Young Scientist Symposium

YS01

Owl or Lark? Stroop-related cerebral activity is modulated by time of day and chronotype

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Introduction: Interactions between circadian and homeostatic systems modulate our sleep-wake cycle but also variations in cognitive performance. Additionally, individuals exhibit differences in their preferred schedules for sleep and activity patterns. Here we investigated the cerebral bases of these differences in the context of an interference task.

Methods: Thirty extreme chronotypes (16 early (ET), 14 late types (LT)) underwent 2 fMRI sessions, 1.5 and 10.5 h after preferred waking up controlled throughout actimetry the week prior testing. Order of the sessions was counter-balanced over subjects. The day before each fMRI session, subjects stayed in dim-light, circadian phase was asserted by detecting melatonin secretion onset (saliva samples). Polysomnography was recorded the nights preceding test sessions. During fMRI scanning, subjects performed a Stroop conflict paradigm where subjects must name the printed colour of a colour name, with congruent (C), incongruent (I) and neutral (N) trials.

Results: ET and LT significantly differed in their sleep timing and mid range crossings of melatonin expression. Circadian phase angles were similar in both LT and ET indicating a stable relationship between the adopted sleep timing and circadian phase. At the behavioral level, RTs were lower for I than N trials, but no significant time of day or chronotype effects were observed. In the morning, the interference-related activation effect (I versus N events) was significantly higher in LT than ET in the inferior and medial frontal gyrus as well as a parietal and a parahippocampal region. Conversely, in the evening, orbital, inferior and medial frontal gyri, superior temporal and occipital regions were more activated in ET than LT.

Discussion: Inferior frontal areas are known to be involved in a conflict resolution network. Interestingly, activation in this area was higher for LT than ET in the morning, whereas it was higher for ET than LT in the evening. This cannot be accounted for by differences in time awake or in circadian phase *per se*. Previously reported chronotypical differences in the dynamics of the sleep pressure, mainly differences in its built up and dissipation are however potential candidates to explain our data.

YS02

Topography of the effects of a PER3 polymorphism on alpha activity in REM sleep under baseline and recovery conditions

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Introduction: EEG characteristics are among the most heritable traits in humans. We previously reported that individuals homozygous for the longer allele of a variable number tandem repeat (VNTR) polymorphism in PER3 have increased alpha activity during REM sleep under both baseline conditions and during recovery from acute sleep deprivation. Alpha activity during REM sleep is known to vary across EEG derivations and to be most pronounced in occipital derivations. We investigated whether this polymorphism affects the topographical distribution of alpha activity in REM sleep and compared its effects to those of sleep deprivation.

Methods: The dynamics of alpha activity in REM sleep were assessed in 24 healthy volunteers who were homozygous for either the long (PER35/5) or short allele (PER34/4) of a PER3 VNTR. Sleep EEG in frontal, central, parietal and occipital brain regions was recorded during baseline sleep and recovery sleep, after a 40 h constant routine.

Results: During baseline sleep, PER35/5 participants displayed greater theta- alpha activity in all derivations. Thus EEG power density differed significantly between the two genotypes in frontal (7–12 Hz, $P<0.05$), central (8–11 Hz, $P<0.05$) parietal (8–10 Hz, $P<0.05$) and occipital (9–10 Hz, $P<0.05$) derivations. Repeated measures ANOVA revealed a significant interaction between genotype, derivation and frequency ($P=0.02$). A very similar pattern was seen during recovery sleep, although smaller differences were also present in slow wave and beta ranges. In contrast, sleep deprivation led to an increase in EEG activity in REM sleep over slow wave and theta activity ranges (Frontal: 2–4 Hz; Central 2–5 Hz; Parietal 2–7 Hz and occipital 3–5 Hz, $P<0.05$).

Conclusion: The polymorphism has a robust effect on EEG activity in REM sleep, which is most pronounced in alpha activity in occipital and parietal derivations which contrasts the effects of sleep deprivation and implies that the polymorphism affects aspects of the EEG that are separate from the effects of sleep homeostasis.

YS03

The impact of prescribing hypnotic medication on compliance with behavioural treatment for insomnia

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The efficacy of cognitive-behaviour therapy (CBT) for insomnia is well established, but improvement is highly dependent on compliance with therapeutic recommendations. Adding hypnotic medication may potentially influence compliance with CBT, either decreasing compliance due to lower motivation to comply with more demanding behavioural procedures, or enhancing compliance because of the rapid sleep relief provided by medication. This study aimed at investigating the impact of medication on compliance with behavioural treatment procedures for insomnia. Participants were 160 adults (aged 30–72 years old, mean = 50.3; 60.6% women) meeting criteria for chronic insomnia. They were randomized to six weekly group CBT sessions either alone ($n=80$) or combined with medication (10 mg zolpidem taken nightly) ($n=80$). Compliance was assessed weekly by the therapists with ratings of the restriction of time spent in bed and stimulus control procedures. Compliance ratings were compared between the two conditions and correlated with several baseline measures. No significant group differences were found for weekly compliance ratings or for the overall six-week averages, except for compliance with restriction of time in bed on week 5, which was higher in the CBT condition. The proportions of participants with high, intermediate, or low compliance were similar in both conditions. Significant correlates of higher compliance were (a) for the combined condition: lower baseline scores of depressive symptoms, fatigue, dysfunctional beliefs and attitudes about sleep, health-related impairment, and insomnia consequences, and (b) for the CBT condition: lower baseline scores on measures of insomnia severity and consequences, shorter insomnia duration, and higher treatment acceptability. These results suggest that adding medication to CBT does not impede nor enhance compliance with behavioural treatment procedures for insomnia. Nonetheless, compliance appears to be associated with different variables depending on whether CBT is delivered alone or in combination with medication. Further studies should investigate more thoroughly potential mediators of compliance for different treatment regimens.

YS04

Regional slow-wave sleep homeostasis in the pigeon (*Columba livia*)

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Aside from mammals, birds are the only other taxonomic group that engages in unequivocal slow-wave sleep (SWS) and rapid-eye movement (REM) sleep. This basic similarity appears to be due to convergent evolution as sleeping reptiles do not show SWS or REM sleep. In addition to sharing the same states of sleep, birds appear to regulate sleep in a manner similar to mammals. We recently demonstrated for the first time that birds show a mammalian-like compensatory increase in SWS-related low-frequency power density following 8 h of sleep deprivation (Martinez-Gonzalez et al. 2008. Journal of Sleep Research). However, it is unknown if birds can increase low-frequency power density during sleep on a regional scale that is dependent on prior use during wakefulness. To evaluate this idea, we provided asymmetrical visual stimulation to seven adult homing pigeons (*Columba livia*) individually housed on a 12L:12D photoperiod. Pigeons were implanted with electrodes over the hyperpallium (i.e., visual Wulst) of each hemisphere. After recording one baseline night, we sleep deprived each bird for the last 8 h of the day while the left eye was occluded with a cap and the right eye was directed towards a monitor showing video of wild birds. We predicted that the left hyperpallium (receiving projections from the right unoccluded eye) would show a greater increase of SWS-related power density relative to the right hyperpallium (receiving projections from the occluded eye). Overall, during the first 3 h of recovery, the increase in SWS-related low-frequency (1.56–4.30 Hz) power density was significantly greater in the left hyperpallium when compared to the right hyperpallium (paired *t*-tests: $P<0.05$), whereas the time spent in SWS was not significantly different between the two time periods ($P>0.40$). Consequently, unilateral visual stimulation in sleep-deprived pigeons results in an asymmetrical increase in SWS-related low-frequency activity with the increase being greater in the hemisphere that was visually stimulated during the sleep deprivation procedure. Thus, as in mammals, power density during avian SWS is related to brain use during wakefulness. These data add yet another level of convergence between the sleep of mammals and of birds.

WFSRSMS–ESRS Joint Symposium
Chronic Insomnia, Sleep and Daytime Function – Understanding the Paradox

S01

Clinical paradoxes in insomnia– implications for human research

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S02

Burden of disease in insomnia patients

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Chronic insomnia is a common sleep disorder affecting about 10% of the adult population. The disorder is associated with cognitive and intellectual impairment, current and subsequent affective disorders, reduced quality of life, and impaired coping abilities. Furthermore, recent studies indicate that insomnia is related to sick leave, long-term work disability and disability pension. These issues will be reviewed in the presentation. Whether insomnia is related to somatic disorders and increased mortality is more controversial. On the other hand, short sleep duration is linked to obesity, diabetes, hypertension and increased mortality. In general, few studies have been able to demonstrate that insomnia is related to objective impairment, such as increased sleepiness (measured by Multiple Sleep Latency Test or reaction time tests). This is considered as a paradox, since insomniacs report a reduced sleep duration. However, a main problem for the insomniacs is a state of hyperarousal, probably explaining the lack of objective sleepiness. Treatment studies have consistently showed that cognitive behavioural therapy (CBT) produces both short- and long-lasting effects on the nocturnal symptoms of insomnia. However, the treatment effects on daytime functioning are less clear, both following non-pharmacological and pharmacological therapies. The reason for this apparent paradox may be lack of adequate instruments measuring daytime impairment in insomnia. These issues will be discussed in the symposium.

S03

Effect of sleep medication on driving ability

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A substantial number of people with insomnia are treated successfully with hypnotic drugs. These sleep medications aid those with sleep complaints in falling asleep, maintaining sleep during the night, or both. Various effective hypnotics have been developed since the introduction of benzodiazepine hypnotics in the 1960s. Benzodiazepines act at the GABAA receptor in the brain. The sedative effects of these drugs help patients fall asleep, but unfortunately next morning residual effects of these drugs are commonly experienced. These residual effects of hypnotics are essentially the same as their therapeutic effects. The residual sedative effects may result in memory deficits, psychomotor problems, and cognitive impairment. Various daily activities such as on-the-job performance and driving a car may be affected by these residual drug effects. Sleepiness and inattention are the main causes of traffic accidents. Reviewing the scientific literature shows that benzodiazepine hypnotics and zopiclone significantly impair driving performance. Tolerance to the impairing effects of these hypnotics develops slowly, and increased traffic accident risks have been reported for patients using these drugs. In contrast, when taken as recommended zolpidem and zaleplon, do not impair next-day driving performance. Indiplon and ramelteon are promising new hypnotics, but their effects on driving are still under investigation.

S04

Insomnia, aging and daytime function– what are we treating?

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Proteomics in Sleep Research – Revealing the Functions of Sleep

S05

Proteomic effects of extended/prolonged wakefulness

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The cellular and molecular processes that underlie the drives and functions of sleep have been the topic of many studies in the last few decades. Discovery-based techniques such as cDNA microarrays have increasingly been utilized in conjunction with sleep deprivation paradigms to examine the molecular mechanisms and functions of sleep. These studies have helped to validate and expand existing hypotheses such as those on the roles of sleep in synaptic plasticity and in energy metabolism. The mechanisms underlying the highly prevalent changes in sleep architecture with age are not known, but likely reflect fundamental changes in the molecular basis of circadian timing and sleep homeostatic processes. Here, we explore the effects and interactions of sleep deprivation and aging utilizing the proteomic technique of difference in gel electrophoresis (DIGE). DIGE, which utilizes cyanine dye labeling of samples, allows for the comparison of multiple experimental groups within and across gels. In this study we compared cerebral cortex tissue from young (2.5 month) and old (24 month) mice that had been sleep deprived for 6 h to tissue from undisturbed young and old control animals. We observed significant differential expression in 7 functional classes based on published characteristics: cell signaling, cytoskeletal, energy metabolism, exocytosis, heat shock proteins, mRNA processing/trafficking, and serum proteins. The identity and characteristics of these proteins relevant to sleep and aging are discussed.

S06

Sleep deprivation-induced changes in proteins in the rat brain

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Prolonged wakefulness is known to lead to decreased neurobehavioral alertness, decreased learning, and overall poorer neurocognitive performance, often referred to as 'sleep debt'. Many of these deficits are associated with basal forebrain, cortex and hippocampus. Previously we have demonstrated that long-term effects of sleep deprivation (SD) include changes in transcription factors and mRNA. Regulatory processes at the level of translation and post-translational mechanisms that either modify the structure and function of the proteins or alter their half-life, their interaction with other proteins, and the rate of synthesis mean that there is not always a direct correlation between mRNA levels and protein function. To discern changes in the expression patterns of proteins in different rat forebrain areas following 6 h of SD (8 AM–2 PM) we performed two-dimensional electrophoresis of total protein and compared with the undisturbed sleeping (control) rats that were killed at the same circadian time (2 PM). Samples from seven rats were pooled and 250 μg gel^{-1} loaded for electrophoretic separation on two pH ranges, pH 5–7 and 4–8 of 2D gels run in duplicate. The silver stained duplicate gels for each pH range for the control and SD were scanned using laser densitometer (Molecular Dynamics Inc.) and analyzed (Progensis Discovery software). The spots showing a three-fold increase or decrease in the spot density were selected for further characterization using MALDI-TOF mass spectrometric peptide analysis of trypsin digested proteins extracted from the gels. The peptide mass spectrum for each protein was matched with SwissProtein or NCBI bank to identify the protein. We observed that SD-induced posttranslational changes in protein structures resulted in shifted spot positions in the Western blots of 2D gels. We have also examined the changes in the protein complexes using immunoprecipitation in order to understand the changes in the function of the proteins that result from protein-protein complex formed with other proteins. These multifunctional proteins are associated with microtubular dynamics, cellular energy mechanisms, molecular trafficking, actin filaments and/or synaptic vesicles endo/exocytosis. Thus sleep deprivation-induced changes in these proteins suggest that dynamic energy changes, cytoskeletal reorganization and synaptic plasticity may underlie the long-term effects of sleep deprivation.

S07

Regional protein expression during spontaneous sleep-wakefulness

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Sleep is an essential behavior orchestrated by the coordinated interaction of a number of brain regions. The biological function (s) of sleep is not known, though a restorative function is widely accepted. Understanding the intracellular response to sleep can provide clues to function. Protein profiling offers the most direct means of assessing the impact of sleep on the intracellular milieu. We used two dimensional electrophoresis (2DE) to analyze protein expression in the frontal cortex of rats after spontaneous sleep-wake bouts. Gels were sequentially stained with SYPRO ruby to detect whole cell protein expression and ProQ Diamond, a stain specific for phosphorylated proteins. Qualitative analyses showed unique protein profiles were detected as a function of the time of day (TOD) and after timed bouts of waking (W), and slow wave sleep (SWS). The percentages of state-related SYPRO ruby spots approximated those reported for mRNA profiles. Phosphorylated profiles showed that distinct cellular activities underlie W and SWS. A total of 18 spots associated with W or SWS were subjected to mass spectrometry analyses. The proteins identified were associated with energy metabolism, cellular transport/cytoskeletal support, the oxidation reduction state, and signal transduction. The expression of GAPDH and actin, associated with SWS, were further examined following sleep deprivation and recovery sleep (SD/RS). There were no changes in gapdh and actin mRNAs following SD/RS. GAPDH protein levels, however, showed an expression pattern characteristic of homeostatic regulation. In contrast, there were no changes in actin protein levels. Western analysis of actin separated by 2DE showed changes in phosphorylation state across SD/RS and spontaneous sleep. Our results show that changes in protein expression occur within the time frames of spontaneous sleep-wake bouts in rats. The functional categories of the state-related proteins are similar to those identified by microarray analyses, indicating that dynamic changes occur within cells in response to sleep. The data suggest that post transcriptional (GAPDH) and post translational (actin) mechanisms underlie state-related expression. Collectively these data are consistent with roles for sleep in many biological functions.

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S08

Human serum protein profile after sleep restriction

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Sleep restriction (SR) might lead to cellular stress. Humans ($n = 6$–8) was subjected to 3 or 6 h of SR and blood were sampled before, during and after the SR-night at the same time points (16, 48 h). Seldi-Tof-MS (Ciphergen), Maldi-Tof-MS (AutoFlex, Bruker Daltonics) and an Hsp70 ELISA-kit (EKS-700 Stressgen biotechnologies) were used to detect changes in the human blood serum proteome. Protein profile changes after SR were searched for by building a decision tree from the information gain in the m/z spectrum. Principal component analysis (PCA, Sirius 7.0-PRS), support vector machine-, decision three-models were also used analyzing the mass spectrometry data. A protein of 71 kDa was decreased in the blood (serum) 0, 3 and 9 h after 3 h SR. Similarly Hsp-70 with molecular weight around 70 kDa was also reduced 0 h, 3 h and 9 h after 3 h SR by the Stressgen-kit measurement. sIgA showed a changed profile after 3 and 6 h SR and the day after the SR night. The protein profile from the Seldi-Tof-MS (2.5–100 kDa, $n = 3$) measurements also showed changed expression for several proteins. Proteins highly expressed at basal level seem to be reduced after SR (not to basal level) the day after or night before. The protein profile from the Maldi-Tof-MS (0.4–15 kDa, $n = 7$) also showed changed expression for several proteins. Several proteins (2.5–100 kDa) where differentially expressed after 3 and 6 h of sleep restriction, specifically Hsp-70 was reduced after 3 h of sleep restriction. The decrease of many proteins as Hsp-70 in the blood during sleep restriction is in line with what has been observed in obstructive sleep apnoeas. Immune parameters as sIgA might reflect a weakened immune response after 3 and 6 h SR and is in line with earlier studies.

Slow Oscillations: fMRI and High-Density EEG Signs During NREM Sleep

S09

Spontaneous and evoked slow oscillations: impact on information processing

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During NREM sleep, cortical neurons are depolarized and fire tonically just as in quiet wakefulness, but these depolarized up-states are interrupted by short, hyperpolarized down-states when neurons remain silent. This alternation involves large populations of cortical neurons and is reflected in the EEG as high-amplitude slow oscillations. This bistability of thalamocortical circuits between up- and down-states appears to be due to depolarization-dependent potassium currents that increase with the amount of prior activation. In my talk I will suggest that intrinsic bistability in thalamocortical networks may represent not only the key mechanism responsible for the occurrence of the spontaneous slow oscillations of sleep, but also the reason why information processing is impaired during NREM sleep. Recent experiments employing a combination of transcranial magnetic stimulation (TMS) and high-density EEG (hd-EEG) have shown that, while during wakefulness the brain is able to sustain long-range specific patterns of activation, during NREM sleep this ability is lost: the thalamocortical system either breaks down in causally independent modules, producing a local slow wave, or it bursts into an explosive and aspecific response, producing a full-fledged slow oscillation. In this perspective, the occurrence of a slow wave, be it local or global, spontaneous or evoked, reflects the inability of thalamocortical circuits to effectively integrate information due to an underlying bistability between up and down states.

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S10

The functional significance of K-complexes: new insights by fMRI

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K-complexes are an essential electroencephalographic hallmark of NREM sleep with still debated functionality. Easily elicited upon external stimulation, these multifunctional phenomena obviously represent a sleep-typical information processing mechanism, but they also subserve the protection of sleep. Using combined EEG/fMRI recordings allows to investigate the neuronal patterns associated with K-complexes. In accordance with a maximum of the electrophysiological deflections over frontocentral regions, we observed prominent negative BOLD responses in the motor/supplementary motor areas extending to medial prefrontal and the cingulate cortices, a patterns also obtained in the successive deepening of NREM sleep. Negative BOLD responses in areas assigned to attentional processing, response selection and motor response may be attributed to sleep defensive mechanisms, delimiting motor arousal reactions upon external disturbances and supporting the consolidation of sleep. However, the appearance of K-complexes could also be associated with regional BOLD increases in prefrontal, temporal and cingulate areas, likely representing a neuronal trace of their active processing and possibly arousing component. In conclusion, fMRI/EEG studies allow to visualize the 'janus-faced' character often ascribed to K-complexes. The strong negative BOLD responses obtained, however, highlights their sleep defensive properties.

S11

Cerebral correlates of non REM sleep oscillations, as assessed by EEG/fMRI

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Using simultaneous electroencephalography and functional magnetic resonance imaging (EEG/fMRI) in non-sleep deprived human volunteers, we characterized the cerebral correlates of spindles, slow and delta waves, considered as identifiable discrete neural events. In humans, some evidence suggests that there are 2 different types (slow and fast) of sleep spindles. An activation pattern common to both spindle types involved the thalami, paralimbic areas (anterior cingulate and insular cortices) and superior temporal gyri. No difference was detected in teh thalamus in the direct comparison between slow and fast spindles although some thalamic areas were preferentially activated in relation to either spindle type. In contrast, at the cortical level, slow spindles were associated with increased activity in the superior frontal gyrus whereas fast spindles recruited a set of cortical regions involved in sensorimotor processing, as well as the mesial frontal cortex and hippocampus. Significant increases in activity were associated with slow waves in several cortical areas including inferior and medial frontal cortices, precuneus and posterior cingulate. As compared to baseline activity, slow waves were associated with significant activity in the parahippocampal gyrus, cerebellum and brainstem whereas delta waves were related to frontal responses. No decrease in activity was ever observed. These results identify regional brain activity increases during spindles and slow waves consistent with the description of the neural underpinnings of these oscillations.

S12

Slow oscillations to consolidate hippocampus-dependent memories

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Sleep strengthens the consolidation of hippocampus-dependent declarative memories. We summarize evidence from studies in humans, epileptic patients and rats indicating that this process of consolidation during sleep relies on a dialogue between the neocortex and hippocampus which is essentially regulated by the < 1 Hz EEG slow oscillation. The slow oscillation is generated within neocortical networks with its amplitude depending on the use of these networks for encoding of information during prior wakefulness, i.e., the more information is encoded during prior waking, the higher the slow oscillation amplitude. The slow oscillation temporally groups neuronal activity into up-states (of strongly enhanced neuronal activity) and down-states (of neuronal silence). Grouping occurs not only in the neocortex but via efferent pathways also in several other structures relevant to memory consolidation, i.e., in the thalamus, generating spindle activity, and in the hippocampus, generating sharp-wave ripples which accompany the replay of newly encoded memories in these circuitries. The synchronizing effect of the slow oscillation enables that inputs fed back from these structures to the neocortex, i.e., the thalamo-cortical spindle activity and the hippocampo-to-neocortical memory replay activity, arrive synchronously at respective neocortical networks. We suppose that this slow oscillation induced synchrony of inputs from thalamus (spindles) and hippocampus (ripples plus memory replay) is critical to the redistribution of memory representations to neocortical networks for long term storage.

Consequences of Restricted Sleep: Adaptive or Maladaptive?

