapy</td>
<td>739, 1022</td>
</tr>
<tr>
<td>Cognitive behavioral therapy</td>
<td>677, 699</td>
</tr>
<tr>
<td>cognitive behavioral therapy for insomnia</td>
<td>734</td>
</tr>
<tr>
<td>cognitive functioning</td>
<td>521</td>
</tr>
<tr>
<td>cognitive impairment</td>
<td>378</td>
</tr>
<tr>
<td>Cognitive Performance</td>
<td>365, 387, 395, 1041, 1052</td>
</tr>
<tr>
<td>cognitive workload</td>
<td>378</td>
</tr>
<tr>
<td>Cognitive-behavioral insomnia therapy</td>
<td>667, 669, 674, 700, 865</td>
</tr>
<tr>
<td>cognitive-behavioral therapy</td>
<td>686, 720</td>
</tr>
<tr>
<td>coherence</td>
<td>1055</td>
</tr>
<tr>
<td>college</td>
<td>1017</td>
</tr>
<tr>
<td>College students</td>
<td>1027, 1049</td>
</tr>
<tr>
<td>Comorbidity</td>
<td>510, 925</td>
</tr>
<tr>
<td>complex sleep apnea</td>
<td>502</td>
</tr>
<tr>
<td>complexity</td>
<td>951</td>
</tr>
<tr>
<td>compliance</td>
<td>274, 476, 490, 505, 528, 532, 545, 558, 570, 594, 628</td>
</tr>
<tr>
<td>conditioned fear</td>
<td>478</td>
</tr>
<tr>
<td>Confusional Arousals</td>
<td>780</td>
</tr>
<tr>
<td>congenital cardiac disease</td>
<td>286</td>
</tr>
<tr>
<td>consumption habits</td>
<td>124</td>
</tr>
<tr>
<td>Continuing Medical Education</td>
<td>998</td>
</tr>
<tr>
<td>continuous positive airway pressure</td>
<td>455, 557, 560, 561</td>
</tr>
<tr>
<td>Continuous Positive Airway Pressure (CPAP)</td>
<td>458, 459, 501, 503, 506, 528, 532, 539, 574</td>
</tr>
<tr>
<td>control of breathing</td>
<td>621</td>
</tr>
<tr>
<td>COPD</td>
<td>479</td>
</tr>
<tr>
<td>Coping</td>
<td>690</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>485</td>
</tr>
<tr>
<td>Cortical arousal</td>
<td>121, 905, 920</td>
</tr>
<tr>
<td>corticosterone</td>
<td>743</td>
</tr>
<tr>
<td>Cortisol</td>
<td>175, 328, 394, 697, 934, 935</td>
</tr>
<tr>
<td>cosleeping</td>
<td>226</td>
</tr>
<tr>
<td>cost effectiveness</td>
<td>712, 899</td>
</tr>
<tr>
<td>Countermeasures</td>
<td>450</td>
</tr>
<tr>
<td>CPAP</td>
<td>325, 468, 470, 481, 490, 491, 497, 505, 512, 524, 526, 527, 570, 594, 628</td>
</tr>
<tr>
<td>CPAP non-compliance</td>
<td>625</td>
</tr>
<tr>
<td>CPAP predictors</td>
<td>560</td>
</tr>
<tr>
<td>cpp treatment</td>
<td>473</td>
</tr>
<tr>
<td>CPAP Utilization</td>
<td>630</td>
</tr>
<tr>
<td>CPAP, Continuous Positive Airway Pressure</td>
<td>471, 623</td>
</tr>
<tr>
<td>CPAP/BiPAP</td>
<td>274</td>
</tr>
<tr>
<td>CRH</td>
<td>37</td>
</tr>
<tr>
<td>CRP</td>
<td>537</td>
</tr>
<tr>
<td>CRT device</td>
<td>965</td>
</tr>
<tr>
<td>CSP ferritin</td>
<td>827</td>
</tr>
<tr>
<td>Cyclic Alternating Pattern</td>
<td>873</td>
</tr>
<tr>
<td>Cyclic-Alternating-Pattern</td>
<td>304, 468, 546</td>
</tr>
<tr>
<td>Cystatin</td>
<td>530</td>
</tr>
<tr>
<td>Cytokine</td>
<td>2, 22, 30</td>
</tr>
<tr>
<td>cytokines</td>
<td>70, 176, 408</td>
</tr>
</tbody>
</table>

**D**

daily activities                      | 371     |
daycare                              | 264     |
daytime functioning                  | 287, 334, 508, 686 |
daylight impact                      | 692     |
daylight sleepiness                  | 218, 328, 344, 562, 581, 662, 781, 883, 1023, 1040 |
DeAnn                               | 253     |
Decision-Making                      | 405     |
Declarative                          | 1039    |
delayed sleep phase disorder         | 184     |
delayed sleep phase syndrome         | 177     |
delta                                | 299     |
delta band                           | 108     |
Delta EEG                            | 128     |
Delta Power                          | 5, 7, 765 |
DELT A SLEEP                         | 125     |
dementia                             | 320, 325, 327, 341, 349 |
demographics                         | 271     |
dental cast                          | 504     |
dependence                           | 133, 134, 135 |
Depression                           | 66, 170, 278, 375, 482, 691, 782, 800, 903, 904, 906, 907, 908, 919, 921, 922, 923, 924, 929, 933 |
depression                            | 74, 115, 444, 446 |
development                          | 27, 44, 231 |
dex-CRH                              | 763     |
impulsivity ........................................... 308
In-Flight Sleep ........................................... 947