S13

Molecular consequences of acute and chronic sleep loss

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Several recent studies have used transcriptomics and proteomics approaches to characterize the molecular correlates of sleep, waking, and sleep deprivation. Although these studies are still limited in number and focus on a few brain regions, some consistent findings are emerging. Sleep, spontaneous wakefulness, short-term, and long-term sleep deprivation are each associated with the upregulation of hundreds of genes in the cerebral cortex and other brain areas. In fruit flies as well as in mammals, three categories of genes are consistently upregulated during waking and short-term sleep deprivation relative to sleep. They include genes involved in energy metabolism, synaptic potentiation, and the response to cellular stress. In the rat cerebral cortex, transcriptional changes associated with prolonged (several days) total sleep loss differ significantly from those observed during short-term sleep deprivation, and suggest that sustained sleep loss may trigger a generalized inflammatory and stress response in the brain. Also, several plasticity-related genes are strongly induced after acute sleep deprivation only, and several glial genes are downregulated in both sleep deprivation conditions, but to a different extent. A recent study in the telencephalon of white-crowned sparrows during the migratory season, when birds lose approximately two/thirds of their normal sleep, shows that migration may also be associated with brain cellular stress and enhanced energetic demands. So far there is no indication, however, that the cellular stress response induced in the brain by prolonged wakefulness is maladaptive, because long-term deprivation in rats does not seem to trigger extensive oxidative damage.

S14

How the activated brain compensates against lack of sleep–evidence from fMRI studies

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Facing the loss of sleep creates a need to counteract reduced levels of alertness, as well as reduced cognitive, behavioural and often also emotional capacities in order to keep up with environmental demands. Imaging approaches such as functional magnetic resonance imaging (fMRI) allow to investigate more precisely the regional-specific brain activation patterns associated with altered functioning following sleep deprivation. Combining fMRI with simultaneous EEG recordings further opens up the possibility to more closely disentangle the brain activation changes in a fine-grained temporal resolution. This approach allows to demonstrate how the waxing and waning of different vigilance levels following sleep deprivation affects neuronal activation patterns underlying the compensatory mechanisms. In addition, EEG responses such as event-related potentials derived from the EEG recordings concomitant to functional imaging can be exploited. We applied these simultaneously obtained modes of information to study several important basic executive functions in young healthy subjects, showing that inhibitory capacities appear more affected by a lack of sleep than basic reactive mechanisms. Furthermore, different degrees of sleep loss, from total sleep deprivation to several days of partial sleep deprivation, have been targeted. Task-specific areas often display increased activation following sleep loss, aiding to maintain intact levels of performance. However, differential up- and downregulation within the neuronal networks underlying task execution are noted, especially in frontal areas. Some of the additionally recruited brain areas following sleep deprivation as e.g. in anterior cingulate structures are associated to loss of concentration and worse performance, thus in fact may represent maladaptive coping mechanism.

S15

The consequences of chronic sleep restriction: changes in neurobiological and neuroendocrine stress systems

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Chronically restricted sleep is a widespread problem in our modern around-the-clock society. It is commonly believed that insufficient sleep, in the long run, may have repercussions for health and perhaps sensitizes individuals to psychiatric diseases. In this context, we applied an animal model of chronic sleep restriction to study effects of sleep loss on neurobiological and neuroendocrine systems that have been implied in the pathophysiology of depression. Adult rats were exposed to a schedule of chronic partial sleep deprivation allowing them about 4 h of sleep/day. Sleep restriction was achieved by placing the animals in slowly rotating drums. EEG recordings performed during the daily 4 h rest periods showed elevated levels of NREM sleep EEG SWA, suggesting an increase in sleep intensity to compensate for the loss of sleep time. This increase in SWA was attenuated after 8 days of restricted sleep, perhaps reflecting adaptation to chronic sleep loss. A week of sleep restriction caused a reduction in adult hippocampal neurogenesis and altered HPA axis regulation and reactivity. These changes may in part be related to alterations in serotonergic signalling since sleep restricted rats displayed blunted physiological responses to direct serotonin-1A receptor stimulation. This desensitization of the serotonin-1A system persisted for many days even with unlimited recovery sleep. While some effects of chronic sleep restriction may reflect adaptational processes to cope with persistent sleep curtailment, other changes may reflect maladaptation. Although no proof exists for immediate health consequences, the data show that chronic sleep restriction gradually causes changes in neurotransmitter receptor systems and neuroendocrine reactivity in a manner that is similar to what is seen in depression. This experimental study provides support for the hypothesis that disrupted and restricted sleep may contribute to the symptomatology of psychiatric diseases.

S16

Regulation of sleep, glucose metabolism and hunger: consequences of recurrent sleep restriction

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Sleep and energy homeostasis display close relationships that evolution has established in a context of scarcity of food. In our modern societies that encourage physical inactivity and overeating, the increasingly common behavior of voluntary bedtime restriction is therefore likely to trigger metabolic responses that may be referred to as "maladaptive". In support of this hypothesis, laboratory studies in healthy young men have shown that sleep restriction (4 h in bed for 2–6 days) is associated with marked alterations in glucose metabolism and neuroendocrine regulation of appetite. The alterations in glucose regulation included decreased glucose tolerance, impaired beta-cell function and a trend for decreased insulin sensitivity, resulting in an increased risk for diabetes. Recent evidence indicates that not only reduced sleep duration, but also reduced sleep quality may play a role in the pathophysiology of diabetes. Indeed, selective suppression of slow wave activity (SWA), without changes in sleep duration, was associated with marked alterations in glucose metabolism. Interestingly, when sleep restriction extends over a week, we did not observe the expected rebound in SWA (well-described after acute total sleep deprivation). These results suggest that when partial sleep deprivation becomes

chronic, the failure to appropriately compensate sleep loss by an increase in sleep intensity may further increase the severity of the associated metabolic alterations. Restricted sleep also resulted in an up-regulation of the appetite-stimulating hormone ghrelin and a down-regulation of the satiety hormone leptin, and these neuroendocrine changes were strongly correlated with increased hunger, which may lead to overeating and weight gain. In a study involving 3 bedtime conditions (4, 8, and 12 h), leptin levels showed a robust dose-response relationship with sleep duration. Consistent with these laboratory findings, epidemiological evidence supports an association between short and/or poor sleep and the risk for obesity and diabetes. In conclusion, chronic sleep loss, a condition that affects millions of individuals in our modern society, may be involved in the current epidemic of obesity and diabetes.

Brain Plasticity and Memory Consolidation

O01

Role of translation and transcription during sleep-dependent cortical plasticity

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Sleep has long been suspected to facilitate memory formation, but direct evidence that sleep promotes the cellular substrate of memory formation (i.e. synaptic plasticity) is lacking. We have shown that cortical activity during sleep consolidates a classic type of developmental in vivo cortical plasticity (ocular dominance plasticity, ODP). In other systems, persistent forms of synaptic plasticity require both messenger RNA and protein synthesis. Activity-dependent translation is though to be controlled at the level of mRNA translation initiation (mediated by the mTOR pathway) and elongation (controlled by eEF2). We propose to determine if protein synthesis is necessary for the consolidation of visual (V1) cortical plasticity during sleep and to identify the responsible mechanisms. We will use Western blots and quantitative RT-PCR to assess changes in expression of key proteins and mRNA involved in activity-dependent protein synthesis and gene expression in remodeling brains after sleep. To determine the necessity of these pathways, we will also inhibit the mTOR pathway with rapamycin and global cortical protein synthesis with cycloheximide. After inducing cortical plasticity (monocular deprivation, MD), the drugs are infused in V1 during sleep and the effect on ODP is assessed with optical imaging of intrinsic cortical signals and single-unit electrophysiology. Preliminary Western-blots results suggest a specific and simultaneous activation of the mTOR and the eEF2 pathways in the remodeling V1 tissue during sleep. This suggests a coordinate process of enhanced translation initiation and reduced peptide chain elongation. The requirement of *de novo* protein synthesis during sleep-dependent ODP was further confirmed by our results showing that both cycloheximide and rapamycin impair the consolidation of ODP during sleep. Finally, RT-PCR performed on the same tissues showed a decrease of 50 to 80% of immediate-early genes (Arc, c-Fos) during sleep specifically after MD compare to control sleeping animals. Taken together, our results suggest that sleep promotes translation of specific mRNA relevant for synaptic function (activation of mTOR pathway) and that this process is accompanied by a shut-down of global translation (eEF2 phosphorylation) and transcription.

O02

Evidence for a 2-step model of sleep and memory: learning-dependent changes in sleep spindles and theta in rats

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How does the brain form enduring memory traces? Sleep has been proposed to play a role in memory consolidation. REM sleep increases following avoidance learning, and memory is impaired if REM deprivation occurs during these post-training periods, termed REM sleep windows (RSWs). Little is known about the characteristics of the RSW involved in memory consolidation.

Method: Twenty male Sprague-Dawley rats (250–300 g) were implanted with four EEG and two EMG electrodes. After recovery, 3 days of acclimatization, and 24 h of baseline (BL) recording, animals were trained on the two-way avoidance task for 100 trials (50 trials day^{-1}) from 9–11 AM and re-tested for 25 trials on day 3. EEG was recorded for 22 h after training on both training day 1 (TD1) and TD2. Rats in the learning group (LG) ($n = 8$) avoided footshock on 60% of the last 20 test trails. The remaining rats ($n = 12$) were assigned to the non-learning group (NLG).

Results: The LG increased avoidances over 5 blocks of 20 trials ($F = 4.16$, $P = 0.006$) and no change in the NLG. The change in REM from BL was higher for the LG ($F = 2.74$, $P = 0.02$) on TD1 during h 17–20 ($t = 3.66$, $P = 0.002$). Theta power increased during REM in the LG from BL to TD1 ($F = 2.83$, $P = 0.03$) in h 17–20 ($t = 2.43$, $P = 0.03$). Sigma power increased for the LG in REM ($F = 3.12$, $P = 0.05$) during h 21–24 ($t = 2.90$, $P = 0.01$) and SWS ($F = 3.37$, $P = 0.04$) during h 21–24 ($t = 2.48$, $P = 0.02$). Sleep spindle density increased for the LG in SWS ($F = 2.55$, $P = 0.03$) during h 21–24 ($t = 2.95$, $P = 0.01$) and in REM ($F = 2.61$, $P = 0.05$) during h 21–24 ($t = 2.52$, $P = 0.03$).

Discussion: REM and theta increased in learning rats during 17–20 h, suggesting that theta is involved in memory consolidation during the RSW. Sigma and spindles increased from 21–24 h in both REM and SWS. Spindles were not identified during tonic theta in REM, thus spindles were likely identified during transition sleep. The results suggest that a 2-step process is involved in sleep-dependent memory consolidation. First, theta increases to organize and consolidate material via hippocampal-neocortical dialogue, followed by subsequent refinement in the cortex by spindles during transition sleep and SWS.

O03

The role of sleep in motor adaptation memory consolidation assessed by fMRI

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The aim of this study was to characterize the cerebral correlates of overnight procedural memory consolidation, using a motor adaptation task. The task, performed with a mouse in the scanner, consisted in reaching a target displayed on the screen. A 60° angular deviation was introduced in the trajectory of the mouse displayed on the screen. Subjects had to adapt their movement to the angular deviation to reach the target as fast as possible. Thirty-one subjects were trained to the task then divided in two groups whether they slept (N = 16) or were totally sleep-deprived (N = 15) on the post-training night. Both groups were tested on the task 3 days later, allowing 2 recovery nights for the sleep-deprived subjects. Functional MRI data were acquired during both training and testing sessions (3T Allegra MR scanner, Siemens) and analysed using SPM2 (http://www.fil.ion.ucl.ac.uk). Performance (speed to reach the target) significantly increased in both groups during training ($P < 0.0001$) and this effect did not differ between groups ($P > 0.9$). A significant response to the practice of the adaptation task modulated by performance improvement was observed bilaterally in the ventral putamen. Performance during retest in sleepers did not improve nor deteriorate but were maintained as compared to the end of training ($P = 0.15$). In contrast, performance in sleep deprived subjects significantly decreased (deterioration, $P = 0.006$) at retest as compared to the end of training and more than in sleepers ($P = 0.04$). Cerebral responses to the adaptation task did not increase from training to retest sessions in sleepers as compared to sleep deprived subjects. In contrast, right intraparietal sulcus, bilateral cerebellum hemispheres, right superior frontal gyrus and anterior cingulate cortex were more activated during retest as compared to training in sleep deprived subjects as compared to sleepers. Our results suggest that post-training sleep, but not sleep deprivation, leads to maintained motor skill performance at delayed retest session. Performance deterioration observed after sleep

deprivation was linked to the activation of a cerebello-cortical network usually observed in the early stages of motor learning.

O04

Low-Resolution Brain Electromagnetic Tomography (LORETA) reveals off-line neuronal re-processing of motor learning during post-training REM sleep

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Introduction: There is increasing evidence that sleep has an important function in motor learning. Smith et al. (Psychologica Belgica 2004;44:81–104) hypothesized that REM sleep is specifically required for tasks new and unfamiliar to the learner.

Methods: Twenty-four young healthy subjects (13 females, 11 males; aged 23.1 ± 2.6 years) participated in an implicit procedural motor learning task (mirror-tracing task). After an entrance examination and a screening/adaptation night subjects underwent two experimental conditions in the sleep lab (control and experimental condition in randomized order). Sleep stages and sleep-related EEG patterns were identified by the Somnolyzer 24×7 system and brain activity was estimated by LORETA (21 EEG-channels, spectral power at discrete frequency pins).

Results: Performance in the mirror tracing test was improved in the morning as compared with the evening retrieval (error time, $P<0.001$). While no correlations between R&K-derived measures of sleep and task performance were observed, LORETA sources in the motor cortex at around 10 Hz and 20 Hz (the two main frequency components of the rolandic mu rhythm) correlated significantly with overnight improvement. Interestingly, the correlations were positive for REM episodes with predominant theta waves ($r=0.76$, $P<0.001$) and negative for REM episodes with low-voltage mixed-frequency EEG ($r=-0.62$, $P<0.001$).

Discussion: Sleep improved task performance in a motor learning task. The significant positive and negative correlations between LORETA sources of the rolandic mu rhythm and overnight task improvements might reflect a desynchronization and synchronization as described in wakefulness after hand movements but also after imagination of movements only (Pfurtscheller and Lopes da Silva, Clin Neurophysiol 1999;110:1842–1857). Similar characteristics of the rolandic mu rhythm during REM and wakefulness have already been described by Duntley et al. (Clin Neurophysiol 2001;112:528–531).

Conclusion: The observed brain-behavior correlations strengthen the hypothesis of off-line neuronal re-processing of a novel motor task during post-training REM sleep.

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O05

Does sleep favour forgetting of irrelevant information?

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Numerous data indicate that sleep favours memory consolidation [1]. However, some authors proposed that sleep may also help to forget irrelevant information [2]. To test this hypothesis, we investigated the effect of sleep and lack of sleep on memory performance using the directed forgetting paradigm. Young subjects performed a directed forgetting task (item procedure). During the encoding phase, words were presented during 1 s, and were followed by the instruction "to be remembered (TBR)" or "to be forgotten (TBF)" during 3 s. Then, subjects were randomly divided in two groups whether they slept (RS group, $n=14$) or not (TSD group, $n=12$) during the first post-learning night. Memory performance was assessed after two recovery nights using a recognition task. This task consisted in the presentation of words that subjects have to categorize as previously encountered (whatever the instruction furnished) or not. The directed forgetting effect is observed when performance for TBR items is better than for TBF ones. A repeated measures ANOVA (with group as between subject factor, and item type as repeated measure factor) conducted on the items categorized as previously encountered revealed a significant effect of group ($P<0.001$), indicating that TSD subjects recalled more words than RS ones. This analysis also disclosed a main effect of the item type ($P<0.001$; TBR $>$TBF) and a significant interaction between both factors ($P<0.03$). Post hoc analyses indicated that TSD and RS subjects did not differ concerning the number of TBR items correctly memorized ($P>0.16$). In contrast, TSD participants recognized more TBF items than RS subjects ($P<0.001$). Finally, a one-way ANOVA carried out on the difference (TBR-TBF) for the items recognized revealed a significant effect of group ($P<0.03$). Thus, the magnitude of the directed forgetting effect is larger in the RS group than in the TSD group. Our data clearly indicate that sleep favours the forgetting of irrelevant information, suggesting that memories inhibited at encoding are not reprocessed and consolidated during sleep.

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2. Crick and Mitchinson 1983, Nature, 304: 111–4.

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O06

Improving memory: a matter of temperature during sleep

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Recent studies have demonstrated that Slow Wave Sleep (SWS) is related to declarative memory consolidation (Marshall et al. 2006). Additionally, it has been shown that increasing skin temperature during the early part of the night leads to an increment of SWS (Raymann et al. 2008). In this study we examined the possibility of boosting the process of memory consolidation during sleep by increasing skin-body temperature. In a repeated measures design subjects learned a list of unrelated word pairs to a criterion of 60%. Afterwards, they spend two nights in the sleep-lab during which, in one of the two nights their skin-temperature was slightly warmed-up (warm condition) whereas in the other it wasn't (cold condition). EEG recordings and skin-temperature recordings where made during the night. Preliminary results show that subjects who reported having noticed the difference in temperature between the two nights performed better at subsequent memory testing after the night in the warm condition compared to the cold condition. This is the first study to provide evidence for a link between body-temperature and memory consolidation during sleep. The data further add to the notion that SWS is directly related to hippocampus dependent memory consolidation and open-up exiting possibilities for boosting this phenomenon.

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O07

Sleep-dependent enhancement of emotional source memory

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A growing body of evidence suggests that mnemonic representations of newly encoded episodes are strengthened during sleep. Two recent behavioural studies extend this literature by showing that such sleep-dependent consolidation is particularly apparent for emotional episodes. The authors of these studies suggest that the selective enhancement of emotional memories during sleep may be due to increases in connectivity between amygdala and hippocampus which are facilitated by sleep physiology. The aims of the current study were 1) to search for sleep-dependent enhancement of emotional source memory, 2) to identify localised regions of sleep dependent neuroplasticity associated with such enhancement, and 3) to test the hypothesis that sleep leads to strengthened connectivity between amygdala and hippocampus during retrieval of emotional memories. To fulfil these aims, we examined negative and neutral source memory for visual stimuli in 22 subjects. All subjects were tested after a 12 h consolidation period, however this contained a night of sleep in only half of them (SLEEP group), while the other half consolidated across a day of wakefulness (NO SLEEP group). Functional magnetic resonance imaging (fMRI) was used to examine neural activity during recall, and data were analysed data using a random effects model in SPM. Our behavioural results show a main effect of emotion, with negative stimuli remembered better than neutral stimuli ($P<0.05$), but no main effect of sleep or interaction between sleep and emotion. Our analysis of localised changes in fMRI activity shows sleep-dependent increases in activation of the parahippocampus and left posterior cingulate in association with the correct recall of negative as compared to neutral background images ($P<0.001$ uncorrected). Analysis of connectivity between the medial temporal lobe and amygdala shows enhanced correlation between the parahippocampus and bilateral amygdala. These results constitute one of the first demonstrations of neuroplasticity in the emotional memory system as a result of sleep, and demonstrate that sleep can lead to enhanced connectivity between amygdala and medial temporal lobe during emotional recall.

O08

Hippocampal-neocortical interactions in long-term memory consolidation depend on sleep

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After encoding, memory traces are initially fragile and have to be reinforced to become permanent. The initial steps of this process occur at a cellular level within minutes or h. Besides this rapid synaptic consolidation, systems consolidation occurs within a time frame of days to years. For declarative memory, the latter is presumed to rely on an interaction between different brain regions, in particular the hippocampus and the medial prefrontal cortex (mPFC). Specifically, sleep has been proposed to provide a setting that supports such systems consolidation processes, leading to a transfer and perhaps transformation of memories. Using functional magnetic resonance imaging (fMRI), we show that post-learning sleep enhances hippocampal responses during recall of word pairs 48 h after learning, indicating intrahippocampal memory processing during sleep. At the same time, sleep induces a memory-related functional connectivity between the hippocampus and the mPFC. Six month after learning, memories activate the mPFC more strongly when they were encoded before sleep, showing that sleep leads to long-lasting changes in the representation of memories on a systems level.

O09

Napping and paired associate declarative memory: effects of semantic relatedness and level of learning

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Existing literature suggests that sleep may differentially benefit memory for related and unrelated word pairs. We have recently shown that pre-existing relatedness, as well as level of word pair learning, moderates the effects of overnight sleep on declarative memory (Lo, Dijk, and Groeger, submitted). Compared to daytime wakefulness, overnight sleep increased the recall probability of poorly-learned related word pairs, but increased the recall probability of well-learned unrelated word pairs. Here, we investigated the effects of daytime napping on declarative memory, while also manipulating level of learning by requiring word pairs to be learned with and without a concurrent distracting task. Participants ($N = 15$) attended four laboratory sessions (nap-distraction, nap-control, wake-distraction, wake-control) during which they acquired the associations of semantically related and unrelated word pairs, with or with concurrent distraction. Thereafter they remained awake, or had a 90-min nap opportunity, before having multiple attempts to recall the learning materials. Nap duration and architecture were similar for the distraction and the no-distraction conditions. Naps lasted 68.6 ± 14.0 min with $4.3 \pm 4.5\%$ S1, $40.7 \pm 11.6\%$ S2, $6.3 \pm 3.7\%$ S3, $19.5 \pm 11.1\%$ S4, and $24.4 \pm 15.6\%$ REM sleep. Distraction reduced learning, resulting in 46% more poorly-learned and 18% fewer well-learned pairs, but did not differentially affect later recall. For poorly learned materials, related word pairs were more likely to be recovered after nap than wakefulness (probability = 0.32 versus 0.13; $t = 4.44$, $P = 0.01$), but this effect was not observed with unrelated pairs (0.03 versus 0.06; $t = 1.41$, $P > .05$). For well learned materials, the advantage of nap was found only in unrelated word pairs (0.81 versus 0.70, $t = 3.04$, $P = 0.01$; related: 0.85 versus 0.83, $t = 0.91$, $P > .05$). Daytime naps benefit recall of both well established and newly acquired declarative knowledge, but this effect is moderated by the extent of learning prior to sleep.

O10

Declarative and procedural memory tasks have a different effect on brain synchronization during subsequent sleep

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Sleep benefits consolidation of memory. This consolidation is presumably accompanied by changes in brain activity during sleep following acquisition of a skill or of information. Local increases in sleep EEG slow-wave activity have been reported following memory acquisition, but it is unknown if changes also occur in neural interactions and network characteristics in humans. We examined twelve subjects who slept in the MEG scanner on two occasions, i.e. after a visuomotor skill task (mirror tracing) or after a declarative task (face-name learning). We selected three 20-sec epochs of stage 2 sleep per subject per session and computed short-range and long-range synchronization likelihood (SL) and the graph theoretical neural network parameters Clustering Coefficient (C) and Pathlength (L) for each of the frequency bands. SL is a measure of synchronization that includes both linear and non-linear coupling (Stam and Van Dijk, Physica D 2002). We

examined these parameters using within-subject statistics. Across frequency bands, mirror tracing induced a higher short-range SL in right frontocentral areas than face-name association learning. In adition we found a higher long-range SL in the right and left hemisphere and between homologous areas in the two hemispheres, which was different for each frequency band. In the delta, theta, sigma and beta bands, overall L was higher for the mirror tracing task, indicating interactions more characteristic of an ordered network. We suggest that neural interactions during sleep are modified by learning experiences occurring before sleep and that these may contribute to consolidation of the information acquired.

What is this Thing Called Insomnia?

O11

Selective attention to sleep is not an artefact of sleep complaint in insomnia: a study with pregnant and postpartum women

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Introduction: Espie et al. (2006) propose a route into primary psychophysiological insomnia (PI) along the attention-intention-effort pathway which focuses on the inhibition of sleep-wake automaticity. A contributing factor to this is selective attention to sleep (alongside explicit attention to sleep and effort in the sleep engagement process). Previous research has established selective attention to sleep in PI by demonstrating altered attentional processing of sleep stimuli in PI compared to normal sleepers. Comparison has not been previously made in the area of attentional bias between PI and another group presenting with a similar sleep complaint but due to other factors. Pregnant and postnatal women represent such a group. Waters and Lee (1996) found significant changes in sleep from the third semester of pregnancy to the first postpartum month, with primiparous first time mothers experiencing a drop in sleep efficiency from 90% to 77%.

Method: An ICB flicker paradigm was employed to investigate whether selective attention to sleep was unique to PI or was an artefact of sleep dissatisfaction/deprivation. A between subjects design was used to analyse responses of pregnant and postnatal women obtained from a computer task presenting images of sleep salient and neutral images. The women taking part in the study were classified by stage of pregnancy (1st, 2nd or 3rd trimester) or postpartum period (3–6 months, 6–9 months or 9–12 months). The reaction time of interest was the time taken to identify an object which changed between two images presented consecutively.

Results: Comparisons were made between means for selected factors. In line with the current models of PI, no relationship was found between pregnancy/postpartum stage and reaction time on the computer task. Saliency of the stimuli also did not have an effect.

Conclusion: This study suggests that selective attention is not an artefact of sleep complaint but an identifiable trait in PI. Also, these results lend support to the attention-intention-effort model (Espie et al. 2006) and the cognitive model of insomnia (Harvey 2002) which considers the importance of selective attention towards salient stimuli in the maintenance of insomnia.

O12

Validation of a misperception index to measure the error in sleep estimation and identify paradoxical insomniacs

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The aim of the present study was to validate statistically a new index, correlated positively with the magnitude of sleep misperception and able to indicate its direction, in a large group of healthy subjects and in another with primary insomnia. An attempt was also made to establish an eventual threshold value for sleep misperception in the diagnosis of PI. A Misperception Index (MI) was established as the ratio between the difference between subjective (sTST) and objective (oTST) total sleep time, which was computed using the following formula: MI = (oTSTsTST)/oTST. The statistical properties of this index, which can range between -1 and $+1$, were analyzed in detail in a group of 288 normal subjects selected among those who participated to the Sleep Heart Health Study and also served to establish the minimum amount of sleep needed for a reliable subjective estimation, in normal condition. Subsequently, MI was computed in a large group of 159 patients with primary insomnia, prospectively enrolled in this study. By drawing a bimodal distribution, the statistical analysis of MI in insomnia patients was able to disclose the presence of two subgroups, one with a moderate sleep misperception (132 patients) and another with high sleep misperception (27 patients). The latter presented MI values ≥ 0.9, exhibiting statistical properties different from those with MI < 0.9 and from normal subjects. The Bland-Altman test demonstrated a reliability of the index for values of oTST > 120 min. This study demonstrates that the application of a standardized and statistically validated approach to the study of sleep misperception in primary insomnia is able to disclose a subgroup o patients with a probable true sleep misperception insomnia which might be as rare as reported in the current classification system.

O13

Minimal Insomnia Symptom Scale (MISS) in patients with persistent insomnia

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Background: Minimal Insomnia Symptom Scale (MISS) was recently introduced as an ultra-short screening instrument for insomnia in the general population (Broman J-E, Smedje H, Mallon L, Hetta J. The Minimal Insomnia Symptom Scale (MISS): A brief measure of sleeping difficulties. Ups. J. Med. Sci. 2008;113:in press). The aim of the present study was to investigate some of its measurement properties in a group of insomnia patients. MISS was compared to two other established insomnia scales, the Insomnia Severity Index (ISI) and the Pittsburgh Sleep Quality Index (PSQI) and to a depression scale, the Montgomery-Asberg Depression Rating Scale-Self-rated version (MADRS-S). Further, possible relationships to polysomnographic (PSG) sleep variables were evaluated.

Method: A consecutive series of 48 patients (31 women and 17 men; mean $\pm$ SD age 44 ± 13 years) were evaluated at a sleep disorders unit. They fulfilled DSM-IV criteria for insomnia. All patients filled in the questionnaires and performed polysomnography during two nights with the second night used for analysis.

Results: MISS total score ranged from 4 to 12 and its mean $\pm$ SD was 8.9 ± 2.0. MISS correlated significantly to ISI (rho = 0.53; $P < 0.001$) and to PSQI (rho = 0.57; $P < 0.001$) but correlated less to MADRS-S (rho = 0.22; n.s.). With regard to polysomnography MISS was significantly related to Sleep Latency (rho = 0.37; $P < 0.05$) but not to Total Sleep Time (rho = -0.10; n.s.). MISS was also significantly related to number of minutes in Stage 1 (rho = 0.29; $P < 0.05$) and Stage 3–4 (rho = -0.46; $P < 0.001$) but not to Stage REM (rho = -0.07; n.s.) or to Stage 2 (rho = 0.16; n.s.).

Conclusion: In this clinical insomnia sample, the brief and easily administrated MISS was significantly related to other established insomnia scales but less so to a depression rating scale. Further it was significantly positively related to PSG sleep latency and amount of Stage 1 and negatively to amount of Stage 3–4. Results indicate that MISS may be a promising tool in the assessment of insomnia.

O14

Subjective daytime sleepiness is associated with mood but not daytime performance in primary insomnia

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Background: The existence of a minority (up to 25%) of People with Insomnia (PWI) reporting symptoms of daytime sleepiness has been consistently described in the literature (Moul et al. 2002; Rosenthal, 2003).

Aim: 1) To assess whether, for some PWI, sleepiness is a stable feature of their symptoms; and 2) To assess whether sleepy and non-sleepy PWI differ on measurements of mood, daytime performance and occupational impairment.

Design: Eighty-six participants aged 25–50 years (43 meeting DSM IV criteria for primary insomnia and 43 controls) completed a 9 month prospective study with assessments at baseline, 4 and 8 months. At baseline, Epworth Sleepiness Scale (ESS) scores did not discriminate between PWI and controls (7.47+3.19 versus 6.93+4.15 respectively; $F = 0.38$, $P > 0.05$). However, within the PWI group, 12 (25%) participants scored >10 (indicating clinically significant sleepiness). PWI were then divided into sleepy (ESS >10) and non-sleepy (ESS<10) sub groups, and compared on a range of outcomes across the study time points.

Results: Relative to the non-sleepy sub group, sleepy PWI showed significantly elevated trait anxiety (42.52+10.23 versus 51+14.73; $F = 4.62$, $P < 0.05$) and (BDI) depression scores (9.58+6.63 versus 16.50+12.59; $F = 6.07$, $P < 0.05$) at baseline. ESS differences between the two subgroups remained stable and significant across the 3 time points (Main Effect $F = 22.88$, $P < 0.001$). While trait anxiety mean differences between the sub groups were observed at each time point, the Main Effect from repeated measures ANOVA fell just outside the level of significance ($F = 3.14$, $P = 0.08$). No differences were found between the sub groups on PVT performance. However, self reported occupational impairment (OISQ score) was significantly higher among sleepy PWI (17.45+13.03 versus 25.08+12.56; $F = 3.02$, $P < 0.05$).

Conclusion: Sleepiness is a stable feature of insomnia for a minority of PWI who are characterised by higher levels of depressive symptoms and anxiety.

O15

Sleep-onset and neuroticism: what is the connection?

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Many people with sleep-onset problems experience neuroticism. To what extent these problems are related is largely unexplored. We used data from a Swedish longitudinal project to examine this relation. Participants reported about sleep-onset problems experienced at ages 16 through 17, 25, and 37. Questions about sleep were from health questionnaires used in the Solna Project (Karlberg, Klackenberg, Engström, Klackenberg-Larsson, Lichtenstein, Stensson, and Svennberg, 1968). Participants also reported about neuroticism experienced at age 16 with the High School Personality Questionnaire (HSPQ) and at age 37 with the Eysenck Personality Questionnaire (EPQ-I). The results showed that sleep-onset problems were predictive of neuroticism over time. Neuroticism, however, was not predictive of future sleep-onset problems. Thus, any relation between neuroticism and the development of sleep-onset problems is likely through indirect paths. There was a significant interaction between adolescent sleep-onset problems and neuroticism in predicting neuroticism in midlife. It appears that early sleep-onset problems may be detrimental for later emotional stability. Based on these findings, we suggest continued research into the mechanisms behind the development and maintenance of sleep-onset problems. We also suggest that future research examines the long-term effects of sleep-onset problems on psychological health and well-being.

O16

Insomnia and neuropsychological performance: a meta-analysis

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Introduction: Individuals with insomnia consistently report difficulties pertaining to their cognitive functioning. However, studies comparing their performance to that of normal sleepers on neuropsychological tests have generated inconclusive findings. This meta-analysis was conducted to quantitatively summarize available data about the magnitude of differences between individuals with insomnia and normal sleepers on neuropsychological test performance.

Methods: Reference databases were searched for studies comparing adults with primary insomnia to normal sleepers on neuropsychological measures. Neuropsychological variables for which effect sizes could be computed were extracted from each study and classified independently by two licensed neuropsychologists according to the main cognitive function expected to be measured. Individual effect sizes (Cohen's d) were weighted by their variability and combined using a fixed effects model. Average effect sizes and their 95% confidence intervals were computed for each cognitive function.

Results: Seventeen studies met inclusion criteria, totalising 324 individuals with insomnia and 301 normal sleepers. Significant impairments ($P < 0.05$) of small to moderate magnitude were found in individuals with insomnia for tasks tapping episodic memory (ES = – 0.38), manipulation in working memory (ES = – 0.36), verbal fluency (ES = – 0.32), problem solving (ES = – 0.30), sustained attention/vigilance (ES = – 0.29) and retention in working memory (ES = – 0.19). Individuals with insomnia also tended to perform worse, although not significantly so, on tasks measuring divided attention (ES = – 0.33), selective attention (ES = – 0.29) and cognitive flexibility (ES = – 0.26). Performance was not significantly impaired for tasks assessing psychomotor functions (ES = 0.14), alertness (ES = – 0.07), visual scanning (ES = – 0.11), procedural learning (ES = – 0.01), and reading speed (ES = – 0.16).

Conclusions: Individuals with insomnia exhibit impairments for several cognitive functions (complex attention, working memory, episodic memory and executive functions). While these impairments appear small in magnitude, further comparisons with normative data are warranted to establish their clinical significance. Future studies should include larger samples and use more sensitive instruments.

O17

Non-restorative sleep: a distinct, stable component of insomnia associated with impaired daytime function

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Introduction: DSM-IV criteria characterize insomnia as difficulty initiating or maintaining sleep (DIS or DMS) or non-restorative sleep (NRS), causing clinically significant daytime distress or functional impairment for $\geq$ 1 month. This is the first study to objectively identify NRS as an distinct symptom of insomnia and demonstrate its stability over 1 month.

Methods: Subjects reporting awakening unrestored or unrefreshed (NRS) $\geq$ 3 times/week over the previous 3 months were assigned to cohorts (DIS, DMS, DIS+DMS, or NRS only) based on self-reports and verified by polysomnography (PSG) on 2 consecutive nights. Subjects in the NRS only cohort had adequate opportunity for sleep (6.5–8.5 h in bed/night) with no DIS or DMS. Healthy volunteers (HV) were also assessed. Initial PSG and repeat PSG after 1 month were performed to obtain objective measures of latency to persistent sleep (LPS) and wake after sleep onset (WASO). Daytime function was assessed at screening and after 1 month with patient reported measures including the Epworth Sleepiness Scale (ESS), Multidimensional Assessment of Fatigue (MAF) and Pittsburgh Insomnia Rating Scale (PIRS).

Results: Self-characterization was confirmed by PSG on enrollment; cohorts were: DIS ($n = 56$), DMS ($n = 18$), DIS+DMS ($n = 37$), NRS only ($n = 115$) and HV ($n = 52$). Initial PSG measures were similar in NRS only and HV: LPS 13 and 10 min, respectively, versus >60 min in DIS and DIS+DMS cohorts; WASO 32 and 30 min, respectively, versus >90 min in DMS and DIS+DMS cohorts. Repeat PSG revealed that more subjects in the NRS cohort had symptom stability over 1 month than in the other insomnia cohorts (78% versus 39–59%). Daytime assessments revealed a different pattern in the NRS cohort compared with HV at enrollment: ESS score was 8.6 in NRS only versus 5.9–7.5 in other insomnia cohorts and 2.4 in HV. Equivalent MAF scores were 24.0, 23.0–26.9 and 3.0, and PIRS scores were 44.6, 61.5–76.4 and 4.7. Repeat assessment showed that similar patterns were observed 1 month later.

Conclusion: A cohort of subjects with NRS in the absence of DIS or DMS was identified (using both patient reports and PSG measures) and shown to have symptom stability over time. Daytime functional impairment in these subjects was similar or greater to those with DIS and DMS.

O18

Anatomical and functional MRI studies in primary insomnia

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Rationale: Primary Insomnia (PI) is thought to be due to a process of psychophysiological hyperarousal. Evidence for this hypothesis stems from investigations on autonomic, neuroendocrine, neurophysiologic and central nervous (PET)parameters. The present study uses Magnetic Resonance Imaging (MRI)both from an anatomical and a functional perspective to further test the hyperarousal concept.

Material and Methods: Ten drug-free patients with PI (5 males, 5 females, mean age: 45.2 years) and 10 Good Sleeper Controls (GSC) matched for age, sex, body mass index and handedness participated in the study. MRI scans were performed on a 1.5 T Magnetom Sonata scanner and included besides anatomical scans of the brain a functional paradigm in which subjects were instructed to open and close their eyes with simultaneous EEG and BOLD effect measurement.

Results: Patients with PI and GSC differed highly significant on the sum score of the Pittsburgh sleep quality index with PI patients displaying higher values corroborating their diagnosis. Anatomical scans revealed significantly decreased bilateral hippocampal volumes in PI compared to GSC. In the functional paradigm patients with PI displayed significantly increased alpha-attenuation. Localization of alpha-rhythm did not differ between PI and GSC.

Conclusion: PI seems to be coupled with reduced hippocampal volumes, which could be viewed as a consequence of long-lasting hyperarousal. In the same vein, alpa attenuation in an eyes open/closed paradigm was increased in PI, also supporting the hyperarousal concept of PI. Brain areas involved in generating the alpha rhythm did not differ in PI compared to GSC.

O19

Structural consequences of chronic insomnia: a voxel-based morphometric study

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Chronic insomnia affects an increasingly large part of the population, especially at later stages of life. Few studies so far, however, describe how this condition affects brain functioning. Functional imaging studies with insomnia patients suggest hypoactivation in the prefrontal cortex during daytime compared to healthy controls. Now investigating structural brain volumetry in insomnia, we compared 24 elderly insomnia patients (age range 50–75 years, 17F) with a group of 13 healthy age-matched well- sleeping control subjects (9F). Using optimized voxel-based morphometry (SPM5), we analyzed grey and white matter differences between groups. A voxel threshold of $P<0.001$ and cluster threshold of 25 voxels was applied. Individual total grey and white matter volume differences and age differences were corrected for. In the left orbitofrontal cortex, corresponding to Brodmann area 47, an area of reduced grey matter was found for the group of insomnia patients compared to healthy controls. Additionally, areas of reduced grey matter were found in the left sensorimotor cortex and left precuneus. Conversely, no grey matter decreases were found for the healthy controls compared to the patients, nor did we find white matter differences in any of the contrasts. Age differences or depression scores did not explain the results. Severity of insomnia showed a strong relationship with grey matter values within the group of insomnia patients in the left orbitofrontal cortex (regression coefficient -0.71, voxel threshold $P<0.001$, cluster threshold 10 voxels). Using arterial spin labeling (ASL) on the same set of subjects, we showed that the reduced grey matter was associated with a left inferior frontal area of lower perfusion in the insomnia patients as compared with the healthy controls. In conclusion, chronic insomnia can lead to reductions in grey matter in brain areas important for cognitive flexibility. The results of this study shed more light on an underdiagnosed condition and its effect on brain functioning.

O20

Baroreceptor sensitivity during wakefulness is not reduced in patients with primary insomnia

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Introduction: Insomnia has been linked to cardiovascular disease and changes in autonomic function. Reduced baroreceptor sensitivity (BRS) is an adverse prognostic cardiovascular risk marker and provides an insight into autonomic control of cardiovascular function. BRS is unknown for patients with primary insomnia.

Methods: Primary insomnia was diagnosed in 21 patients (18 female/3 male) according to DSM-IV criteria. A posteriori, patients also hold characteristics of psychophysiological insomnia according to ICSD-2. Patients were assessed using history, PE, standardized interviews (MINI), questionaires (PSQI/BDI/ESS/sleep protocol), bloods, EKG and drug screening. Nighttime related respiratory events as well as PLM were investigated using an Embletta polygraphic 6-channel device with nasal canula, abdominal and thoracic movement, body position and activity, pulsoximetry and leg movement sensors. The healthy sleepers control group had been established similarily with additional attended polysomnography (PSG). Spontaneous BRS was cross spectrally analysed from heart rate and blood pressure variability which had been extracted from ECG data and noninvasive Portapres technology blood pressure data. BRS was calculated from 3 min periods as alpha index of Pagani. Measurements followed a standardized

protocol which controlled for breathing frequency (12 breaths per minute (bpm)) and for daytime (9 to 12 am). 21 Patients and 21 controls were matched for age, gender and BMI. The mean age was 48.2 (SD 10,4) and 48.5 (SD 11.1) years. None were overweight or obese. Mann-Whitney-U-Test at a level of significance of 5% of statistical significance and 10% for statistical trends was used.

Results: Daytime BRS showed no significant differences or trends between patients with primary insomnia and healthy controls (median (25-; 75-percentile)): 8.1 (5.8; 14.7) versus 9.6 (6.9; 15.8) msec/mmHg, $P = 0.554$. Neither did absolute or low or high frequency bands of heart rate or blood pressure variability or BRS as secondary additional markers of autonomic function differ between groups.

Conclusion: Our data demonstrate an unimpaired BRS as an indicator of unelevated cardiovascular risk and of intact baroreflex functioning in patients with primary insomnia.

Ten Things You Did Not Know About Sleep Apnoea

O21

Differential control of the upper airway and diaphragm muscles induced by 5-HT1A receptor ligands and electrical stimulation of selective medullary Raphe Nuclei

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Oropharyngeal obstructive apneic events in Sleep Apnea Syndrom (OSAS) in human and dog involve anatomical abnormalities, muscular atonia in sleep and selective inhibition of upper airway muscles (UAM) respiratory activity while the DIA remains active (1). Based on previous studies (2,3), we explored: (i)the role of 5-HT system via the 5-HT1A receptors, (ii) the role of the medullary raphe (MR) using High-frequency stimulation (HFS), on the differential control of breathing between UAM and DIA in no-apneic animal. 8OHDPAT (ago 5-HT1A) and WAY100635 (antago 5-HT1A) were injected alone or mixed, by central route and compared to saline solution ($n = 35$). HFS was selectively performed within the Raphe Obscurus (Rob), Raphe Magnus (RMg) and Raphe Pallidus (RPa) ($n = 7$). Responses were evaluated on several UAM innervated by different cranial nerves, DIA activities, oxygen saturation, respiratory rate (RR) in anesthetized rats. The inspiratory bursts of the whole of the UAM were selectively increased after 8OHDPAT injection (+200%, $P < 0.05$) for about 30 min, the RR was also increased (+43%, $P < 0.05$) while the DIA remained lightly increased. Opposite responses of UAM were obtained with WAY100635 at 300nmol. RMg and dorsal ROb HFS induced central apneas (12sec at 160 μA) with a increase of UAM activity (+32%, $P < 0.05$) while the DIA remained unchanged. Ventral ROb and RPa HFS induced tachypnea (+22%, $P < 0.05$) with an off-switch of the UAM inspiratory bursts. These data supported the hypothesis that 5-HT system via the 5-HT1A receptors supports the respiratory differential modulation of the whole of the UAM versus DIA. Future experiments should investigate if hypercapnia and vagotomy reinforce these responses. As 5-HT and MR have a sleep-wake states dependant activity, these structures could be implied on differential respiratory modulation during sleep-wake states transition in healthy and OSAS conditions. Serotonin neurons of Rob which was reported as immature in sleep infant death syndrome (SIDS) could be also involved in physiopathology of central apnea.

1. Katz et al. AJRCCM 2004 2. Sood et al. JAP 2006 3. Dreshaj et al. Respi Physiol Neurobiol 1998.

O22

The influence of increased genioglossus activity and increased end-expiratory lung volume on pharyngeal collapsibility

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Both increased genioglossus muscle activity (GG) and increased end expiratory lung volume (EELV) improve airway patency in humans. However, these effects may occur through different mechanisms with increased GG primarily causing airway dilation whereas increased EELV likely stiffens the pharyngeal airway walls through caudal traction. It is possible that the ability of the GG to dilate the airway is enhanced when the EELV is increased and airway walls stiffened. The first aim of this study is to determine whether increased GG and EELV have an additive or synergistic effect on airway patency. In addition, patients with OSA may have smaller improvements in airway collapsibility for a given change in GG activity or EELV than healthy controls. The second aim is to test this hypothesis.