In-home sleep studies ............................. 915, 938
Inbred Strain ............................................. 19
Index .................................................. 665
indiplon .................................................. 681, 682, 683, 684, 685
direct costs ............................................. 735
individual difference ............................... 361, 364
infant ................................................... 231, 238, 239, 250, 280
infant sleep ............................................. 267, 911
Infant Temperament .................................... 296
infants ..................................................... 248
Infants sleep ............................................ 223
inflammation ......................................... 241, 266, 268, 348, 544, 572
influenza .................................................. 1005, 1009
inheritance ............................................ 815
Inhibition .................................................. 433
inmate immunity ..................................... 408
insomnia ................................................ 130, 138, 141, 151, 224, 233, 265, 291, 295, 312,
331, 332, 345, 479, 480, 482, 538, 665, 666, 667, 669, 670, 671, 673,
675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688,
689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 701, 703, 705,
706, 707, 709, 710, 711, 712, 713, 714, 717, 718, 722, 725, 727, 728,
729, 730, 731, 733, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744,
746, 747, 749, 750, 751, 753, 754, 755, 756, 757, 758, 759, 760, 761,
762, 763, 764, 850, 902, 907, 916, 917, 918, 923, 925, 933, 937, 943,
955, 967, 1040
insomnia and depression ......................... 916, 917, 918
insomnia subtype .................................... 734
instrumentation .................................... 940, 984
Integrated Selective .................................. 995
Intelligence .......................................... 429
inter-individual differences ......................... 395
inter-individual variability .......................... 399
inter-observer ........................................ 987
Interferon ............................................. 127
Interleukin 1 beta .................................. 1011
interleukin-1 ........................................... 22
intermittent hypoxia .................................. 24, 47, 55, 72, 79, 96, 627
Interscorer correlation ............................. 979
Intertrigeminal region ................................ 90
Intractable pain ....................................... 890
Interscorer correlation ............................. 979
IRLS .................................................. 813

J
Japanese .............................................. 564, 847
Jet lag .................................................. 163
Jill ..................................................... 837
Josefinita .............................................. 612
Juvenile .................................................. 84
Juvenile - Arthritis ................................... 304
juxtacellular labeling ................................ 76

K
K-complex .............................................. 128, 299
kidney function ...................................... 530
Kindergarten .......................................... 302
kleine levine .......................................... 830
kleine-Levin syndrome ............................. 846
KLS .................................................. 831
knock-out ............................................... 74
knock-out mice ....................................... 60, 62
Korean .................................................. 1021

L
L-Dopa .................................................. 808
Labial Closure Force .................................. 900
laboratory adaptation ................................ 168
Laboratory Evaluation ......................... 812
Late-life Insomnia ................................. 339
latency ................................................... 262, 391, 958
Lateral hypothalamus ................................ 29
Lateral Position Sleep ................................ 515
lateralization .......................................... 905
Learned Helplessness ................................ 919