Methods: Patients with CPAP treated obstructive sleep apnea and age matched healthy controls are being recruited. Subjects are instrumented with an epiglottic catheter (respiratory drive and pharyngeal mechanics), intramuscular GG electrodes (GG electromyogram EMG_{GG}), magnetometers (lung volume) and a nasal mask/pneumotachograph (CPAP delivery, airflow and mask pressure measurement). Subjects sleep supine in a head out plastic chamber in which the extra-thoracic pressure could be lowered (to raise EELV) while on nasal CPAP with a variable deadspace to allow periodic re-breathing (and EMG_{GG} activation). The pharyngeal critical closing pressure (P_{CRIT}) was measured in 4 conditions: a) at baseline, b) with ~500cc increased EELV, c) with ~50% increased EMG_{GG} and d) with combined ~500cc increased EELV and ~50% increased EMG_{GG}.

Results: 5 patients with OSA and one control have been studied to date. Data have been analysed in 3 OSA patients (aged 52 ± 5 years, AHI 66 ± 19 events/h). The actual increase in GG/EELV for conditions b-d were 593cc, 110% and 563cc+58% respectively. P_{CRIT} was 3.7 ± 1.0 cmH_2O at baseline and was reduced by 4.2 ± 1.8, 2.1 ± 0.9 and 4.7 ± 1.9 cmH_2O in conditions b-d respectively.

Conclusions: These preliminary data indicate that increasing EELV by ~600cc reduces P_{CRIT} to a greater degree than doubling EMG_{GG}. Increased GG and EELV do not appear to act synergistically to reduce P_{CRIT} in OSA patients.

O23

The effect of continuous positive airway pressure (CPAP) treatment on the acute cardiovascular response to arousal from sleep in male obstructive sleep apnoea patients

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Introduction: Obstructive sleep apnoea (OSA) is an independent risk factor for hypertension. Long-term treatment of OSA with continuous positive airway pressure (CPAP) has been shown to reduce 24 h ambulatory blood pressure (BP). However, the influence of CPAP on the acute cardiovascular response to arousal from sleep is unknown. Therefore, we tested the hypotheses that the cardiovascular response to an arousal from sleep following apnoea/hypopnoea would be reduced in OSA patients after 3 months of CPAP treatment.

Methods: Ten male OSA patients (Mean (SEM); Age, 56 (3) years; BMI, 35 (2) $kg\,m^{-2}$; AHI, 63 (13) events h^{-1}) were studied before and after 3 months of CPAP (mean (SEM) duration of CPAP usage 115 (9) days). The BP and heart rate (HR) responses to arousal were measured at the termination of obstructive apnoeas/hypopnoeas induced by rapid reduction of CPAP during stable stage 2 NREM sleep. The mean of three to 15 interventions were compared pre and post CPAP treatment for each patient using.

Results: The increase in mean BP associated with arousal from sleep at the termination of obstructive apnoeas/hypopnoeas was reduced post CPAP (mean (SEM): pre, 17 (3) versus post, 13 (1) mmHg; $P = 0.045$); when adjusted for age, BMI and arousal grade the mean BP response to arousal was reduced by 3 mmHg following 3 months of CPAP treatment (95% CI −6.22–0.02, $P = 0.05$). The HR response to arousal, post apnoea/hypopnoea following three months of CPAP treatment was not significant.

Summary: Following 3 months of CPAP treatment there was a reduction in the acute cardiovascular response to arousal from sleep at the termination of an obstructive apnoea induced by rapid CPAP dialdown. Project funded by the Wellcome Trust.

O24

Influence of thermal drive on central sleep apnea in the preterm neonate

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Background: The incidence of apnea in neonates depends on a number of factors, including sleep state and thermoregulation. This study was performed to assess the role of thermal drive in the mechanisms underlying short episodes of central apnea during active and quiet sleep in neonates. It was hypothesized that apnea is not specifically induced by changes in air temperature but, rather, through processes controlling the overall body heat loss (BHL, taking into account conductive, convective, radiative and evaporative heat exchanges).

Material and Method: Twenty-two neonates (postconceptional age: 36.3 ± 0.9 weeks) were exposed at thermoneutral (incubator temperature: 32.5 °C), warm (34.2 °C) and cool (30.4 °C) conditions during 3 consecutive morning naps. Oxygen consumption (VO_2), skin and rectal temperatures and short central apnea (>3 sec) were analyzed during active sleep and quiet sleep scored polygraphically. The thermal drive was expressed as BHL ($kJ.h^{-1}.kg^{-1}$) calculated using indirect partitional calorimetry.

Results: As expected, apnea occurred more frequently in active sleep than in quiet sleep ($P<0.001$). The frequency of apnea in active sleep was higher in the warm condition ($P<0.05$). In contrast, apnea episodes were less frequent ($P<0.05$) and shorter ($P<0.05$) in cool exposure, during which VO_2 and rectal temperature increased. The frequency ($P<0.001$, $r^2=0.31$), mean ($P<0.05$, $r^2=0.06$), and maximal ($P<0.001$, $r^2=0.19$) durations of apnea were correlated with the BHL: the greater the BHL (i.e. body cooling condition), the less frequent and the shorter the apnea episodes. This was observed in active sleep and in quiet sleep. In contrast, no significant relationship exists between apnea and mean skin or rectal temperature.

Conclusion: During sleep, apneic events were more closely related to BHL than to body temperatures. In cool exposure, the decreases in the duration and frequency of apneic episodes suggest that these events depend on the metabolic drive (which is proportional to energy expenditure).

O25

Impact of oximeter signal averaging time on the oximetry dip rate in sleep disordered breathing is significant

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Background: The impact of signal averaging time (Tavg), a selectable parameter in most oximeters, on oxygen desaturation index (ODI) has not been extensively described.

Aim: To assess the impact of different Tavg's on the 2% ODI (ODI2) using an oximeter with a high sampling rate for memory storage (Masimo Rad 9, sampling rate 0.5 Hz).

Methods: Twenty-six patients free of PLMS symptoms, in whom SDB was suspected, underwent full PSG (Compumedics, Melbourne, Australia) whilst simultaneously connected to two Rad 9 oximeters (Masimo, Irvine, CA, USA) with memory storage time set for 24 h (ie 0.5 Hz sampling rate): one set with a long (16 sec) and the other with a short (2 sec) Tavg. Oximeters were downloaded and ODI2 (events per hour [eph]) analysed automatically using Download2001 (Stowood Scientific, Oxford, UK). ODI2 long versus short Tavg were then compared.

Results: Comparing long and short Tavg ODI2, the mean difference ($n=26$) was -6.9 eph (95% CI -4.0 to -9.8, $P<0.0001$) and limits of agreement were -21.7 to 7.9eph. The differences between the long and short Tavg ODI2 increased with increasing mean ODI2 ($y=-0.37\times-0.11$, $R^2=0.56$, $P<0.0001$).

Conclusion: Long Tavg settings, reduce the ODI2. Oximetry metrics are significantly influenced by recording settings, this may also impact on the clinical interpretation of the test.

O26

Psychological variables as predictors of adherence to continuous positive airway pressure

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Background: Compliance to Continuous Positive Airway Pression (CPAP) is a problem for many patients, and there is some evidence that education and support can improve observance rates.

Study objectives: We examined whether psychological variables enable us to predict adherence with CPAP in order to construct a predictive model to identify patients at risk of abandoning treatment.

Methods: One hundred and twenty-two Obstructive Sleep Apnoea (OSA) patients were studied before and 1 month after they initiated CPAP treatment. All patients completed four psychological instruments: a quality of life questionnaire (Nottingham Health Profile: NHP), a mental health rating scale (Hospital Anxiety and Depression Scale: HADS) and two disease-specific questionnaires that measure the patients' understanding of their illness and its treatment (Apnea Knowledge Test: AKT), and their attitude to OSA and CPAP (Apnea Beliefs Scale: ABS).

Results: 30% of the participants were inobservant at one month (less than 4 h/night of CPAP use). Decision-tree analysis indicated that it was possible to correctly classify 85.7% of inobservant patients using three baseline factors (Emotional reactions score (NHP), patient age, and total score on ABS). Logistic regression analyses confirmed these two psychological variables as independent predictors of observance.

Conclusion: Assessing subjective health status at onset of CPAP enables the identification of patients at risk of abandoning CPAP treatment. This subgroup could then be targeted early to receive supportive and educational measures to improve compliance rates.

O27

The risk factors of sleep-disordered breathing as predictors of pre-eclampsia

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Introduction: Sleep-disordered breathing is associated with pre-eclampsia. This study investigated the possibility of a causal link between the risk factors of sleep-disordered breathing and pre-eclampsia.

Methods: One hundred and sixty-seven healthy pregnant and 84 pre-eclamptic women were consecutively recruited in the third trimester of singleton pregnancies. Subjects completed a sleep questionnaire. Height, weight, neck, waist and hip circumferences were measured in the third trimester of pregnancy. The relationship between predictive variables and pre-eclampsia was assessed using univariate and multiple logistic regressions.

Results: Habitual snoring was associated with a 21-fold increase (95% confidence interval (CI)1.58–281.46, $P=0.021$) in the risk of

developing pre-eclampsia independent of neck, waist and hip circumferences, pregnancy body-mass index (BMI), BMI gain during pregnancy, age and smoking. Witnessed sleep apnoea was not related to the development of pre-eclampsia. After multivariable adjustment, the odds ratio (OR) of developing pre-eclampsia for women with large neck circumference was 3.40 (95% CI 1.59 to 7.23, $P<0.002$), with high BMI gain during pregnancy 1.74 (95% CI 1.07 to 2.82), and with large waist circumference 0.81 (95% CI 0.65 to 0.99, $P=0.043$). Age was also associated with pre-eclampsia with an adjusted OR = 0.78 (95% CI 0.63–0.96, $P=0.019$). Being an ex-smoker was a positive risk for pre-eclampsia with an adjusted OR = 0.03 (95% CI 0.001–0.75, $P=0.033$).

Conclusion: Women with the risk factors of sleep-disordered breathing may be predisposed to pre-eclampsia.

O28

The effect of 12-month growth hormone treatment on obstructive sleep apnea in abdominally obese men

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Background: Obstructive sleep apnea (OSA) is associated with a state of relative hyposomatotropism. Risk factors are male, obesity, and soft tissue abnormalities in the neck. This study aimed to investigate the effect of human Growth Hormone (GH) treatment on OSA indices in abdominally obese men.

Patients and Methods: Thirty-seven men with abdominal obesity and glucose intolerance, were randomized in a prospective 12-month, double-blind placebo controlled trial to either GH ($n=18$, mean (SD) age: 61 (7.1) years) or placebo ($n=19$, 64 (6.1) years). Groups were stratified regarding Body Mass Index and waist circumference. Overnight ambulatory polysomnography and computerized tomography (CT) for assessment of muscle and fat distribution in the neck were performed at baseline and after 12 months.

Results: In contrast to placebo, GH treatment was associated with a worsening from baseline to follow-up of all OSA indices; Apnoea/Hypopnea Index (AHI) (n/h) 31 (20) versus 43 (25) ($P=0.003$), Oxygen Desaturation Index (ODI) (n/h) 18 (14) versus 29 (21) ($P=0.008$), NREM-AHI 29.4 (19.7) versus 41 (26.9) ($P=0.003$). GH treatment was also associated with increases in serum Insulin-like-Growth-Factor-1 (IGF-1) (168 (71.8) to 292 (116.8), $P=0.0001$), total neck area (172 (20.5) to 179 (19.6), $P=0.02$) and neck circumference (47 (2.6) to 48 (2.6), $P=0.01$).

Conclusions: GH treatment increased the severity of OSA in men with abdominal obesity. The parallel changes in neck circumference and AHI after GH treatment possibly suggest that exacerbation of OSA may be related to trophic effects in the neck.

O29

Platelet prothrombotic phenotype in obstructive sleep apnea is normalized with treatment

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Obstructive sleep apnea (OSA) constitutes an independent risk factor for cardiovascular morbidity. Platelets maintain vascular homeostasis by clot formation and wound healing, but also participate in atherosclerosis. We hypothesized that the apnea-induced intermittent hypoxia promotes a prothrombotic phenotype by increasing platelets/platelets and platelets/leukocytes aggregates, promoting cardiovascular risk. Platelet interactions with monocytes and polymorphonuclear leukocytes (PMNs) were determined in polysomnographically diagnosed, co-morbidity free 16 OSA and 16 age sex and BMI matched controls (RDI = 44 ± 24 versus 5 ± 3 events/h respectively), in 7 OSA patients at baseline and after 3 months of dental device treatment, and in 7 additional CPAP treated patients tested on two consecutive nights with/without CPAP. Also, platelet receptors CD41/CD61and CD62P, fibrinogen and reactive oxygen species (ROS) generation by PMA activated platelets were determined. Percentage of cells expressing receptors (%) and their density of expression using mean fluorescence intensity (MFI) were determined for all measures by flow cytometry. Platelets/monocytes and platelets/PMNs aggregates were higher in OSA (296 ± 177 versus 177 ± 106MFI, $P<0.03$; 219 ± 158 versus 103 ± 54MFI, $P<0.06$, respectively), while treatment with dental device significantly decreased both types of aggregates (168 ± 68 versus 100 ± 23MFI, $P<0.03$; 168 ± 61 versus 79 ± 16MFI, $P<0.003$). Only platelets/PMNs interactions were significantly increased by removing CPAP (from 71 ± 14 to. 243 ± 77MFI, $P<0.01$). Platelets/PMNs aggregates correlated with RDI ($r=0.37$, $P<0.04$). Platelet/platelet aggregates and CD62P were increased in OSA (680 ± 416 versus 375 ± 253MFI, $P<0.02$; 48 ± 14 versus 29 ± 9, $P<0.002$, respectively). Also plasma fibrinogen and ROS generation by PMA stimulated platelets were higher in OSA patients then in controls (402 ± 64 versus 360 ± 25 mg dl^{-1}, $P<0.03$; 242 ± 141 versus 126 ± 82MFI, $P<0.05$, respectively). A pro-atherogenic platelet phenotype is evident in OSA via increase in adhesion molecules, fibrinogen receptors, platelets/platelets and platelets/leukocytes aggregates and ROS generation. Effective treatment attenuated platelet/leukocyte aggregates. These atherogenic sequela most likely contribute to the development of cardiovascular morbidity in OSA.

O30

Unexpected survival advantage in elderly with moderate sleep apnea

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Breathing disorders in sleep is a prevalent finding in the elderly but their clinical significance is unclear. The present study compared the rate of mortality in a cohort of elderly patients investigated by polysomnography because of symptoms suggesting sleep apnea with the mortality of age, gender and ethnicity matched cohort of the standard general population. The survival status of 611 elderly (442 men 169 women) investigated in the sleep laboratory during January 1st 2001 and December 31st 2005 was ascertained. Their age at sleep examination was 70.4 ± 4.8 years, BMI was 30.4 ± 5.9 kg m^{-2} and RDI was 28.9 ± 20.1 events h^{-1}. The mean follow-up period was 4.4 ± 0.96 years. Patients had high rates of co-morbidities most notably hypertension (59%), ischemic heart disease (25.9%), and diabetes (23.2%). Fifty six (9.16%) patients (14 women, 42 men) died during the study period. The comparison of the survival of the sleep laboratory cohort with mortality in the general population using the one-sample log-rank test revealed that the standardized mortality rate was 0.621 (95% CI 0.469–0.806; $\chi^2=12.96$, $P<0.0003$). The expected number of deaths was 90.19 while only 56 deaths were observed. To determine if survival was associated with sleep apnea, standardized mortality rates were calculated separately for patients with RDI < 20 ($n=251$), RDI 20–40 ($n=214$) and RDI > 40 ($n=146$). This revealed a significant survival advantage only for the moderate group. While the expected number of deaths in this group was 32.8 only 13 were

observed, resulting in a standardized mortality rate of 0.39 ($P<0.0005$). The survival of patients without or with mild sleep apnea and of patients with severe sleep apnea was no different than that of the matched population cohorts. We hypothesize that paradoxically, the apneic events which are the hallmark of the sleep apnea syndrome, provide elderly with moderate sleep apnea with cardioprotection by activating gene programs associated with ischemic preconditioning.

Working 5 to 9: A Shift Work Session

O31

Working during nights or in evening shifts – does it affect your health?

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Background: Shiftwork has a potential impact on health status due to the effects of changes in sleep patterns. The ideal methodology is to follow a population over many years. This impact has usually been studied on men of particular ages in specific occupations and addressing particular diseases. Additionally, the healthy shift worker effect makes studying this issue more complex.

Aims: Our study addresses the relationship between shiftwork and health status, highlighting the impact of working nonstandard times on the health of British men and women.

Methods: We used secondary analysis of longitudinal data from the British Panel Household Survey (BHPS). A subsample of people aged 26–75 years old was selected from the 2005 wave who had been followed annually from 1995 to 2005 ($n = 11860$). Variables were constructed to measure the number of years working nightshifts and evening shifts. Health status was measured by self-assessed health and health problems reported in 2005. Nested logistic regression models were used to examine the impact of the duration of shiftwork on men's and women's health, controlling for age, sex, education, marital status and number of years employed/self-employed (1995–2005).

Results: Undertaking shiftwork in the evening for one year increased odds of poor self-assessed health by 26% (total), and it increased odds of reporting heart or blood pressure problems by 50% (total) and by 85% (men). Working for 2–4 years during evenings also resulted in poor self-assessed health and elevated reporting health problems (e.g. breathing problems, asthma, bronchitis and anxiety/depression). Undertaking nightwork for 2–4 years increased odds of reporting health problems, e.g. for arms/legs/feet for women (by 85%), chest (breathing problems, asthma, bronchitis) by 106% (women), digestive problems by 127% (men), and anxiety/depression by 86% (women). For men who undertook 5+years nightwork, the odds of reporting health problems like anxiety/depression were almost 6 times higher than for those who never worked during nights (OR = 5.70).

Conclusion: Working nights and evenings has negative consequences for self-assessed health and reported health problems for both men and women, especially when shiftwork is undertaken for 2–4 years.

O32

The effects of a brief nap during night shift

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Introduction: The sleepiness and fatigue experienced during night shift work has important implications for personal, workplace and public safety. Napping has been suggested as a potential countermeasure to this sleepiness. Research into the effects of napping during the day has often shown considerable alerting benefits. However, naps on a night shift following prolonged wakefulness (18–24 h) from the previous morning have not consistently produced alerting effects. This study investigated the benefits of a 30-min night time nap, in a simulated night shift environment, when a prophylactic daytime sleep was allowed prior to the night shift.

Methods: A repeated measures, counterbalanced design with 22 subjects, was used to investigate the benefits of 30 min of sleep in a night nap, relative to no nap. In both conditions subjects obtained 2-h sleeps in the afternoon (1500 h-1700 h) and had the night time nap from 0230 h-0300 h. Subjective alertness (SSS, KSS, VAS) and fatigue (POMS), cognitive performance including the PVT, and objective sleepiness (SOL) were measured prior to the nap or no nap and then following the nap or no nap from 0315 to 0700.

Results: Relative to the no-nap condition the 30-min nap resulted in some impairment of alertness and performance for a relatively brief period (up to 20 min) following the nap. Generally, for the rest of the night (0400–0700 h) following this brief impairment, alertness and performance were better following the 30 min nap than with no nap.

Conclusions: The findings demonstrate that, when a prophylactic 2-hour sleep is allowed in the afternoon, a 30-min nap during night shift, is a significant countermeasure against the sleepiness and fatigue shift workers endure for most of the remaining night shift. However, there appears to be a brief period of sleep inertia immediately following the 30-min sleep during which alertness is impaired.

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O33

A brief practical exercise as a strategy against sleepiness and fatigue during night work

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Introduction: Night workers are strongly affected by circadian rhythm, thereby suffering from sleep loss and chronic fatigue. Considering the practicality for real workplaces (ex. airline pilot, plant operator, driver), we developed a brief exercise workers can easily do anywhere without expert instruction. Although exercise is recommended as one effective strategy against sleepiness and fatigue, little is known about the impact of exercise during the night period. Therefore, we examined the impact of exercise on reducing sleepiness and fatigue during simulated night work.

Method: Eight males (Mean age: 19.3 year, SD: 1.3) participated in this experiment. They attended 3 experimental conditions: 3 min×9 times exercise (exercise every hour; EE [22, 23, 0, 1, 2, 3, 4, 5, 6 h]), 9 min×3 times exercise (exercise 3 times; 3E [0, 2, 4 h]) and no exercise. During a period of night work (2200–0800), they were required to complete a task (30 min), a test battery (15 min) and break (15 min) every hour during the night work. The task was an English transcription typing task. The test battery was composed of a visual analogue scale (VAS) for sleepiness and fatigue, and a visual vigilance test (VVT). During each break, they were required to complete the exercise according to an animation on their personnel computer.

Result and Discussion: Two-way repeated ANOVA (Condition×Time-of-day) showed that a marginally significant difference among conditions was observed on VAS for sleepiness ($F1,7 = 3.45$, $P = 0.060$), while there was no significant difference on VAS for fatigue. One-way repeated ANOVA (Condition) showed that, at the time of the circadian trough (3:00–4:00), VAS for sleepiness and VVT for reaction times on 3E was significantly reduced compared with other conditions ($F2,14 = 6.19$, $P = 0.012$, $F2,14 = 3.83$, $P = 0.047$, respectively), although no significant findings were observed on VAS for fatigue. In conclusion, the exercise of 3E is a more effective strategy for reducing sleepiness without increasing fatigue. Furthermore, our results suggested that the impact is more evident around the time of the circadian trough.

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O34

Change from 8-h shifts to 12-h shifts: effects on sleep and sleepiness

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Objective: The present study examined the effects of a change from 8-h shifts to 12-h shifts on sleep and sleepiness in process operators. The effects were studied immediately and two years following the shift change.

Methods: A total of 22 process operators (aged 30–56 years) participated in the study. Thirteen of them served as subjects during the shift change in 2005 and also in the two-year follow-up and the rest nine only either in 2005 or in 2007. Prior to the shift change the participants worked two morning shifts (07–15 am), two evening shifts (15–23 am) and three night shifts (23–07 am) in a row followed by four days off. In the 12-h shift system, they had two consecutive morning shifts (07–19 am) and night shifts (19–07 am) followed by six days off. Sleep was measured with a sleep diary and actigraphy between the shifts. Sleepiness was assessed with the Karolinska Sleepiness Scale (KSS), the Psychomotor Vigilance Task (PVT), and pupillography during the shifts.

Results: Following the shift change in 2005, the main finding was a 20 percentage point decrease in napping and a 1-h increase in the main sleep period prior to the night shifts. Results of PVT response time and lapses were slightly better for the 12-h shifts than the 8-h shifts ($P<0.05$ and $P<0.001$). In the 2-year follow-up, the main finding was a 21 percentage point increase in napping prior to the night shifts compared to the situation immediately following the shift change. PVT response time showed some improvements ($P<0.001$), but the number of lapses remained the same. The results of the pupillography and KSS measurements did not show marked changes between the three measurements.

Conclusion: A change from 8-h shifts to 12-h shifts does not necessarily lead to impairments in sleep or sleepiness, but even slight positive changes can occur.

O35

Is the type of employment considered a predictive factor for accidents among truck drivers?

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Introduction: The recent changing organization of work has brought new challenges in the workplace. One of these challenges is the nontraditional employment practice of utilizing temporary work and contractor-supplied labor. In the case of truck drivers, workers outside the traditional workforce can be exposed to a higher number of risk factors than those regularly employed. These drivers drive and sleep at irregular times and have worse sleeping, eating and resting conditions. Consequently, the observed sleepiness at work among truck drivers might be a consequence of working under these inadequate conditions. This study aimed to evaluate factors associated with reported accidents among truck drivers.

Methods: The study was conducted with 470 truck drivers. They filled in a questionnaire about sociodemographic data; working conditions (type of employment, reported accidents in the past 12 months, shift schedule, working time, seniority on the job, having a second job); health outcomes (BMI, risk for obstructive sleep apnea derived from Berlin questionnaire, smoking, alcohol consumption, drug use, sleeping behind the wheel, sleep quality, etc). Chi-square tests were used and a logistic regression analysis was performed considering reported work accidents in the past 12 months as a dependent variable.

Results: The significant factors ($P<0.05$) resulting from the chi-square analyses were: temporary work, being a long-haul driver, unscheduled stops during work, working at night, sleeping behind the wheel and excessive body weight. The predictor of work accidents was sleeping behind the wheel (OR = 1.9, 95% CI = 1.01–3.57) and temporary work was a protection factor against accidents (OR = 0.4, 95% CI = 0.24–0.08).

Conclusion: Our findings were not expected, since temporary work was not a predictor for accidents. One might speculate that the flexibility of the temporary work might be more relevant than the worse conditions of this type of organization. Further studies are necessary to investigate the association between different types of work organization and the occurrence of accidents in this population.

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O36

A 6-h workday– effects on sleep and sleepiness

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Long work days may reduce sleep duration, but what happens when the work day is shortened? The present study looked into this question. Twenty-five work units in the public service sector participted with 800 individuals in a longitudinal study of the effects of a reduction of the work day from 8 to 6 h day^{-1} (40 to 30 h week^{-1}) with full salary. Half the participants were assigned to the experimental group and the other to a control group. Sleep and other aspects of health was measured before the reduction and twice with one-year intervals. Questionnaires, two-week sleep diaries, one day of saliva collection were obtained for the three points of measurement. The results showed that TST changed from 7.2 ± .7 h to 7.6 ± 7.4 h (7.4 ± .7 to 7.3 ± .9 ns) for the control group; $P<0.001$ for interaction). A number of sleep quality ratings showed a similar pattern of improvement in the intervention group. The change in TST was due to earlier rising (0600 h ± 42 to 0600 h ± 42 min $P<0.001$) while bedtime remained at 2242 h ± 43 min, regardless of condition or group. Mean sleepiness (karolinska sleepiness scale (KSS)) decreased from 4.2 ± 01 to 3.4 ± .1 (scale 1–9) as a day average for the intervention group, whereas no difference was seen for the control group (mean KSS = 4.2 ± .1 for before and after). The interaction effect was highly significant. When days off were studied the effect was considerably weaker (3.4 ± .1 versus 3.0 ± 1 for the intervention group and no change for the control group. It was concluded that a 6 h work day will increase sleep duration and rated sleep quality as well as reduce sleepiness, all effects apparently due to a delay of the time of awakening made possible by the reduction in daily work h.

O37

Use of timed light treatment to hasten circadian adaptation of offshore nightshift workers returning to day life

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Introduction: Research has shown that subjects working 12 h shift schedules (18.00–06.00 h) offshore for 2 weeks adapt to the

nightshift. However, if adaptation occurs, shiftworkers will be out of synchrony when they return home with consequent problems of poor night sleep.

Aim: To investigate the effectiveness of timed light treatment to hasten circadian and sleep adaptation in nightshift workers returning home to day life.

Methods: Eight male shift workers (mean age ± SD) 47.1 ± 8.1 years, BMI 28.8 ± 2.1kg m^{-2}, worked 19.00–07.00 h ($n = 2$) or 18.00–06.00 h ($n = 6$) offshore shift schedules, at latitudes 58/59°N. They were assessed for the last 7 days of a nightshift offshore and the following 14 days at home. Subjects received light treatment/sunglasses or no light treatment/no sunglasses in a crossover design. Sequential urine was collected for the last 3 days of the nightshift and the subsequent 7 days. Light was administered with a portable lightbox, Litebook®. After completion of their nightshift (day1) subjects wore specialised sunglasses (Litebook®) until 13.00 h. On day 2 subjects wore sunglasses until 13.00 h and then received light treatment for 1 h. For the following 3 days the sunglasses and light treatment were scheduled an hour earlier each day. The light regimen was designed to phase advance the circadian system. Subjects wore an Actiwatch-L (Cambridge Neurotechnology) throughout the study period to monitor light and activity and completed daily sleep diaries. Sleep parameters derived from the actigraphy and diaries included sleep onset/offset, sleep latency, fragmentation index, sleep duration and sleep efficiency.

Results: Mean actigraphic sleep duration after the light treatment (days 6–14) was significantly longer on the light treatment leg (6.47 ± 0.33 h, mean ± SEM) compared to the "no light" condition (5.44 ± 0.35 h; paired Student's t-test, $P = 0.04$). There was also a trend for improved sleep quality when subjects received light treatment. Sleep efficiency following light administration was 84.5 ± 2.5% compared to 81.1 ± 2.2% and fragmentation index was lower at 32.2 ± 3.5 compared to 34.8 ± 2.5.

Conclusions: Timed light administered to hasten adaptation to day life after working a night shift improved some aspects of sleep.

O38

Reducing nighttime attentional failures with bright light exposure: timing it right

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Exposure to bright light can effectively counteract nighttime deterioration in attention, but timing of the light exposure is critical. Here, we compared the efficacy of two different nocturnal bright light exposures in reducing attentional failures: Early (2300–0300) and Late (0300–0700) bright light exposure.

Method: Fifty-one healthy young subjects were randomly assigned to one of three light exposure conditions during an 8 h nighttime wake episode (2300–0700): Early, Late and Control (no bright light). The bright light exposure included one of two illumination levels: (~600 and ~2500 Lux maximum). Except during the bright light exposure, the average illumination in the room during wake was ~150 Lux. We measured attentional failures (proportion of reaction time outliers) in the Psychomotor Vigilance Task (PVT) four times, every two hours, during a baseline (day) episode and the nighttime wake episode.

Results: Nighttime attentional failures were greater than baseline attentional failures (0.29 ± 0.01 versus 0.1 ± 0.01; $P < 0.01$). However, there were fewer nighttime attentional failures in the Early (0.24 ± 0.03) subjects than in the Late (0.3 ± 0.03) and Control (0.32 ± 0.03) subjects ($P < 0.01$). Furthermore, attentional failures tended to increase more rapidly across the nocturnal wake episode for Late (last session-first session = 0.18 ± 0.02) and Control (0.16 ± 0.02) subjects than for the (0.13 ± 0.02) subjects (session×condition $P = 0.08$).

Conclusion: We conclude that bright light exposure before the circadian trough is more effective against nighttime attentional failures than bright light exposure during the circadian trough. This suggests that light exposure during the early night would be most beneficial for an initial night shift or an extended duration shift, but for subsequent night shifts, the circadian resetting effects of light would have to be taken into account.

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O39

Effect of bright light on sleep and readaptation after night work

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Introduction: The process of adapting to night work is initiated already during the first night shift by inducing a phase delay of circadian rhythms. The need for readaptation to diurnal rhythms during days after night work is important for adapting to day-oriented work schedules, for social reasons and possible health. During the dark Scandinavian winter a natural morning day light exposure is not possible at travel home from work. This present study aimed to evaluate the effect of bright light exposure on sleep and readaptation of the circadian rhythm after working nights during winter.

Methods: Fifteen female night nurses were exposed to both moderate intensity light (ML, 2200lux), and bright light (BL, 7000lux), for 2 consecutive free days preceded by 2 night shifts. Light was administered for 30–60 min in the morning at a distance of 50 cm from the eyes by use of light boxes at home. Both light conditions were compared to a baseline condition with normal home light conditions. Sleep and sleepiness were assessed through motion loggers and sleep diaries.

Results: After BL exposure workers reported enhanced alertness (effect of condition; $F = 4.62$, $P = 0.0187$). Sleep length and sleep efficiency was not affected as measured through motion loggers but subjective sleep quality improved (effect of condition; $F = 6.59$, $P = 0.0F = 052$) in connection with both BL and ML conditions.

Conclusion: Bright light treatment trough light boxes seemed to have a mild positive effect on self-evaluated sleep. An elevated alertness may indicate an accelerated readaptation by bright light treatment. A detectable difference was observed comparing a moderate bright light box or bright light box, the alerting effects being stronger with a strong light intensity dosage.

O40

Assessment of sleep-wake cycle resynchronization after a light:dark cycle phase shift by a probability distribution estimation method

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Phase shifting the L:D cycle conveys an acute disarrangement and a resynchronization process. The 24-h distribution of sleep states and of relevant EEG elements will eventually be identical to the original one at the new phase. However, the resynchronization process will not necessarily occur by the progressive shifting of the original 24-h distribution, but internal desynchronizations will occur. These are thought to be critical for jet-lag and shift-work disturbances. The methodology proposed here quantifies both the global coherence of the distribution of W, NREM and REM and its characteristic EEG

elements as well as the specific distribution of each state. Eight rats were subjected to one of four 6-h phase shift paradigm: advances by shortening the light or dark phase and delays by lengthening the light or dark phase. Delta, theta, sigma and EMG activities were quantified in each 5-sec epoch by zero-crossing and FFT techniques. Indexes of the incidence both of states and of trains of waves of a given amplitude and frequency were firstly determined for each hour of the basal pre-shift condition. Vectors were thus generated that characterize the 24-h segment at one hour shifts. The procedure then calculates the probability that a given 24-h segment corresponds to a given phase shift. This is achieved by a logistic model whose inputs are the characteristic vectors and whose output is a vector with 24 components that represent the probability distribution of the segment belonging to each phase. The model is adjusted with the basal days and each experimental day can be represented graphically by a strip that color codes the probability of belonging to each phase with one hour resolution. The peculiarities of the resynchronization process can be visually assessed strip by strip until it is completed and a high probability is displayed throughout the strip. Differences in resynchronization and their critical phases are readily recognized between states and paradigms; such as a faster mobility of delta-rich NREM as compared to REM and of delta-rich NREM in the phase advance by a short light phase paradigm.

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Neurological Sleep-wake Disorders

O41

What is the impact of changes to the ICSD electrophysiological diagnostic criteria for narcolepsy?

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Background and Objectives: The 2nd edition of the International Classification of Sleep Disorders (ICSD) was recently published (1). In it revision of the diagnostic criteria for narcolepsy with cataplexy includes changes made to the electrophysiological criteria. We examined the impact of the new electrophysiological criteria and compared them to those from the previous ICSD (2).

Patients and Methods: Sixty-one patients (27 male) were selected from a clinical database. Inclusion criteria: clinical diagnosis of classical narcolepsy with cataplexy; polysomnogram (PSG) and multiple sleep latency test (MSLT) performed free of narcolepsy pharmacotherapy; HLA DQB1*0602 positive status. PSG & MSLT data were retrospectively reviewed.

Results: Median (IQR) age at PSG was 39.7 (29 to 63) years. Sixty subjects (98.4%) fulfilled 1 or more of the 1997 ICSD PSG or MSLT diagnostic criteria for narcolepsy, with multiple sleep onset REM periods (SOREM) on MSLT being the most sensitive (87%). Fifty-one patients (84%) met the 2005 ICSD electrophysiological diagnostic criteria for narcolepsy with cataplexy, which require a combination of multiple SOREM and mean sleep latency <8 min to be present on MSLT.

Conclusions: The sensitivity of the new ICSD electrophysiological diagnostic criteria for narcolepsy is poor when applied to classical cases with clinical features as the diagnostic arbiter. Revision of the MSLT criteria has not improved their accuracy sufficiently to justify the discriminatory role they have been given. This study does not allow a ROC analysis, which in any case remains challenging for a disease which it could be argued remains without a true diagnostic gold standard. Given the limitations of the MSLT, a more central role should be considered for cerebrospinal fluid orexin assay (3) which is the new addition to the ICSD diagnostic criteria (1).

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O42

REM Sleep Behavior Disorder (RBD): genetic dissection of relevant neural circuitry

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REM sleep behavior disorder (RBD), a parasomnia typically manifested as dream enactment behavior, may represent an early pathophysiologic manifestation of Lewy body diseases (LBD), such as Parkinson disease and dementia with Lewy bodies. Preclinical investigation of possible underlying neural mechanisms of RBD suggest that glutamatergic neurons located in the sublaterodorsal nucleus (SLD), which project to GABA/glycine interneurons in the ventral horn, are responsible for atonia during REM sleep (Lu et al. 2006). Based upon these findings, we hypothesize that a loss of glutamate from these neurons in the SLD produces REM sleep without atonia, an animal equivalent of RBD. To assess this question, we selectively eliminated glutamate release from SLD by injecting adeno-associated virus-Cre recombinase (AAV-Cre) into the SLD of mice with lox P sites flanking exon 2 of the vesicular glutamate transporter 2 (VGLUT2) gene. In addition, we examined the role of the ventromedial medulla (VMM) in REM atonia by injecting orexin-saporin in rats and AAV-Cre into flox-VGAT (vesicular GABA transporter) and flox-VGLUT2 mice. Consistent with our hypothesis, these data show that loss of the VGLUT2 gene in the SLD produces REM sleep without atonia (walking and running) without alteration of total amount of REM sleep. Furthermore, loss of the VGLUT2 but not the VGAT gene in the intermediate VMM results in myoclonic jerking against the background of tonic atonia during REM sleep. Based upon these observations, we propose that suppression of muscle activity during REM sleep is controlled by the activation of excitatory glutamatergic projections from the SLD (with collaterals targeting the intermediate VMM) and from the intermediate VMM, which terminate at inhibitory interneurons in the spinal cord. Collectively, this work provides insight into the control of muscle tone during REM sleep, which may have implications for our understanding of neurological conditions that precede the onset of neurodegenerative disease.

O43

Fatigue, level of alertness and driving performances in patients suffering from traumatic brain injury

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Almost one in every two patients, suffering from traumatic brain injury (TBI), report chronic fatigue. A previous study showed that sleepiness could account for fatigue in TBI patients. In this new study, we looked at the relationship between both objective and subjective sleepiness, fatigue and drug treatment in TBI patients. In a TBI subgroup versus matched controls, we focused on the relationship between fatigue or sleepiness and driving performance. Nocturnal polysomnography, 5×40-min maintenance of wakefulness test (MWT) trials, Epworth Sleepiness Scale (ESS) and a Fatigue Severity Scale (FSS), were collected in 36 TBI patients (28 males, mean age [± SD] = 33 ± 11 years). Twenty two patients (16 males, mean age [± SD] = 33 ± 12 years) out of the TBI and 22 controls (16 males, mean age [± SD] = 33 ± 10 years) performed an hour simulated driving session to estimate their mean standard deviation from the centre of the road (SDS). In TBI patients, FSS, ESS and MWT latency mean [± SD] scores were, respectively, 27 ± 10, 8 ± 4 and 35 ± 7 min only. In control subjects, FSS, ESS and MWT latency mean [± SD] scores were, respectively: 15 ± 2.5, 5 ± 3 and 37 ± 5 min. TBI patients reported more subjective fatigue (U Mann-Whitney, FSS: $U = 99$, $P < 0.001$) than controls. Their driving performance was also significantly worse than controls (SDS: $U = 79$, $P < 0.001$). In TBI patients, fatigue were correlated to deviation from the center of the road (Rho de Spearman. $r = 0.455$, $P < 0.05$) and with MWT ($r = -423$, $P < 0.05$). In conclusion, our TBI patients complained of subjective fatigue and presented normal levels of sleepiness (ESS and MWT). Interestingly, subpathological level of sleepiness at the MWT correlates in TBI patients with fatigue when it does not in control subjects; and fatigue is associated with poor driving performance. Treating TBI patients, with alerting drugs even if MWT scores are subnormal, could improve fatigue and cognitive performances.

O44

EEG mapping during sleep in fibromyalgia and controls

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Background: Controversy concerning Fibromyalgia Syndrome (FMS) pathophysiology remains an open issue, specially on the pain processing, the role of brain structures for a lower pain

threshold and patients bad limit definition concerning effort and fatigue. The links between sleep disturbances and pain processing are strong with mutual feedback interactions.

Objective: To determine if sleep EEG mapping in the conventional frequency bands (δ, θ, α1, α2,σ and β) in FMS is a useful tool in understanding of the pathophysiological processes.

Methods: One group of 11 FMS patients without any medication for, at least, 1 month, with no other recognized pathology, namely rheumatologic, neuro-psychiatric disorders, underwent a full PSG with a 19 channels EEG. One group of 10 healthy controls was submitted to the same procedure. All PSG were staged and corrected by an expert. All the sleep parameters were collected and introduced in tables for statistical analysis. Through spectral analysis (FFT) power maps were computed for all EEG frequency bands at all the EEG channels, at specific times (ST): minutes 1, 5 and 15 of NREM2 and of SWS of the first sleep cycle, normalized by the total power. From these data a one-way ANOVA analysis for repeated measures ($P<0.05$) was applied (Statview®5.0.1.0.).

Results: All collected data confirm the worse sleep quality in FMS. All patients, and none of the controls, had a sleep alpha-delta EEG pattern. The evolution of the EEG activities in FMS revealed a consistent reduction of delta during NREM2 ($P = 0.0002$ for the diagnostic groups (DG) and $P<0.0001$ EEG topography (ET)) and a persistent dominance of more rapid frequencies, particularly α1 and 2 ($P = 0.0302$ for DG and $P<0.0001$ for ET at 1st min. and $P<0.0001$ for ET at 5th min.) andζ (sleep spindles) ($P = 0.0317$ for DG and $P<0.0001$ for ET at 1st min. and $P = 0.0040$ for DG and $P<0.0001$ for ET at 5th min).

Conclusion: Beyond the more classical results we assume that the presence of sleep spindles and fast frequency abnormalities in SWS of FMS may translate abnormal thalamo-cortical relationships. These data may be the specific markers of an abnormal pain processing during sleep, involving the thalamo-cortical pathways, adding some arguments for the neuropathological hypothesis of FMS.

O45

Independent replication of association of restless legs syndrome to MEIS1, BTBD9 and MAP2K5/LBXCOR1 in the European population

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Restless legs syndrome (RLS) is with prevalence of up to 10% in the Causacian population one of most common sleep disorders. There is a marked genetic component in the pathogenesis. Up to date, six linkage regions for RLS on chromosomes 2q, 9p, 12q, 14q, 19p and 20p, under a recessive or autosomal dominant model of inheritance have been identified. Only recently, association of RLS with three intronic and intergenic variants of MEIS1, BTBD9, and MAP5K/LBXCOR1 on chromosomes 2p, 6p and 15q was described by means of a genome wide association study. The aim of our study was to investigate whether these variants are also relevant in RLS patients originating from Czech Republic, Austria and Finland. Our study population consisted of a total of 679 RLS patients and 1230 controls of Czech, Austrian and Finish origin, respectively. We tested the association using 10 single nucleotide polymorphism markers (SNP) by means of mass spectrometry (Sequenom MassArray system). We replicated associations for all loci in the three samples combined (rs2300478 in MEIS1, $P = 1.26\times10$–05, odds ratio (OR) = 1.47, rs3923809 in BTBD9, $P = 4.11\times10$–05, OR = 1.58 and rs6494696 in MAP5K/LBXCOR1, $P = 0.04764$, OR = 1.27). Logistic regression showed no significant interaction with country for any SNP tested, and Breslow-Day test shows homogeneity ORs in all samples. The best models observed for individual loci are in agreement with previous findings. BTBD9 among the known loci seems to be the most consistent in its effect to RLS across populations and also most independent of familial clustering. We conclude that the observed genetic determinants are risk factors for RLS in multiple populations.

Acknowledgement: The study was partially supported by MSM0021620849.

O46

Simultaneous deep brain and polysomnographic recordings in humans: REM sleep-related activity within the subthalamic nucleus of Parkinson's disease patients

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Introduction: Psychobiological models of REM sleep and dreaming have proposed a role of the basal ganglia in the diffusion and modulation of REM sleep phenomena. We sought to identify and characterize phasic and synchronized oscillatory activity recorded through Deep Brain Stimulation (DBS) electrodes implanted in the human subthalamic nucleus (STN).

Methods: We studied 14 patients implanted with bilateral DBS for Parkinson's disease who had a free-incidence post-surgical period. The clinical course, psychological, neurophysiologic assessments, and magnetic resonance neuroimaging revealed a positive therapeutic localization of the DBS-electrode's contacts within the STN. Local field potentials (LFPs) from bilateral subthalamic DBS-electrodes and electrophysiological (EEG, EOG, EMG, EKG etc.) activity were simultaneously recorded following a standard overnight polysomnography (PSG) protocol for human subjects. Both, LFPs recorded through DBS-electrodes and electrophysiological PSG derivations were analyzed in terms of amplitude, time and frequency domains, and submitted to statistical analyses. Visual scoring of sleep stages was performed blind from STN traces according to R & K standard criteria.

Results: A bilateral pattern of phasic and synchronized beta oscillations was recorded as LFPs showing phase reversal in the STN during REM sleep. These activities were time-related to the occurrence of rapid eye movements and EMG atonia.

Conclusion: Our results are in agreement with the proposal of an active role of an ascending basal ganglia activation network in the modulation of REM sleep phenomena.

O47

Orexin (hypocretin) gene transfer improves narcoleptic symptoms in orexin null mice

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Introduction: Narcolepsy is a neurodegenerative disorder linked to the loss of orexin neurons. A behavioral phenotype that

resembles narcolepsy occurs in mice when the orexin gene is deleted. Gene transfer has proven to be an effective neurobiological tool in a number of neurodegenerative diseases but it is not yet known if it can also correct a sleep disorder. Here we constructed a replication-defective herpes simplex virus-1 (HSV-1) amplicon-based vector to test if orexin gene transfer could reverse the symptoms of narcolepsy in orexin knockout mice with narcolepsy phonotype.