learning .................................................. 80, 1019
learning modules ..................................... 995
leptin .................................................... 94, 213, 676, 800
leukocytes ............................................. 408, 415
levodopa ................................................. 823, 825
Lewy bodies disease .................................. 779
lifestyle ................................................. 366, 694
light ...................................................... 162, 163, 164, 198, 199
light environment .................................... 201
light exposure ......................................... 698
Light treatment ....................................... 672
lipecalin 2 .............................................. 999
Lipopolysaccharide ................................... 33
liquid diet .............................................. 93
Liver Cirrhosis ......................................... 866
Liver Disease .......................................... 799
local field potentials ............................... 1055
local sleep processes ............................... 4, 45, 78
Localized Sleep ....................................... 64, 70
locomotion .......................................... 784
locomotor activity .................................... 3, 173
Locus coeruleus ...................................... 29, 101
long-term .............................................. 682, 684
Long-term depression .............................. 73
long-term insomnia therapy ...................... 713
longitudinal study .................................... 249
low-dose acetazolamide ........................... 109
LTP .................................................. 410, 434, 435
Lung Cancer Survivors ............................. 875
Lung volume .......................................... 534

M
magnetic resonance imaging .................. 495
Maintenance of Wakefulness Test ............. 400
mammals ............................................... 46
Mandibular Advancement Splint .................. 511
Mandible ............................................... 495
mapping ................................................. 45, 78
marksmanship .......................................... 417
Mars sol ................................................. 1050
maternal sleep ........................................ 911, 949
mathematical model ............................... 166, 383, 392
mathematical modeling ............................ 205
Matrix .................................................. 668
MCH .................................................. 99
MDMA .................................................. 142
Measure ............................................... 666, 963
Medical Education .................................. 403
<table>
<thead>
<tr>
<th>Term</th>
<th>Page Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical errors</td>
<td>1031</td>
</tr>
<tr>
<td>Medical Residents</td>
<td>432</td>
</tr>
<tr>
<td>Medical Students</td>
<td>997</td>
</tr>
<tr>
<td>medication</td>
<td>553, 701</td>
</tr>
<tr>
<td>meditation</td>
<td>929</td>
</tr>
<tr>
<td>melanin concentrating hormone</td>
<td>31</td>
</tr>
<tr>
<td>melatonin</td>
<td>162, 163, 164, 182, 187, 189, 200, 202, 203, 204</td>
</tr>
<tr>
<td>melatonin onset</td>
<td>188</td>
</tr>
<tr>
<td>memory</td>
<td>21, 372, 478, 514, 936, 1039</td>
</tr>
<tr>
<td>Memory consolidation</td>
<td>445, 1044</td>
</tr>
<tr>
<td>Menopause</td>
<td>319, 326, 350, 755, 944</td>
</tr>
<tr>
<td>Mentation</td>
<td>914</td>
</tr>
<tr>
<td>Meta-analysis</td>
<td>317</td>
</tr>
<tr>
<td>metabolic</td>
<td>315, 859</td>
</tr>
<tr>
<td>metabolic rate</td>
<td>649</td>
</tr>
<tr>
<td>metabolic syndrome</td>
<td>55, 535</td>
</tr>
<tr>
<td>metabolism</td>
<td>94, 213, 463</td>
</tr>
<tr>
<td>methamphetamine</td>
<td>633</td>
</tr>
<tr>
<td>methamphetamine HCL</td>
<td>662</td>
</tr>
<tr>
<td>methodology</td>
<td>295</td>
</tr>
<tr>
<td>mice</td>
<td>19, 20, 373</td>
</tr>
<tr>
<td>microarray</td>
<td>1000</td>
</tr>
<tr>
<td>microdialysis</td>
<td>8, 35, 36, 54</td>
</tr>
<tr>
<td>Middle-age</td>
<td>200, 342</td>
</tr>
<tr>
<td>migraine</td>
<td>834</td>
</tr>
<tr>
<td>military</td>
<td>1049</td>
</tr>
<tr>
<td>milnacipran</td>
<td>641</td>
</tr>
<tr>
<td>minority</td>
<td>258</td>
</tr>
<tr>
<td>mirtazapine</td>
<td>924</td>
</tr>
<tr>
<td>misperception</td>
<td>722, 750</td>
</tr>
<tr>
<td>MMPI</td>
<td>562</td>
</tr>
<tr>
<td>modafinil</td>
<td>143, 146, 362, 444, 781</td>
</tr>
<tr>
<td>modeling</td>
<td>192</td>
</tr>
<tr>
<td>monoamine</td>
<td>61</td>
</tr>
<tr>
<td>mood</td>
<td>380, 386, 672, 742</td>
</tr>
<tr>
<td>Mood States</td>
<td>931</td>
</tr>
<tr>
<td>mood, pain</td>
<td>427</td>
</tr>
<tr>
<td>morningness-eveningness</td>
<td>167, 168, 674</td>
</tr>
<tr>
<td>morningness/eveningness</td>
<td>179, 181, 214, 447</td>
</tr>
<tr>
<td>morphine</td>
<td>8</td>
</tr>
<tr>
<td>mortality</td>
<td>139, 348, 469</td>
</tr>
<tr>
<td>motherB4 smoking</td>
<td>236</td>
</tr>
<tr>
<td>motivation</td>
<td>1015</td>
</tr>
<tr>
<td>Motoneuron</td>
<td>39</td>
</tr>
<tr>
<td>motor sequence learning</td>
<td>1044</td>
</tr>
<tr>
<td>motor skill learning</td>
<td>1046</td>
</tr>
<tr>
<td>mouse</td>
<td>206, 430</td>
</tr>
<tr>
<td>mouth breathing</td>
<td>272</td>
</tr>
<tr>
<td>movement disorder</td>
<td>814, 818</td>
</tr>
<tr>
<td>MRI</td>
<td>595</td>
</tr>
<tr>
<td>MSLT</td>
<td>517, 520, 605, 608, 656, 845, 961, 974, 1014, 1015</td>
</tr>
<tr>
<td>Multiple Sclerosis</td>
<td>842, 852</td>
</tr>
<tr>
<td>multiple system atrophy</td>
<td>559</td>
</tr>
<tr>
<td>muscarinic</td>
<td>25</td>
</tr>
<tr>
<td>muscle and capillary</td>
<td>789</td>
</tr>
<tr>
<td>Muscular Symptoms</td>
<td>874</td>
</tr>
<tr>
<td>mutagenesis</td>
<td>1001</td>
</tr>
<tr>
<td>MWT</td>
<td>517, 656, 961</td>
</tr>
<tr>
<td>myeloperoxidase</td>
<td>415</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>601</td>
</tr>
<tr>
<td>myoclonic twitch</td>
<td>44</td>
</tr>
<tr>
<td>myoclonic twitching</td>
<td>50</td>
</tr>
<tr>
<td>myoclonic twitching</td>
<td>218, 843, 844, 845</td>
</tr>
<tr>
<td>naloxone</td>
<td>221</td>
</tr>
<tr>
<td>nasal cannula</td>
<td>556</td>
</tr>
<tr>
<td>nasal CPAP</td>
<td>556</td>
</tr>
<tr>
<td>nasal CPAP Interfaces</td>
<td>584</td>
</tr>
<tr>
<td>nasal obstruction</td>
<td>988</td>
</tr>
<tr>
<td>nasal surgery</td>
<td>592</td>
</tr>
<tr>
<td>nasal transducer</td>
<td>952</td>
</tr>
<tr>
<td>Natural Bright Light</td>
<td>118</td>
</tr>
<tr>
<td>Neck Circumference</td>
<td>457, 464, 607</td>
</tr>
<tr>
<td>Neominal audio exposure</td>
<td>107</td>
</tr>
<tr>
<td>Neominal REM sleep deprivation</td>
<td>66</td>
</tr>
<tr>
<td>neominal</td>
<td>84</td>
</tr>
<tr>
<td>Nervous lesions</td>
<td>587</td>
</tr>
<tr>
<td>neuroanatomy</td>
<td>77</td>
</tr>
<tr>
<td>neurobehavioral impairment</td>
<td>383, 390, 392</td>
</tr>
<tr>
<td>Neurobehavioral Performance</td>
<td>391, 1030</td>
</tr>
<tr>
<td>NeuroCAP</td>
<td>432, 974</td>
</tr>
<tr>
<td>neurocognition</td>
<td>316</td>
</tr>
<tr>
<td>neurocognitive</td>
<td>146</td>
</tr>
<tr>
<td>neurocognitive function</td>
<td>344, 1045</td>
</tr>
<tr>
<td>Neurocognitive test battery</td>
<td>566</td>
</tr>
<tr>
<td>Neuroendocrine</td>
<td>174</td>
</tr>
<tr>
<td>neurofibromatosis</td>
<td>839</td>
</tr>
<tr>
<td>Neurogenesis</td>
<td>385</td>
</tr>
<tr>
<td>neuroimaging</td>
<td>691</td>
</tr>
<tr>
<td>Neuroimmunology</td>
<td>2, 22, 30</td>
</tr>
<tr>
<td>Neurormedical</td>
<td>836</td>
</tr>
<tr>
<td>NeurormetPlus</td>
<td>836</td>
</tr>
<tr>
<td>neuronal transition probability model</td>
<td>110</td>
</tr>
<tr>
<td>Neuropeptide</td>
<td>29</td>
</tr>
<tr>
<td>Neuropeptide S</td>
<td>49</td>
</tr>
<tr>
<td>neurophysiology</td>
<td>50</td>
</tr>
<tr>
<td>neuropsychological deficits</td>
<td>569</td>
</tr>
<tr>
<td>neuropsychology</td>
<td>242, 244, 318, 331, 332, 507</td>
</tr>
<tr>
<td>neurotensin</td>
<td>12</td>
</tr>
<tr>
<td>neurotrophin</td>
<td>82</td>
</tr>
<tr>
<td>Next Day Function</td>
<td>705</td>
</tr>
<tr>
<td>NF-kB</td>
<td>6</td>
</tr>
<tr>
<td>NICU</td>
<td>970</td>
</tr>
<tr>
<td>night shift work</td>
<td>203</td>
</tr>
<tr>
<td>night work</td>
<td>181, 196</td>
</tr>
<tr>
<td>Night-shift</td>
<td>186</td>
</tr>
<tr>
<td>night-waking</td>
<td>250</td>
</tr>
<tr>
<td>Nightmires</td>
<td>155, 772</td>
</tr>
<tr>
<td>Nitric Oxide</td>
<td>33, 63, 68, 431</td>
</tr>
<tr>
<td>NMDA antagonist</td>
<td>90</td>
</tr>
<tr>
<td>no-treatment</td>
<td>130</td>