Methods: First, the mouse prepro-orexin gene was inserted into the HSV-1-PrpUC vector and then the expression of transferred orexin gene was confirmed by reverse-transcription PCR and immunohistochemistry in cultured cells. Then the same vector was delivered into the lateral hypothalamus (LH) of orexin knockout mice, and mice were then sacrificed at various intervals after delivery to determine the lifespan of the expression of the gene product. Lastly we injected the vector into the LH of another batch of orexin knock out mice ($n = 13$) and we examined its effects on sleep-wake paying special attention to changes in cataplexy attacks and the REM sleep. Sleep was measured during the 2nd and 4th days post-injection. Control mice ($n = 9$) were injected with vector carrying solely the reporter gene (GFP). Sleep was also recorded from wildtype (WT) mice ($n = 9$) of the same background strain (C57BL/6J) and age (3–7 months old; 20–35 g) as the orexin knockouts.

Results: Numerous orexin-A immunoreactive neurons in the LH of orexin knockout mice were evident 1–3 days after gene transfer followed by a decline after the 4th day. Orexin gene transfer into the LH decreased the incidence of cataplexy by 60% (versus control vector), and the levels of REM sleep during the second half of night were same as WT.

Conclusions: HSV-1 vector-based orexin gene transfer reorganized and improved REM in knockout mice. This methodology provides an efficient tool to determine how sleep becomes reorganized in an animal model where the underlying network exists but the sleep abnormality results from a missing gene.

Acknowledgement: Support: NIH grants (NS030140, NS052287) and VA Research Service.

O48

Emotional motor control in narcolepsy-cataplexy

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Background: Narcolepsy with cataplexy (NC) is a chronic sleep-wake disorder presenting with excessive daytime sleepiness and cataplexy. Cataplexy consists of a sudden loss of muscle tone triggered by intense emotions suggesting the possibility of an abnormal emotional motor control in these patients. Our previous data using functional magnetic resonance (fMRI) and electrophysiology demonstrate an amygdala dysfunction in narcoleptic patients.

Objectives: To test the effect of emotions on voluntary motor control, we developed an emotional version of a stop-signal task. This task provides a measure of inhibitory motor control, which is independent of motor execution and other unspecific cognitive functions, in particular from speed of reaction time.

Design and Methods: Eleven drug free HLA-DQB1*0602 positive NC patients (mean age: 37.8 ± 8.8 years, hypocretin-1 deficient in 5/6 tested) and 11 controls (mean age: 34.7 ± 9.2 years) participated the study. Reaction times to "go" stimuli and the latencies needed to stop a motor response (SSRT = stop signal reaction time) were measured under different emotional conditions (neutral and fearful stimuli). SSRT was determined by a dynamic tracking algorithm which converges to a 50% probability of successfully suppressed motor response. Data were analyzed using ANOVAS with EMOTION as within-subject repeated factor and GROUP as between-subject factor and post-hoc *t*-tests.

Results: Reaction times to Go trials were slower for NC patients for emotional and neutral stimuli (all $P = 0.05$; emotional NC: 702 ± 97 ms versus C: 502 ± 56 ms; neutral NC: 701 ± 99 ms versus C: 496 ± 65 ms). SSRT measures revealed an interaction GROUP by EMOTION ($P = 0.02$) because SSRTs were faster for emotional stimuli in controls but not in patients (emotional NC: 238 ± 70 ms versus C: 269 ± 45 ms, $P = 0.2$; neutral NC: 216 ± 45 ms versus C: 275 ± 54 ms, $P < 0.05$). The probability of inhibition was 0.5 for each group and in each condition.

Conclusions: Although NC patients were generally slower than controls during Go trials, they showed effective inhibitory motor control. Remarkably, motor inhibition was affected by emotions in NC but not in controls. These preliminary results suggest a relevant emotional influence on motor inhibition in narcolepsy-cataplexy.

O49

Familial narcolepsy-cataplexy, obesity, and type 2 diabetes with hypocretin deficiency

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Aim: To report the findings from a unique Spanish family of four generations including dizygotic male twins in the third generation who were concordant for narcolepsy with cataplexy, obesity and type 2 diabetes mellitus.

Patients and Methods: The family was assessed by history, physical and neurological examinations, Epworth Sleepiness Scale and Ullanlinna Narcolepsy Scale; PSG standard recordings followed by MSLT; HLA DQB1 genotyping, mutation analysis of Prepro-hypocretin (HCRT), Hypocretin-Receptor-1 and -2 gene as well as CSF hypocretin-1 measurements, immunohistochemical screening for antibodies against lateral hypothalamic neurons, and laboratory tests including detection of diabetes-related auto-antibodies.

Results: Six family members were diagnosed with narcolepsy-cataplexy. Seven other family members were known to have suffered EDS. Furthermore, the family consists of several members affected by type 2-diabetes and/or obesity, which partially cosegregates with narcolepsy or EDS. One of the affected sons of the twins was affected by idiopathic thrombocytopenic purpura. HLA genotyping in the twins and in both sons of one twin showed no association with DQB1*0602, while CSF measurements in both twins revealed a hypocretin deficiency. The twins' cousin and his son were DBB1*0602 positive and had no diabetes. We found Anti-Gad 65, anti-IA2 and anti-insulin auto-antibodies < 5 U mL^{-1} in both twins and in both sons of one twin. We found no antibodies against hypocretin cells or other lateral hypothalamic neurons with immunohistochemical screening. Mutation analysis ruled out any pathogenic mutation in the coding regions and exon-intron boundaries of the hypocretin ligand and receptor genes.

Conclusion: This family clearly represents a genetic form of narcolepsy with an autosomal-dominant mode of inheritance, not necessarily associated with HLA-DQB1*0602 and/or mediated by auto-antibodies or a mutation in the gene coding for pre-prohypocretin, but with hypocretin deficiency. Our findings point to the possibility of a common genetic contribution to narcolepsy, obesity, and type 2 diabetes as already suggested in sporadic narcolepsy.

O50

Does age at onset of narcolepsy influence the course and severity of the disease?

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Introduction: The aim of the study is to compare the course and severity of narcolepsy in relation to different age at the disease onset.

Patients and Methods: Clinical interview with the completion of the Stanford questionnaire, Epworth Sleepiness Scale (ESS) and polysomnographic data (nocturnal PSG followed by MSLT) were evaluated in 105 patients (44 males, 61 females, mean age 45.4 ± 19.2, BMI 29.2 ± 5.8) suffering from narcolepsy. In 87 cases narcolepsy with cataplexy (N-C), in 18 patients narcolepsy without cataplexy (NwC) was diagnosed. The severity of the disease was judged by the clinical condition-number of sleep and cataplectic (in N-C) attacks, presence of sleep paralysis and hypnagogic hallucination, subjective value of ESS and objective measurements of MSLT mean latency and number of SOREMs. ANOVA, two-sample *t*-test and chi-square test were used for statistic analysis.

Results: The age at onset of excessive-daytime sleepiness (EDS) was in 50% cases before the age of 19 years, cataplexy appeared in N-C cases most frequently with a 3-year latency after EDS. Most of the patients reported reaching maximum severity immediately after the disease onset. No correlations with the age at onset and the presence of hypnagogic hallucinations and/or sleep paralysis were found. There was no correlation between the number of sleep and cataplectic attacks (in N-C) and the age at onset, nor did subjective ESS show any significant difference. Similarly, neither the MSLT mean latency nor the number of SOREMs depended on the age at onset. The only significant correlation was found between the BMI and the severity of the disease. The higher the patients BMI, the shorter MSLT values and the higher the rate of cataplectic attacks ($P < 0.05$) were found.

Conclusion: The severity of narcolepsy does not depend on the age at onset. The results did not confirm the clinical presumption that narcolepsy appearing in childhood is predictive of a more severe course of the disease in adulthood.

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WASM-ESRS Symposium
Translational Research Interaction of Scientific Studies and Clinical Sleep Medicine: Prion Disease and Sleep Disordered Breathing

S17
Sleep-wake disorders in sporadic Creutzfeldt-Jakob disease
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S18
Clinical presentation of fatal familial insomnia
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S19
Pathophysiology of sleep apnea in children and difference from adults
C. GUILLEMINAULT
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S20
Diagnosis and treatment of sleep apnea in children
M. P. VILLA
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Genetic Contribution to Sleep Regulation

S21

Heritability of sleep homeostasis in humans

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S22

Role of clock genes in sleep homeostasis in humans

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Circadian and homeostatic processes are central to sleep regulation and these two processes have long been considered to be independent. However, there is growing evidence that the circadian and homeostatic process interact and this interdependence can be observed at the behavioral and molecular-genetic level. Thus, the apparent amplitude of the circadian rhythms of sleep propensity, alertness and performance all depend on homeostatic sleep pressure. A polymorphism in the clock gene PERIOD3 affects several markers of sleep homeostasis as well as the overt circadian amplitude of waking performance when wakefulness is extended into the biological night. The question arises whether these diverse observations can be reconciled with a model of sleep regulation in which the sleep-homeostat and circadian process interact. New analyses and computer simulations will be presented to illustrate how clock genes, through their effect on sleep homeostasis, may affect circadian organisation of sleep and wakefulness.

S23

Studies in inbred mouse strains to elucidate genetics of sleep homeostasis

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Twelve years ago we initiated a series of experiments with the aim to genetically dissect sleep in mice. We utilized several complementary approaches towards this goal, including forward, molecular, and reverse genetics. In a first set of experiments we characterized sleep and its regulation in six commonly used inbred strains of mice and discovered that most aspects of sleep greatly varied with genotype. These traits include the amount and distribution of NREM and REM sleep and the consolidation of NREM sleep under baseline conditions. Moreover, we discovered the greatest contribution of genetic factors for EEG derived variables, including the frequency of theta oscillations during REM sleep, the contribution of delta oscillations to the NREM sleep EEG, and the homeostatic regulation of EEG delta power with heritabilities well over 80%. We assumed that each of these aspects of sleep has to be regarded as a complex and quantitative trait. We therefore used QTL (Quantitative Trait Loci) analysis as a forward genetics approach to map genomic regions that segregate with our traits in various recombinant inbred, inter- and backcross panels of mice. For two of the three EEG traits mentioned we have successfully localized the underlying gene while for the homeostatic regulation of EEG delta power we identified a strong candidate gene, homer1a. We obtained support for the implication of homer1a in the homeostatic regulation of sleep from a molecular genetics approach, using micro-arrays, aimed at identifying brain specific transcripts that co-varied with EEG delta power both under baseline and sleep deprivation conditions and from an in-silico analysis approach. By generating a transgenic mouse model, we found that in homer1-expressing cells specifically, apart from homer1a, three other activity-induced genes are overexpressed with sleep deprivation. All four genes play a role in recovery from glutamate-induced neuronal hyperactivity suggesting a role for sleep in intracellular calcium homeostasis, thus protecting the cells from neuronal over-activation associated with prolonged wakefulness. We discovered another, novel molecular pathway involved in the homeostatic regulation of sleep using a reverse genetics approach. We and others found that sleep homeostasis is compromised in mice lacking functional circadian clock genes such as cryptochrome1 and -2, bmal1, clock, and npas2. Furthermore, the transcription of the circadian genes period1 and -2 in the mouse forebrain follow the sleep-wake distribution and are induced by sleep loss. In npas2 KO mice period2 no longer follows the sleep-wake distribution. Together these observations suggest a non-circadian role for clock genes in sleep homeostasis. The mechanism by which clock gene expression is coupled and feeds back to wakefulness (and sleep) is the topic of our current research.

S24

Use of in silico approaches to identify likely candidate genes

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Electroencephalographic oscillations in the frequency range of 0.5–4 Hz, characteristic of slow-wave sleep, are often referred to as delta power. Delta power reflects sleep intensity and correlates with the homeostatic response to sleep loss. A survey of inbred strains of mice demonstrated that the time course of accumulation of delta power varied among inbred strains and that the segregation of the rebound of delta power in recombinant inbred strains identified a genomic region referred to as the delta power in slow wave sleep (Dps1) using quantitative trait locus (QTL) analysis. This region contains genes that modify the accumulation of delta power after sleep deprivation. Although QTL is an important method for identifying a genomic region underlying a phenotype, finding a causal relationship between a gene in a region and a phenotype remains difficult. The narrowing of a QTL interval can be performed through additional mouse crosses or using bioinformatics and statistical tools. We used in silico tools to investigate in detail the Dps1 QTL. We narrowed the QTL using interval-specific haplotype analysis and performed a comprehensive annotation of the remaining genes in the region. Sequence comparisons identified polymorphisms within the coding and regulatory regions of all genes present in a narrowed interval. We established the expression pattern of selected genes located in the Dps1 interval in sleep and wakefulness in parental strains used for QTL mapping. Taken together, these steps reduced the number of potential candidate genes that may underlie the accumulation of delta power after sleep deprivation and explain the Dps1 QTL. The strongest candidate gene was Homer1, which was supported by expression differences between sleep and wakefulness and the SNP polymorphism in the upstream regulatory regions.

The New AASM Manual for the Scoring of Sleep and Associated Events: The ESRS Task Force Report

S25

Technical and digital specifications

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S26

Visual rules for adults

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S27

Respiratory and cardiac rules

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S28

Movements rules

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S29

Visual rules for children

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S30

Respiratory rules for children

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Early Morning Shift Work and Shift Work Disorder

S31

Prevalence of Shift Work Disorder (SWD)

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Shift work disorder involves disturbed or non-restitutive sleep in connection with primarily night shifts. The problems should not occur during day work or days off. The prevalence of SWD is debated and there does not to seem to exist any donclusive study that takes all criteria into account. This presentation will present one approach to estimating prevalence through asking a representative sample of the shift working populattion about the extent to which their disturbed sleep is a major problem in life and about how often it is disturbed, as well as how often night shifts are associated with fatigue (without any disturbances occuring during day work or days off. The resulting estimate will vary between 0.1% and 30% of the shift working population, depending on restrictiveness. In addition, morning work is not part of the diagnosis although a number of studies indicate that morning work is associated with reduced sleep (1–2 h depending on start-time) and increased sleepiness during most of the shift. Disturbed sleep, however is rarely reported in connection with morning shifts-only insufficient sleep. Thus, morning work should be part of the SWD diagnosis, but the question is the criteria.

S32

Implications of shift scheduling for sleep duration and excessive sleepiness

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Disturbed sleep, which itself is a major health risk of shift work, may be an important pathway for the long-term health effects of night and shift work. As indicated by the different models explaining the variation of sleep and sleepiness, the major factors predicting sleep and excessive sleepiness at work are related to the circadian variation of body functions, time spent awake, and sleep recovery. Sleepiness immediately after waking up, the so called ''sleep inertia'' is a separate factor increasing sleepiness immediately after waking up. In addition to the general circadian and homeostatic factors, work demands influence the expression of sleepiness during the work shifts. Although shift systems vary greatly in relation to how they influence the expression of the homeostatic factors of sleep regulation, there is still insufficient amount of controlled intervention studies to support definitive conclusions regarding the preference of different shift systems. Compared to slower rotating shifts systems, the use of very rapidly rotating shift systems (only 1–2 consecutive night shifts) seems to support the fastest recovery of the sleep/wakefulness. There is also evidence in favour of the forward rotating shift systems compared to the backward rotating shift systems. Forward rotation allows more time between the shifts for sleep. Especially in irregular shift systems, the avoidance of quick returns as well as the avoidance of early morning and night shifts are related with longer night sleep and improved possibilities for daytime napping. The starting time of the morning shift is critical. Each hour delay in the starting time of the morning shift is related with 40–50 min extension in the main sleep length. Since sleepiness at work grows hand in hand with the time spent awake and the inability to nap before the shift, the use of extensive long and/or early starting night shifts should be avoided. Finally, adaptation to shift work is highly individual. Good employee control on working h is related with better subjective health.

S33

Clinical consideration and factors influencing tolerance to early morning shifts

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Shift work sleep disorder is the most frequent complaint of shift and night workers, mainly due to de-synchronization of sleep/wake cycle due to night work, early awakening on morning shifts, and work-non work conflicts for people with family and social burden. It is one of the main causes of intolerance to shift work, which is related to several aspects pertaining to different domains, dealing with personal characteristics and coping strategies, family and social conditions, working situations and, particularly, working hours organization: that explains the high inter-individual variability. Concerning individual aspects, the influence of some personality and behavioural aspects such as age, morningness/eveningness, rigidity/flexibility of sleeping habits, sleep strategies (e.g. napping) has been emphasized. From the social point of view, work/non work conflicts related to difficulties in combining irregular working schedules with family commitments, are the main causes of sleep problems and chronic fatigue, especially in women. As concerns working time organisation, too early starts of morning shifts, backward shift rotations, and too short intervals between shifts, are the most important aspects to be considered. More specifically, intolerance to early morning shifts is more common among evening types, in case of too early starting time, and when a too fast backward shift rotation (i.e. ''quick returns'' related to a morning shift following an afternoon shift) is planned. Occupational health physicians (OHP) have to deal with different and concurrent approaches at both group and individual level, with epidemiological and clinical perspectives, enacting preventive and therapeutic strategies. Epidemiological inquiries concerning sleep troubles and complaints help the OHP assess the scope of the problem at group level and establish appropriate preventive (e.g. shift schedule arrangements, medical surveillance) and compensative (e.g. life styles, sleep strategies) measures. On the other hand, the crucial point of clinical evaluations deals with the ability to differentiate ''tolerable'' troubles (compatible with transitory perturbation of the sleep/wake cycle) from more severe or pathological disorders, asking for prompt interventions at work (transfer to day work) and personal (treatment, rehabilitation) levels. For the latter, the OHP needs the constant help and support by sleep experts for a careful diagnostic process, considering all possible intervening and confounding factors. This is needed not only for establishing the most appropriate actions, but also for the forensic implications connected with the diagnosis of Shift Work Sleep Disorder as a work-related disease.

S34

Treatment strategies for early morning shift work and shift work disorder

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Contributions of Adenosine and Dopamine in Mediating Arousal: Inseparable Partners?

S35

Dopamine, stimulants, and wakefulness in Drosophila

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In mammals, the wake-inducing actions of stimulant drugs such as caffeine (CAFF) and methamphetamine (METH) have been linked to increased dopaminergic signalling. We have investigated changes at the molecular level underlying CAFF-mediated wakefulness in Drosophila. We have also examined the behavioral effects of CAFF in wild type flies and in flies carrying mutations in different components of the dopaminergic system, including different dopaminergic receptor types. The results indicate that the dopaminergic system mediates the wake-promoting effects of CAFF in Drosophila.

S36

Potential role of A2A adenosine receptors in the activity of VLPO neurons during sleep

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GABA/galanin neurons within the ventrolateral preoptic nucleus (VLPO) are crucial for sleep by inhibiting wake-promoting systems. Since sleep induced by adenosine (ADO) requires activation of brain A2AR, we examined the hypothesis that ADO could directly activate VLPO neurons via A2AR in rat brain slices. Following on from our initial *in vitro* identification of the sleep-promoting neurons as inhibited by NA and Ach arousal transmitters, we established that the VLPO comprises two intermingled subtypes of neurons, either inhibited (Type-1, 47%) or excited (Type-2, 53%) by 5-HT. Since both cell types co ntained galanin and expressed GAD-65/67 mRNAs, they potentially correspond to the sleep-promoting neurons. Besides, ADO and CPA (A1R agonist) inhibited Type-1 and Type-2 neurons. In contrast, ADO unmasked a reversible and selective excitation of Type 2-cells, while in presence of DPCPX (A1R antagonist).This effect involved the activation of post-synaptic A2AR since reproduced by CGS21680 (A2AR agonist) in synaptic uncoupling conditions and reversed by ZM241385 (A2AR antagonist). The present study is the first demonstration of a direct activation of the VLPO sleep-promoting neurons by ADO. Our results further support the cellular heterogeneity of these neurons, which could e nable their differential contribution to the sleep regulation. ADO and 5-HT accumulate during waking. Thus, we propose that Type-2 neurons are involved in sleep induction while Type-1 neurons would play a role in sleep consolidation through inhibitory interactions with arousal systems.

S37

Adenosinergic and dopaminergic signaling as targets for wake-promoting therapeutics: insights from mouse genetic models

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The use of pharmacological agents to promote and maintain wake is ubiquitous in the developed world, and for the most part the actions of these agents can be attributed to their effects on adenosinergic or catecholaminergic signaling in the brain. The widely used non-prescription wake-promoting agent, caffeine, is an adenosine antagonist. Some of the most widely prescribed wake-promoting therapeutics potentiate catecholaminergic (dopaminergic and noradrenergic) signaling. Studies performed in mouse genetic models have provided key insights into the pharmacological targets of these wake-promoting compounds. I will review these studies with the goal of conveying to the audience the diversity of mouse genetic models relevant to the study of wake promoting therapeutics and the value of these models for improving our understanding of the neurobiological basis for waking and vigilance.

S38

Pharmacogenetics of central nervous system stimulants in humans

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The subjective psychostimulant actions of caffeine and modafinil are highly variable among individuals. Caffeine promotes wakefulness by antagonizing adenosine receptors in the brain. We found in an internet survey among 20′000 students that high habitual caffeine consumption is associated with symptoms of insomnia in self-rated caffeine sensitive individuals, but not in caffeine insensitive individuals. Follow-up studies showed that the genotype distribution of a common 1083T >C single nucleotide polymorphism (SNP) of the adenosine A2A receptor gene (ADORA2A; SNP-ID: rs5751876) differs between subgroups of highly caffeine sensitive and insensitive adults. Moreover, the ADORA2A 1083T >C genotype determines how closely the caffeine-induced changes in the sleep EEG resemble alterations typically observed in patients with primary insomnia. These data demonstrate that a common variation in ADORA2A contributes to subjective and objective responses to caffeine on sleep. The findings also suggest a role for adenosine A2A receptors in the generation of the sleep EEG. The mode of action of modafinil is not fully understood. The available data indicate that increased dopaminergic and/or adrenergic neurotransmission underlies modafinil-induced wakefulness. The enzyme catechol-O-methyltransferase (COMT) is primarily responsible for dopamine metabolism in the prefrontal cortex. A functional Val158Met polymorphism of COMT (SNP-ID: rs4680) is associated with 3- to 4-fold reduced enzymatic activity, and was previously shown to modulate sleepiness and modafinil efficacy in narcolepsy. We found in healthy men after one night of sleep deprivation that the subjective and objective effects of modafinil differ between homozygous Val/Val and Met/Met allele carriers. More specifically, modafinil improves vigor, mood, vigilant attention and executive function in individuals with the Val alleles, but not in subjects with the Met alleles. These data indicate that dopaminergic mechanisms contribute to waking-induced impairment of subjective state and cognitive functions. These examples demonstrate that pharmacogenetic studies provide a powerful approach to gain new insights into the molecular mechanisms underlying sleep-wake regulation in humans.

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Advances in Treatment of Sleep Disorders

O51

Combined CBT plus medication versus CBT alone for persistent insomnia: acute and maintenance treatment effects

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CBT and hypnotic medications are efficacious for short-term treatment of insomnia, but few patients achieve complete remission with any single treatment. Whether combined or maintenance therapies would enhance outcome is unclear. This study examined two research questions: (1) Is combined CBT plus medication more effective than CBT alone for acute treatment of insomnia? (2) Does maintenance therapy (individualized CBT, intermittent medication) enhance long-term outcome? A total of 160 adults (61% women; mean age of 50.3 years) with persistent insomnia were randomized to CBT alone or CBT plus medication (zolpidem) for the initial treatment phase (6 weeks); 148 treatment completers were randomized a second time for extended treatment (6 months). Patients treated with CBT alone initially received extended CBT or no additional treatment, and those receiving the combined CBT plus medication approach initially were randomized to an extended treatment consisting of CBT plus medication (used on an as needed schedule) or CBT without medication (tapering). CBT was equally effective when used alone or combined with medication during the initial therapy, with sleep efficiency reaching 83% and 84%, respectively. However, the combined approach produced a greater reduction of WASO (69 versus 83 min) and a larger increase in total sleep time (-6 versus 10 min). Both conditions resulted in a significant but similar remission rates (39 versus 44%) as defined by an Insomnia Severity Index score smaller than 8. For the extended therapy phase, the addition of maintenance CBT did not enhance outcomes relative to no additional treatment. For the combined condition, patients who tapered their medication achieved better outcomes than those who continued using medication intermittently. All four conditions significantly increase their total sleep time during the extended treatment. A higher remission rate was observed after the extended treatment for both combined conditions compared to CBT alone (57 versus 45%). The addition of medication to CBT during initial therapy may produce some added benefits, mostly in preserving total sleep time, but it appears preferable to discontinue medication after initial therapy in order to enhance long-term outcome.

O52

Evaluation of an internet intervention for adult insomnia

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Approximately 10% of adults report chronic insomnia, but fewer than 15% of those receive treatment. Although cognitive-behavioral therapy for insomnia (CBT-I) has been shown to be effective, it is not widely available due to expense, time constraints, and lack of trained professionals. This presentation will showcase a CBT-I intervention that is delivered via the Internet (SHUTi: Sleep Healthy Using The Internet), a program that could be broadly disseminated, potentially filling the treatment gap. Based on face-to-face CBT-I, SHUTi is a 6 week self-guided, interactive, and tailored intervention. Forty-five participants with primary insomnia were randomized to either receive SHUTi immediately or as wait-list controls. All subjects completed a battery of measures and two weeks of sleep diaries at pre- and post (3 months after pre) assessment. Based on pre-post diary comparisons, treated participants outperformed controls on multiple sleep parameters, including Sleep Efficiency (SE) and Wake After Sleep Onset (WASO). Specifically, those who received the intervention significantly improved SE (76.8% to 89.2%) while controls did not (79.6% to 81.6%), $P = 0.005$. Treated subjects also decreased WASO (68.6 ± 40.9 to 29.9 ± 20.3) while controls did not (56.4 ± 19.4 to 51.8 ± 26.6), $P < 0.001$. Participants who received the intervention strongly credited the program with their success. 42.9% reported that SHUTi had improved their sleep "very much," and nearly all (95%) stated that SHUTi had at least "somewhat" improved their sleep. In addition, treated subjects indicated a significant change in their sleep pattern over time, greater satisfaction with their current sleep pattern, a sense that insomnia was not as much of a problem for them, and less of a need for additional treatment (all $P < 0.001$). All treated participants indicated that SHUTi was either "mostly" or "very" (3 or 4 on a 0 to 4 scale) easy, convenient, and useful. Clearly, the Internet intervention had a substantive positive impact on those who had used it. These findings suggest that an accessible, tailored, self-help approach to treating adult insomnia has significant potential.

O53

Psychological effects of Cognitive Behaviour Therapy (CBT) for persistent insomnia associated with cancer: randomised controlled trial (RCT)

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Introduction: Insomnia can be caused, or exacerbated, by the stress of having cancer, and up to 40% of patients report persistent sleep problems. Whereas CBT is effective for primary insomnia, the treatment literature on insomnia related to cancer is sparse. Moreover, little in known about psychological changes following CBT for insomnia in this population.

Methods: Pragmatic, two-centre RCT of CBT versus treatment as usual (TAU). Patients meeting diagnostic criteria for persistent insomnia recruited after completion of active anti-cancer therapy for breast, prostate, colorectal or gynaecological cancer. Major assessments at baseline, post-treatment and 6-month follow-up. CBT comprised 5, weekly, 1-h, small group sessions led by a cancer nurse following a validated CBT manual. TAU comprised usual care. Outcomes measured using validated and reliable questionnaires/rating scales of dysfunctional thinking and attribution.

Results: Data from 150 participants (103F; mean age 61 year) analysed on intention-to-treat basis. Significant reductions in subscales of the Dysfunctional Beliefs and Attitudes about Sleep scale (range of ES = 0.65–1.04), and the Sleep Disturbance Questionnaire (range of ES = 0.95–1.18), observed in CBT at post-treatment, relative to TAU. These ES increased to .95–1.33 for DBAS, and .82–1.37 for SDQ at follow up.

Conclusion: Cognitive adjustment associated with successful CBT treatment for insomnia in cancer patients appears similar to that observed in primary insomnia, supporting the notion that insomnia associated with cancer may be treated similarly to the primary insomnia syndrome.

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O54

Efficacy of cognitive behavioural therapy for insomnia in group format

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Introduction: Although CBTI has been established as one of the standard treatments for chronic insomnia, at present, it is not widely available because limited number of clinicians are trained to deliver this type of therapy. We report clinical significance of a 7-session, 9-week CBTI delivered in group format by a behavioral sleep medicine clinician, in Milan, Italy.

Methods: Data were from 83 consecutive series of sleep clinic patients (41 women, 41 men; age 19–72 years, $M = 41.9 \pm 12.7$ years) with chief complaint of insomnia and enrolled in group CBTI. Each group consisted of 10–14 patient. The 7 treatment sessions occurred at Week 1 (assessment and goal setting), 2 (sleep education), 3 (anxiety and stress management), 4 (stimulus control and sleep restriction), 6, 7 (cognitive restructuring, and SC & SR continued) and 9 (review and relapse prevention).

Results: Compared to baseline sleep diary data, CBTI resulted in significant improvement, including sleep latency (38 ± 40 min versus 20 ± 14 min), WASO (57 ± 49 min versus 23 ± 20 min), TST (5.9 ± 1.3 h versus 6.2 ± 1.0 h), sleep efficiency ($78 \pm 14\%$ versus $88 \pm 8\%$), and sleep quality (5.0 ± 2.1 versus 6.0 ± 2.1 on 1 = very poor 1/4 10 = excellent Likert scale). Among patients (77%) who took sleep medications at baseline, 1/4 of them completely got off sleep medication and an additional 31% decreased medication by $\geq 50\%$ by Week9. Patients rated $68 \pm 24\%$ accomplishment of their personal treatment goals. Drop out rate was 6%, and 89% of patients rated moderate or higher level of treatment satisfaction. Based on Insomnia Severity Index score classification, 85% of patients no longer have clinical insomnia (ISI score ≤ 14; ISI score 17.0 ± 5.0 at baseline versus 9.6 ± 5.0 at Week9).

Conclusions: CBTI in group format result in clinically meaningful improvement in sleep and facilitated substantial reduction in sleep medication use. CBTI is well received by patients. In light of high prevalence of chronic insomnia, group CBTI represents a cost-effective and a mechanism of dissemination for making this therapy more available.

O55

Sleep restriction mechanisms in insomnia: preliminary outcomes on treatment efficacy

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Sleep restriction therapy is recommended as a non-pharmacological treatment for insomnia. However, there is little attention concerning its efficacy when used alone and the underlying treatment mechanisms. The objective was to evaluate the efficacy of sleep restriction alone and to explore its process in insomnia treatment. The sample included 5 participants (4 women, mean age 41 years) meeting diagnostic criteria for primary insomnia. A multiple baseline across subjects design was used. Participants completed daily sleep diaries from baseline to post-treatment and for two weeks at the 3-month follow-up. They wore an actiwatch during treatment and spent a total of eight nights in the laboratory. Sleep restriction consisted of curtailing the time spent in bed to the actual amount of time estimated to sleep. There were four to six treatment sessions. Sleep Efficiency (SE), Sleep Onset Latency (SOL), Total Wake Time (TWT), and Total Sleep Time (TST) were derived from sleep diaries. These data were examined for each participant with intervention time series analyses to determine if there was significant improvement while introducing treatment. The statistical modeling of sleep variables explained an average of variance ranged from 50.4% for TST to 79.6% for SOL. Four participants showed a significant decreased in SOL for an average of 30 min; five had a significant decreased in TWT for an average of 96 min while three participants achieved a significant increase in SE for an average of 15.9%. Three participants presented a significant decreased in TST for an average of 56 min. Visual inspection of the follow-up showed that sleep remained improved for four participants and initial decreases in TST were improved. Polysomnographic data confirmed sleep changes for four participants. Weekly percentages of compliance varied greatly among participants and weeks with an average of 57% (SD = 31). These preliminary results suggest that sleep restriction is effective when used alone despite variation in treatment compliance. Decrease of about an hour in sleep duration during treatment indicates that sleep restriction has an acute effect on TST. Although sleep restriction has long term benefits, this acute effect could have negative consequences during treatment.

O56

Patient satisfaction in insomnia: development of a psychometric based assessment

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Objective: Although treatment satisfaction has been addressed in other disease states, there are no questionnaires currently available to examine the effects of therapy on treatment satisfaction or the value of therapy for patients with insomnia. The goal of the study was to develop a psychometric based assessment instrument of treatment satisfaction for patients with insomnia.

Methods: An expert panel of researchers and clinicians identified specific patient satisfaction items from the existing literature. Two focus groups consisting of 8 to 10 patients with insomnia (based on diagnosis and history of sleep disturbances) were surveyed. A preliminary assessment instrument was developed consisting of 42 items (scale: 1 = not important at all to 5 = extremely important), including demographic characteristics and co-morbidities. This instrument was pretested in 14 additional patients prior to validation testing.

Results: A total of 109 patients (mean age 50+11.5 years, 67.9% female) participated in the initial testing of the instrument. Principal components exploratory factor analysis (KMO = 0.85) reduced the assessment instrument to 17 items (Cronbach $\alpha = 0.90$) in 5 domains (contentment, dosing flexibility, outlook, value, and treatment satisfaction). Cronbach α for the 5 domains ranged from 0.73 to 0.86. Goodness of fit measures for the measurement model (AMOS, version 7; $\chi^2 = 50.8$, df = 53, $P = 0.559$; CFI = 1.00, GFI = 0.94, NFI = 0.92, RMSEA = 0.001) support the relationship between the data and the hypothesized model.

Conclusions: Preliminary results from the structural equation model revealed a 17-item assessment instrument consisting of 5 important domains (contentment with therapy, dosing flexibility, and outlook with respect to treatment satisfaction and value). Further testing and validation of the instrument with additional patients is planned. This novel assessment instrument may provide greater knowledge regarding the impact of psychological domains on treatment satisfaction for patients with insomnia.

O57

Sleep enhances antigen-specific T helper cells after hepatitis A and B-vaccination in healthy men

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We tested the common notion that sleep supports immune defense in a vaccination study. Healthy young men were inoculated with a combined hepatitis A and B vaccine at 0800 h and assigned to two groups who either slept ($n = 13$) or were sleep-deprived ($n = 14$) during the following night. Immunizations were completed by a second and third inoculation after eight and 16 weeks, respectively, that were as well followed by a night of sleep or sleep deprivation according to the experimental group. After each vaccination, blood was drawn repeatedly for up to 20 weeks to determine hepatitis A and B antigen-specific T helper cells. For this purpose peripheral blood mononuclear cells were stimulated with overlapping peptides spanning the surface antigens of hepatitis A and B viruses for 6 h in the presence of brefeldin and costimulants CD28 and CD49. By means of multiparametric flow cytometry T helper cells were identified by forward and side scatter and surface markers CD3 and CD4. Intracellular CD40L was used as an early activation marker to determine hepatitis A and B antigen-specific cells. Within this cell population we additionally analysed percentages of interleukin (IL)-2, interferon (IFN)-gamma, tumor necrosis factor (TNF)-alpha and IL-4 positive cells. Ten subjects of the sleep group and eleven subjects of the sleep deprivation group completed the whole observation period of 20 weeks. Two weeks after the first inoculation percentages of hepatitis A and B antigen-specific cells in peripheral blood increased in both groups, followed by further strong increases after booster vaccinations. The majority of antigen-specific cells were IL-2, TNF-alpha and IFN-gamma positive with a minor proportion of IL-4 positive cells. Sleep compared to sleep deprivation increased the percentages of antigen-specific cells after all three vaccinations. This effect was more pronounced for hepatitis A than for hepatitis B antigen-specific cells and equally affected IL-2, TNF-alpha and IFN-gamma positive cells. In contrast, IL-4 positive cells were higher in the sleep group only after the second and third vaccination. We conclude that sleep supports adaptive immune defense after vaccination with particular increases in proinflammatory antigen-specific T helper cells.

O58

24-h growth hormone, prolactin and cortisol levels: the effect of hormone therapy and relationship between growth hormone and slow wave sleep in pre- and postmenopausal women

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Aging and menopause increase sleep complaints. Menopausal hormone therapy (HT) reduces these complaints in women. Sleep studies, however, have not been able to confirm these findings. Since growth hormone (GH), prolactin (PRL) and cortisol are affected by aging and important in sleep physiology, changes in their concentrations across menopause and during HT are of interest. In men GH secretion is linked with slow wave sleep (SWS) through all age ranges. In women daytime GH pulses are more frequent. The relationship between GH and SWS in women seems more complex. In this randomized, placebo-controlled trial GH, PRL and cortisol were sampled every 20 min for 24 h in 18 postmenopausal (aged 58–70 years) and 17 premenopausal (aged 45–51 years) women before and after six months of estrogen-progestin treatment (EPT). Polysomnography was used to evaluate sleep. At baseline the mean 24-h GH (1.0 versus 1.8 mU L^{-1}, $P = 0.033$) and PRL (6.8 versus 10.0 ng mL^{-1}, $P = 0.009$) concentrations were lower in post- than in premenopausal women but after EPT the postmenopausal levels did not differ from premenopausal baseline levels. Postmenopausal mean 24-h GH ($P < 0.001$) and PRL ($P = 0.002$), daytime GH ($P < 0.001$) and nighttime PRL ($P = 0.004$) were higher during EPT compared to placebo. Cortisol levels did not differ. Premenopausal mean nighttime PRL ($P = 0.026$) and cortisol ($P = 0.018$) were higher during EPT compared to placebo. Postmenopausal PRL and premenopausal GH and PRL concentrations were higher at night than during the day and EPT did not alter this pattern. SWS heralded between 40 to 20 min the first nocturnal GH peak in both pre- and postmenopausal women. The total percentage of SWS did not differ between the groups but in premenopausal women the SWS was less scattered ($P = 0.048$). We conclude that menopause decreases the GH and PRL levels and that EPT returns their levels towards those of the middle-aged premenopausal women. In contrast, the 24-h cortisol production is independent of menopause, EPT or age. As expected, in middle-aged premenopausal women EPT has fewer effects, which are limited to nighttime increases of PRL and cortisol. Pre- and postmenopausal women do not differ in terms of SWS but the time link between GH and SWS seems weaker in postmenopausal women.

O59

The effects of melatonin on sleep-wake rhythm of daytime hemodialysis patients: a randomized placebo-controlled cross-over study (EMSCAP study)

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Background: End-stage renal disease is associated with an increased prevalence of sleep disturbances. A mechanism involved in sleep regulation is the circadian sleep-wake rhythm. The pineal hormone melatonin plays an important role in the synchronization of the sleep-wake rhythm. The onset of the evening rise in endogenous melatonin is associated with the onset of sleep propensity. The absence of the nocturnal melatonin surge in hemodialysis patients has been described earlier. Aim of this study were to investigate the effects of exogenous melatonin on melatonin rhythm and sleep parameters in hemodialysis patients.

Methods: The study design is a randomized double-blind placebo-controlled cross-over study of 3×6 weeks melatonin 3 mg or placebo. Hemodialysis patients were asked to fill out a sleep questionnaire and to wear an actometer to objectify their sleep problems. Furthermore, melatonin concentrations in saliva were measured on the night after daytime hemodialysis and the consecutive night at 21:00, 23:00, 1:00, 7:00 and 9:00 h. After each period of 6 weeks actigraphy was performed, sleep questionnaires were filled out and melatonin concentration in saliva was measured. All parameters were tested by Wilcoxon signed- ranks test (2-tailed), significance level $P \leq 0.05$.

Results: In total, 24 patients (6 female, median age 71) were included. After treatment with melatonin a significant improvement of objective sleep onset latency ($Z = -2.20$, $P = 0.03$) and sleep

fragmentation ($Z = 2.41$, $P = 0.02$) were found. Sleep onset latency decreased from a median of 29.9 to a median of 15.5 min. The fragmentation index was reduced from 3.9 to 3.1 wake bouts per hour of sleep. Circadian melatonin concentration normalized. The nocturnal melatonin surge was recovered. In addition to objective sleep parameters subjective sleep parameters improved as well. Patients reported less time needed to fall asleep ($Z = -1.96$, $P = 0.05$), an increase in sleep time ($Z = -2.73$, $P = 0.02$) and an improvement in feeling well-rested in the morning ($Z = 2.13$, $P = 0.03$).

Conclusion: Treatment with melatonin resulted in an improvement of subjective and objective sleep parameters, as well as a normalization of circadian melatonin rhythm with a recovered nocturnal melatonin surge.

O60

Eplivanserin, a novel sleep compound, reduces night-time awakenings in patients with sleep maintenance insomnia without evidence of residual effects

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Introduction: Eplivanserin, an Antagonist of Serotonin Two A Receptors (ASTAR) with no affinity for GABA receptors (unlike benzodiazepines), is being developed at the 5-mg dose for the treatment of insomnia with sleep maintenance difficulties. It increases slow wave sleep (SWS) or deep sleep, and so is expected to decrease night-time awakenings.

Methods: This was a multicentre, double-blind, placebo (PBO)-controlled, 3-parallel-arm study in male and female outpatients ($n = 351$) with primary insomnia (DSM-IV criteria) and predominant complaints of difficulty in maintaining sleep (Wake After Sleep Onset [WASO] $\geq$ 30 min) for $\geq$ 1 month before entry. Patients were randomly assigned to receive PBO, eplivanserin 1 mg or 5 mg orally, once a day with their evening meal for 4 weeks. Patient-reported sleep parameters were recorded in the morning, using a sleep questionnaire. Efficacy variables included sleep quality (primary endpoint), WASO, number of awakenings and total sleep time (TST). Standard safety assessments were performed including rebound and next-day residual effects.

Results: A reduction in WASO (-11 min; $P = 0.009$) was seen with eplivanserin 5 mg versus PBO. In addition, there were fewer awakenings with eplivanserin 1 mg and 5 mg versus PBO ($P = 0.025$ and 0.008, respectively), and an improvement in refreshing sleep quality for eplivanserin 5 mg compared with PBO ($P = 0.049$). TST tended to increase with eplivanserin 5 mg. There was no significant effect of eplivanserin 1 mg or 5 mg on change from baseline in quality of sleep. Treatment emergent adverse events ($\geq$ 5%) with a higher frequency in the eplivanserin (1 or 5 mg) groups versus the PBO group respectively were: headache (9.4%, 12.3%, versus 9.2%), dry mouth (2.6%, 5.3%, versus 1.7%), and dizziness (5.1%, 1.8%, versus 2.5%). No serious adverse events were reported. No residual effects (on sleepiness or ability to concentrate, from morning questionnaire) or rebound insomnia after treatment discontinuation were reported.

Conclusion: Eplivanserin 5 mg day^{-1} improves sleep continuity by decreasing WASO and number of awakenings in patients with insomnia and is well tolerated with no evidence of residual or rebound effects.

It's About Sleep Homeostasis

O61

Period3 and the effects of sleep deprivation on executive function: the importance of circadian phase

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Introduction: Extreme preferences for waking and sleeping times are associated with a length variant polymorphism of the PERIOD3 gene. Those homozygous for the long variant (PER35/5) appear to operate under a higher sleep pressure than those homozygous for the short variant (PER34/4), and perform worse while undergoing extended sleep loss, particularly on tests of executive function. Here we describe how the genotype dependent effects of sleep deprivation on executive function critically depend on taken circadian phase into account.

Methods: Fourteen PER34/4 and 10 PER35/5 healthy, young (mean 25.0 ± 1.0 year) volunteers participated in an approximately 40-h constant routine, during which they remained awake in a semi-recumbent position in dim light. Blood was drawn hourly to establish the timing of individual melatonin rhythms. Every 2 h, volunteers underwent 20 min of cognitive testing. Tests had been practiced during the baseline days, and assessed: Working Memory (Verbal and Spatial N-Back), paced serial addition (PVSAT), unpaced digit-symbol substitution, sustained attention (SART), reaction time, motor sequence learning and control (Pursuit tracking and Serial Reaction).

Results: When plotted in terms of time since waking, executive function of both genotypes was not significantly different between the genotypes for any time point. However, when testing periods were re-aligned with respect of the circadian rhythm of melatonin, marked inter-group differences were evident late the biological night. During the period 2 to 4 h after the melatonin peak, performance of the 2 and 3- back verbal and spatial Working Memory tasks, and Paced Visual Serial Addition deteriorated significantly more in PER35/5. Thereafter, PER35/5 performance in these tasks recovered to PER34/4 levels. No statistically significant differences between the genotypes were observed for any non-executive tasks.

Conclusion: Individuals homozygous for the long variant of the PER3 polymorphism, have selectively impaired executive performance following sleep deprivation during the circadian trough.