</tr>
<tr>
<td>Nociceptin/orphanin FQ</td>
<td>71</td>
</tr>
<tr>
<td>Nocturia</td>
<td>475, 497, 878</td>
</tr>
<tr>
<td>nocturnal events</td>
<td>975</td>
</tr>
<tr>
<td>Nocturnal Seizures</td>
<td>780</td>
</tr>
<tr>
<td>nocturnal sleep</td>
<td>869</td>
</tr>
<tr>
<td>nocturnal sleep disturbance</td>
<td>883</td>
</tr>
</tbody>
</table>
physical activity ........................................... 177, 351, 353, 461
physician identification .................................. 496
physician trainees ........................................ 185
pilot ......................................................... 424
Pittsburgh Sleep Quality Index ....................... 868, 946
placebo effect ............................................ 130, 659
plasmapheresis ............................................ 664
plasticity ..................................................... 13, 15, 435
plexiform neurofibroma .................................. 839
PLM ......................................................... 260, 816, 820
PLMD ......................................................... 219
PLMS ......................................................... 818, 844
Polysomnography (PSG) ................................ 841
polycystic ovary syndrome ................................ 455
polymorphisms ............................................. 1002
polysomnogram ............................................ 363, 949
Polysonomographic ....................................... 160
Polysonomographic characteristics .................. 794
Polysonography ........................................... 202, 440, 492, 502, 550, 555, 568, 604,
741, 758, 777, 787, 881, 935, 941, 985
poly[rI:rC ...................................................... 122
pons ........................................................ 26, 32
pointis oralis .............................................. 25
population-based .......................................... 945
portable monitor .......................................... 956
Portable monitoring ..................................... 969
portable sleep data recorder ................................ 938
post partum depression .................................. 911
Post-operative complications ......................... 547
post-test questionnaire .................................. 519
postpartum .................................................. 267
Postpartum Depression ................................... 935
Pramipexol ................................................... 775
pramipexole .................................................. 822
Prasomniass .................................................. 294
pre-coeruleus ................................................. 95
Pre-Frontal Cortex ........................................ 1029
Pre-operative sleep evaluation ......................... 547
pre-sleep ethanol ......................................... 742
prediction .................................................... 192
Predictors .................................................... 593, 623
Predisposition ............................................. 689
pregnancy .................................................... 360, 437, 568, 880, 906, 908, 977
premature ventricular contraction ..................... 473
Premenstrual Dysphoria .................................. 912
premenstrual symptoms .................................. 153
premenstrual syndrome .................................. 864
preoptic ....................................................... 51, 58
preoptic area ............................................... 42
pressure support ventilation ............................ 548
preterm ....................................................... 280
preterm birth ............................................... 880
prevalence .................................................... 859
Prevalence .................................................... 799, 826
primary care ............................................... 695, 821
primary care medicine ................................... 971
Primary Insomnia ......................................... 708, 715, 716, 720, 721, 726, 734, 745
primate ........................................................ 198
priming ....................................................... 936
prognosis ..................................................... 657
program evaluation ....................................... 671
progressive muscle relaxation ......................... 761
prostaglandin .............................................. 999
protein expression ........................................ 75
protein/mRNA expression ............................... 100
proteins ....................................................... 452
Pseudotumor Cerebri ..................................... 835
PSG .......................................................... 707, 770, 845
PSG sleep ................................................... 340
Psychiatric ................................................... 301
psychiatric disorders .................................... 932
Psychiatric Features ..................................... 160
psychiatric illness ........................................ 718
psychiatric outpatients .................................. 909
psychological symptoms ................................ 472
Psychomotor Performance .............................. 140
psychomotor vigilance ................................... 416, 417, 428
psychopathology .......................................... 772
psychophysiological insomnia ......................... 1022
PTSD ......................................................... 915, 934, 936
Pulmonary Function Tests ................................ 557
Pulmonary Hypertension .................................. 889
Pupillometry .................................................. 368, 954
PVT .......................................................... 413, 964, 1050
PVT, psychomotor vigilance .............................. 379
Q
QOL .......................................................... 1047
QTL analysis ............................................... 1013
quality ........................................................ 941
quality child care .......................................... 314
Quality of life ............................................. 265, 281, 460, 541, 652, 657, 687
Quantitative PCR .......................................... 102
quantitative sleep EEG ................................... 167, 168
questionable dementia ................................... 1045
Questionnaire .............................................. 214, 279, 617, 634, 748, 811, 944, 959, 960, 972
questionnaires .............................................. 971
R
Race .......................................................... 826
racial differences ......................................... 277
ramelton .................................................... 132, 133, 134, 135, 136, 137, 479, 480, 679, 680
rapid eye movements ..................................... 985
Rat ............................................................ 16, 18, 48
rat brain ...................................................... 388
rat model ..................................................... 34, 757
Rat Strain ..................................................... 17
Rational thought .......................................... 157
RBD ............................................................ 765, 774, 777, 805
RDI ............................................................ 518, 520, 542, 967
reaction time ............................................... 379
Real-Time Algorithm ..................................... 981
rebound ....................................................... 658
RECOVERY .................................................. 396, 398, 400, 407, 411
recovery sleep ............................................. 63, 65, 374, 438, 440
Recurrent Abdominal Pain .............................. 255
reliability .................................................... 948, 979, 986
REM .......................................................... 31, 44, 442, 542, 549, 626, 928, 1020
REM deprivation .......................................... 377, 389, 445
REM Rebound .............................................. 438, 872
REM sleep .................................................... 26, 28, 40, 42, 53, 91, 203, 317, 376,
478, 603, 776, 914, 1003, 1053
REM sleep behavior disorder .......................... 159, 767, 775, 779
REM sleep induction ..................................... 145