O62

Polymorphism in period3 predicts fMRI-assessed inter-individual differences in the effects of sleep deprivation

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A variable number tandem repeat polymorphism in PERIOD3 (PER3) is a genetic marker for inter-individual differences in sleep homeostasis and the effects of sleep loss on cognitive performance, in particular during the circadian alertness nadir. Individuals homozygous for the longer repeat (PER3_5/5) are more susceptible than individuals homozygous for the shorter allele (PER3_4/4). However, the brain bases of the effects of the polymorphism on cognitive performance are unknown. Brain responses to an auditory 3-back working memory task were recorded in 15 PER3_4/4 and 13 PER3_5/5 individuals during 4 fMRI sessions separated in 2 visits. These subjects had not previously participated in any of our PER3 related research projects. During each visit, subjects were recorded in the evening, close to the circadian alertness crest, and the following morning, close to the circadian alertness nadir. During one visit they slept in the laboratory between the evening and morning sessions (sleep condition), whereas in the other they remained awake (sleep deprivation condition; SD). The order of the sleep and SD condition was counterbalanced. Performance and fMRI results showed that subjects could perform the task during all sessions and were affected by SD. FMRI data revealed striking differences between genotypes in the changes in brain responses observed after SD. In PER3_4/4 subjects, activity increased in frontal and temporal cortices, thalamus, cerebellum, and parahippocampus. By contrast, PER3_5/5 subjects exhibited marked deactivations in frontal, temporal, parietal and occipital cortices. The ability to recruit higher cognitive prefrontal areas after SD is maintained in PER3_4/4 but not in PER3_5/5. These data provide a brain basis for genetically determined interindividual differences in susceptibility to the effects of increased homeostatic sleep pressure during the circadian alertness nadir.

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O63

The COMT Val158Met polymorphism affects the sleep EEG in healthy men independent of homeostatic sleep pressure and modafinil

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The genetic and neurochemical mechanisms underlying homeostatic sleep regulation in humans are largely unknown. Catechol-O-methyltransferase (COMT) is an important breakdown enzyme of dopamine. The human COMT gene contains in healthy adults a common substitution of methionine (Met) for valine (Val) at codon 158, which leads to 3–4 times reduced enzyme activity. Individuals with Met alleles presumably have higher dopaminergic signaling in prefrontal cortex than individuals with Val alleles. We hypothesized that this functional polymorphism affects markers of sleep homeostasis, and the effects of modafinil, which is thought to promote wakefulness through a dopamine-dependent mechanism of action. Twelve homozygous Met/Met and 10 Val/Val allele carriers (all men; mean age: 23.4 years) completed two 40-h waking periods. After 11 and 23 h of wakefulness they received 100 mg modafinil and placebo in randomized, double-blind, cross-over fashion. Baseline and recovery sleep, as well as subjective state and neurobehavioral performance at regular intervals during sleep deprivation were analyzed. Sleep variables did not differ between COMT genotypes. In contrast, EEG power in nonREM and REM sleep was higher in the 8–13.5 Hz range in Met compared to Val allele carriers. This difference was present before and after sleep deprivation, and persisted after modafinil intake. In comparison to placebo, modafinil did not affect the well-established, sleep loss-induced EEG changes in recovery sleep in either genotype. These results contrast with the effects of the stimulant on the evolution of state and performance during prolonged waking, which were clearly modulated by the Val158Met polymorphism. In conclusion, a functional variation of the COMT gene is associated with robust inter-individual differences in the sleep EEG. These differences, however, do not reflect a genetically-determined influence on sleep homeostasis associated with altered dopamine signaling. Our data challenge the notion that modafinil inhibits the homeostatically regulated increase in sleep intensity after prolonged waking, and indicate that the effects of sleep loss on sleep EEG and performance are separately regulated.

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O64

Cortical excitability and sleep homeostasis in humans: a TMS/hd-EEG study

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In this work we explore directly the relationships between cortical excitability and sleep homeostasis in humans. Our experiments are inspired by a recent hypothesis about the function of sleep-The Synaptic Homeostasis Hypothesis (Tononi and Cirelli 2005). The hypothesis predicts that 1) after a night of sleep cortical excitability should decrease due to a global reduction of synaptic weights 2) during wakefulness, and after a night of sleep deprivation, cortical excitability should progressively increase, due to increased synaptic weights. To test this hypothesis we employed a combination of transcranial magnetic stimulation and high-density electro-encephalography (TMS/hd-EEG), a technique that allows for a direct and non-invasive measure of the excitability of cortical circuits in humans. In 5 subjects, we performed TMS/hd-EEG measurements at several (9) time points during a 72 h experiment (including a night of sleep, one of sleep deprivation and one of recovery sleep). At each time point, we probed with TMS/hd-EEG the excitability of both occipital and frontal cortex by measuring the amplitude and the slope of the first EEG response to direct cortical stimulation. In all sessions, measurements were corrected for contingent fluctuations in the level of vigilance by rejecting the trials that fell during periods of drowsiness, as detected by a continuous visuo-motor task (compensatory tracking task, CTT, Van Orden et al. 2000). To further control for the level of vigilance, pupil size was also continuously monitored during each TMS/hd-EEG session. In all subjects, the profile of cortical excitability in both frontal and parietal areas fluctuated coherently with sleep homeostasis, decreasing after sleep, increasing during prolonged wakefulness and decreasing again after recovery sleep. In particular, comparing the morning after sleep and the morning after sleep deprivation resulted in an increase of cortical excitability (slope of the first evoked component) ranging between 27% and 32% in all subjects. These finding reveal sleep pressure-related changes in intrinsic cortical excitability that are independent on the level of vigilance and on the circadian factor.

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O65

EEG dynamics during repeated sleep restriction and recovery support robust homeostatic responses to lost sleep over time

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The strong reciprocal balance between time awake and slow wave sleep (SWS), also called sleep homeostasis, has not been confirmed in studies with chronic sleep loss. The purpose of the present study was to investigate which parts of sleep physiology that react in a compensatory manner during repeated sleep restriction and subsequent recovery. Nine healthy males (age range 23–28 years) went though a laboratory protocol including 2 baseline days (sleep 23–07 h), 5 days with sleep restriction (03–07 h) and three recovery days (23–07 h). NREM-sleep EEG was analyzed with respect to spectral analysis. Sleep restriction resulted in an acute reduction of all NREM-sleep frequencies (0.50–8.00 Hz constituting the delta and theta frequency bands) if total sleep is considered ($P<0.05$). However, if only the first 3.8 h of sleep are analyzed-equalling sleep time between conditions-most sleep frequencies (1.50–8.00 Hz) increased already the first night with restricted sleep and continued to increase in a gradual fashion, levelling off after 3–4 days (P's$<$05). Although the compensatory increase is most obvious in the lower frequencies (2–4 Hz), which is within the traditional SWS-delta band, ''all'' sleep frequencies (0.75–8.00 Hz) were augmented also during the first recovery night. Limited frequency ranges were increased the second- and third recovery nights (1.75–5.25 Hz, 2.25–3.75 Hz, respectively; P's<0.05). The gradual increase of power in all sleep frequencies, during the accumulation of lost sleep, suggests that all NREM-sleep frequencies are part of a compensatory response. Our findings supports the notion that sleep homeostasis responds in a robust dose-response manner also during repeated sleep loss. Hence, our data contradicts recent findings interpreted as a failure for the homeostatic sleep-wake system to compensate for and adapt to chronic partial sleep loss. Furthermore, our data suggests that compensation to lost sleep occurs primarily in the upper part of the delta band as well as most of the theta band and that restricting the analysis to the delta band only might lead to misleading results in terms of sleep homeostasis and recovery.

O66

Analysis of sleep and sleep homeostasis under constant conditions

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NREM sleep EEG Slow-wave activity (SWA) reflects a sleep homeostatic process S, and the time course of SWA can be simulated on the basis of vigilance state distribution. In a simulation of SWA in the rat adaptation of the decreasing time constant (Td) of S was needed depending on time of day. It remained unclear whether these daily changes were caused by external or endogenous factors. Rats ($n = 11$) were implanted with EEG and EMG electrodes and adapted to the recording room in constant darkness (DD) for at least a week. A baseline day was followed by a 6-h sleep deprivation and 18-h recovery. Vigilance states were scored and EEG spectral analysis was performed. Simulations were performed as in Franken et al. 1991. In addition, the time course of SWA within individual NREM sleep episodes (10-s intervals) was analysed. With a Td of 3.2 h the simulation was consistently lower than SWA during the rest phase and higher during the active phase ($r = 0.555$ $P<0.01$). A variable Td (3.9 h rest phase, 2.5 h active phase, Franken et al. 1991) improved the correlation ($r = 0.682$ $P<0.01$), but systematic differences remained. A variable Td of 4.8 h (rest) and 1.6 h (active phase) turned out to be the optimal solution ($r = 0.748$ $P<0.01$). The rate of increase of SWA within individual NREM sleep episodes changed systematically over circadian phase, independent of the level of SWA. To optimize simulations of S in DD conditions, Td needs to vary between the active and rest phase suggesting that endogenous factors influence sleep homeostasis. Analysis of the time course of SWA within NREM sleep episodes indicates that the simulation systematically under- or overestimates SWA. This may explain the necessity of circadian changes in Td.

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O67

Influence of sleep homeostasis on per1 and per2 expression in the forebrain of SCN lesioned and intact mice

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Sleep is regulated by two main processes, a circadian process (C) and a homeostatic process (S). Process C depends on the master pacemaker, the suprachiasmatic nucleus (SCN), and its rhythmic expression of several clock genes, including period1 (per1) and period2 (per2). Recent reports of sleep alterations in several different clock-gene knockouts suggest an additional role for these genes in sleep homeostasis. This is also consistent with our observations that per1,2 expression in extra-SCN brain regions increase with wake and decrease with sleep. To study the relative contributions of these two processes on clock-gene expression outside the SCN, we determined by real-time PCR and *in situ* hybridization, per1,2 mRNAs expression in the brains of arrhythmic (SCN lesioned-SCNx) and rhythmic (intact) mice across the sleep homeostasis process. The measurements were performed after 6-h sleep deprivation (SD) beginning at light onset, after 2 h sleep rebound, and in respective time-matched controls. We also recorded sleep in SCNx mice to assess the degree by which the circadian process affects sleep homeostasis. Behavioral and histological examinations verified the effects and size of each lesion. The EEG analysis showed that sleep homeostasis is conserved in the absence of circadian drive as compared with control (sham lesion) mice. We also observed that SD elevated per1,2 cortical expression in SCNx and intact mice. Higher per1,2 baseline levels displayed in SCNx mice are also consistent with the higher daytime activity in these mice relative to controls. In intact mice, SD produced no change in SCN expression of per1,2, consistent with the primary role of these genes in regulating circadian timing in the SCN. In conclusion, our results show that sleep homeostasis as well as sleep-wake dependent changes in clock-gene expression in extra-SCN brain regions are preserved in mice without a functional circadian pacemaker. Our results support the idea that outside of the SCN, clock genes may not always follow a 24-hr periodicity, but are also driven by sleep homeostasis.

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O68

Recovery sleep stage dynamics following chronic sleep restriction

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Theoretical models of sleep homeostasis suggest an exponential rebound of Slow Wave Sleep (SWS) during recovery sleep from total sleep deprivation. However, there has been little systematic examination of recovery sleep stages after multiple days of sleep restriction. A sleep dose-response study was conducted to determine the nature of sleep stage rebound following chronic sleep restriction. $N = 88$ healthy subjects (age range 22–45 year; 43 females) participated in a laboratory-controlled chronic sleep restriction protocol. Subjects underwent 2 nights of baseline sleep (10 h TIB) followed by 5 nights of sleep restriction (4 h TIB) and a recovery night (R1) where TIB was given in different doses (2, 4, 6, 8 and 10 h TIB). Subjects were monitored during sleep polysomnographically using a standard montage (C3/A2, EOG and EMG). Sleep was scored by a trained technician according to R&K criteria. The durations of SWS, stage 2, REM, total sleep time (TST), sleep latency (SL), and the percentage sleep efficiency (EF) were calculated on R1 in each of the sleep doses. Linear and quadratic models were fit to the sleep dose functions for every sleep variable. A quadratic model best fit SWS ($R^2 = 0.187$), while a linear model best fit stage 2 ($R^2 = 0.68$), REM ($R^2 = 0.86$), TST ($R^2 = 0.89$), SL ($R^2 = 0.19$), and EF ($R^2 = 0.16$). Greater TIB at R1 resulted in more of each of the sleep stages, shorter SL, and greater SE, with the exception of SWS which was similar for all R1 doses of 4 h and more (all $P < 0.001$). These data suggest that rebound of sleep stages during recovery sleep following chronic sleep restriction is primarily linear with increases in TIB up to 10 h. Only SWS was characterized by a quadratic model, suggesting that the exponential process instantiated in theoretical models of sleep homeostasis based on total sleep deprivation studies extends to recovery sleep following chronic sleep restriction.

O69

The effects of acute sleep deprivation on a cross-modal divided attention task: a functional neuroimaging study

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Sleep deprivation (SD) can have a detrimental effect on occupational and cognitive performance. In particular, impairment of divided attention performance may significantly impact on an individual's ability to perform effectively when sleep deprived. The current fMRI study examined the influence of SD on selective and divided cross-modal attention. Twelve healthy male subjects (Mean age $\pm$ St.D = 39.0 $\pm$ 8.1 years) were screened prior to participating for sleep disorders, drug use, and other medical conditions contraindicating sleep deprivation prior to participating. Participants attended two functional magnetic resonance scans; after normal sleep, and following 27-h SD. During each session, participants completed a task that involved selective visual and auditory attention, and a divided attention task (visual and auditory). After normal sleep, visual and auditory selective attention resulted in cortical activation in sensory association areas related to these modalities (fusiform and temporal cortices respectively). The divided attention task further activated the orbitofrontal gyrus, anterior cingulate, and association sensory areas. There was no effect of SD on behavioural performance. Following SD, the increased processing due to divided attention was further enhanced in postcentral gyrus, precuneus and right parietal cortex, compared to after normal sleep ($P < 0.005$). Following SD there was increased activation in brain regions associated with divided attention, and further, additional brain regions located in the parietal region were also activated. As no behavioural changes were observed, this suggests that these additional activations may act as compensatory mechanism.

O70

Origins of contemporary concepts of sleep regulation

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The analysis of the origins of contemporary concepts of sleep regulation such as sleep homeostasis contributes to their critical evaluation. In this respect the biological theory of sleep proposed in 1905 by Edouard Claparède, professor of psychology at the University of Geneva, is quite remarkable. In accordance with present views of sleep homeostasis he stated that sleep propensity is proportional to fatigue, which is determined either by the duration of waking or by the work performed during waking. He claimed that fatigue is a factor disposing to sleep but is not a constituent of sleep. Awakening was seen to occur when the sleeper became tired of sleeping. Claparède's biological theory was distinct from contemporary physiological theories by focusing on the entire process rather than on specific mechanisms of action. He regarded sleep as an instinct in view of typical instinctual attributes such as globality, suppleness, plasticity and internal disposition. This line

of argument was taken up and expanded by Giuseppe Moruzzi who stated in his 1972 review of the sleep-waking cycle that "the compulsory striving of the animal as a whole-as an individual not as a 'mere collection of organs' – for a functionally integrated pattern of behavior seems to characterize instinctive life". He considered that despite sleep subserving "cerebral homeostasis" the requirements of instinctive behavior dominate. Moruzzi proposed that sleep is preceded by an appetitive behavior that is then followed by a chain of consummatory actions. The concept of sleep as an instinct has merits that deserve renewed consideration.

Ten Things to Remember About Sleep Apnoea

O71

Working memory in Obstructive Sleep Apnea (OSA) patients: a functional MRI study

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Introduction: Obstructive Sleep Apnea syndrome (OSAs) is associated with cognitive (attention, memory and executive-functions) and functional deficits. The real contribution of daytime-somnolence and of intermittent hypoxemia is still controversial. We assessed cognitive performance and cerebral activity during cognitive challenge in OSA, using neuropsychological tests and functional-magnetic-resonance-imaging (fMRI).

Methods: Fifteen male untreated severe (AHI >30) OSA patients (mean age 43.7 ± 7.5) and 15 age-education matched healthy controls. OSA diagnosis was made with polysomnography (AHI >30 h). During fMRI-scanning participants performed a 2-back working-memory task.

Results: Patients scored significantly below controls in short and long-term-memory, executive-functioning. Behavioral results during fMRI-scanning did not show significant differences between groups. Imaging results showed bilateral activations related to task difficulty in both groups in the posterior parietal cortex, insula, pre-supplementary motor area, left ventro-lateral and dorso-lateral frontal cortex and cerebellum. Significant Increased activations in patients versus controls were observed in the left superior, middle and inferior frontal gyri, dorsal medial precuneus, putamen and cerebellum. Decreased activations in patients were observed in the middle-occipital-gyrus and in the pontine reticular formation.

Conclusion: Stronger activations in patients were observed in frontal regions associated with sub-vocal verbal rehearsal and strategic organization of information, suggesting a compensatory-recruitment response to support normal performance. The results extend previous reports on the cognitive impairments and the altered functional neurocircuity associated with OSAs.

O72

A fMRI study of verbal memory encoding in obstructive sleep apnea patients

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Introduction: Obstructive sleep apnea (OSA) is a sleep-related breathing disorder which affects up to 5% of the population in Western countries. Several behavior studies have demonstrated an association between OSA and cognitive impairment in executive and attentional functions, memory, learning ability and psychomotor performance. In the present study we use the functional magnetic resonance imaging (fMRI) technique to uncover the cerebral correlates of verbal memory (VM) encoding in patients with untreated OSA and compare the results to previous fMRI studies of healthy subjects.

Methods: Brain activation during word encoding was measured using a block-design fMRI task in 24 patients with untreated moderate or severe OSA. Task blocks alternated between semantic and lettercase decision blocks. A delayed recall task was administered after the scan.

Results: As expected, semantic decision condition yielded a higher level of subsequent recollection as compared to the lettercase condition. Left frontal, bilateral occipital and thalamic regions showed significantly higher BOLD activations (whole brain, $P = 0.05$, FWE corrected for multiple comparisons). This pattern is consistent with findings previously described in the healthy population. Furthermore, task-related activation of several brain regions (right frontal and parietal) showed a significant negative correlation with the respiratory disturbance index (RDI), which reflects OSA severity. Several regions showed a trend for significance for a positive correlation with RDI.

Conclusions: OSA patients show a similar pattern of brain activation on a VM encoding task as healthy subjects as reported in previous studies. However, several other brain regions task-related activation demonstrated a significant negative correlation with RDI, which indicates that OSA severity has an impact on cerebral activation pattern even in regions remote from those classically involved in a VM task.

O73

A visual working memory parametric fMRI study in obstructive sleep apnea patients

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Introduction: Functional magnetic resonance imaging (fMRI) studies enable the investigation of neural correlates underlying behavioral performance. In the present study we investigate the working memory (WM) function of patients with untreated obstructive sleep apnea (OSA) and compare the results to previous fMRI studies of healthy subjects as well as the only previous fMRI study of WM in OSA patients.

Methods: A parametric fMRI experiment with four levels of a spatial N-back task was used to investigate the pattern of cortical activations across the various degrees of load in 21 patients with moderate or severe OSA.

Results: We found activations in a similar cortical network in patients as the one previously described in healthy subjects, involving the supplementary motor area, dorsolateral prefrontal cortex (DLPFC), precentral and parietal regions. The activity in these regions increased linearly with increasing load. Similarly, a deactivation pattern was found in posterior and anterior cingulate, bilateral parahippocampal gyri and medial frontal regions previously described as a "default network". Activation in these regions linearly decreased with increasing load. Furthermore, an inverted-U shape trend of activation was observed in posterior cingulum, thalami and occipital regions, as well as right insula and left parietal and left DLPFC. The latter observation may represent a reflection of the observed decrease of behavioral performance at maximal load.

Conclusion: Our results indicate that the same cortical regions are involved in WM function in OSA patients as in healthy subjects and that, similarly, some components of this network demonstrate a capacity-constrained response. This is in contrast with the results of the prior WM fMRI study (Thomas et al.), which revealed an absence of activation in the DLPFC of OSA patients.

O74

Diffusion Tensor Imaging (DTI) in Obstructive Sleep Apnea (OSA)

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Introduction: DTI is used to assess the integrity and organization of white matter; in particular, diffusion anisotropy maps give information about the impact of degenerative or vascular changes on white matter. OSA causes hypoxemia and fragmented sleep, which lead to neurocognitive deficits. The aim of the study is to assess with DTI whether OSA may be associated with significant modifications in brain diffusion maps, possibly reflecting the effects of hypoxemia.

Methods: Fifteen untreated male patients (mean age 43.7 ± 7.5) with severe OSA (AHI $> = 30$) and 15 normal controls matched for age, verbal IQ, education, gender, and hypertension were studied with a high-resolution magnetic resonance scanner. Measures of fractional anisotropy (FA) were assessed in patients and normal controls. We preliminary report 9 patients with OSA and 13 normal controls. Functional abilities were assessed with neuropsychological tests as well as with functional brain imaging techniques and are described elsewhere.

Results: The comparison between patients and normal controls showed decreases in FA in the long fronto-parietal fiber tracks belonging to the superior longitudinal fasciculus, bilaterally. The reverse comparison (controls versus patients) did not reveal significant regional differences, supporting the correctness of normalization preprocessing. Decrease of FA might be attributed to hypoxic damage.

Conclusion: Long fronto-parietal white matter tracks appear to be affected in OSA. These preliminary results need to be confirmed in the whole sample of patients and normal controls. The results about the effects of PAP treatment will clarify whether the white matter changes may be related to inflammation and ischemia.

O75

Neurocognitive deficits before and after treatment for obstructive sleep disordered breathing in children

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Introduction: Obstructive sleep disordered breathing (SDB) describes a range of upper airway obstruction during sleep from primary snoring to severe obstructive sleep apnoea (OSA). Significant neurocognitive deficits accompany childhood SDB, but it is unclear whether treatment by adenotonsillectomy (AT) improves neurocognition. This study assessed the severity of SDB and neurocognitive performance in children both before and after treatment, as compared to non-snoring matched controls.

Methods: Snoring children aged 3–12 years and awaiting AT for suspected SDB and non-snoring controls from the general community were recruited. Participants underwent overnight polysomnography (PSG) and comprehensive neurocognitive assessment (before AT for snoring children). Repeat testing was completed 6 months later.

Results: Ninty-one children completed both baseline and follow-up testing. Following baseline PSG, snoring children were categorised as having OSA ($n = 20$, 6.8 years $\pm$ 3.1; 14 males) or primary snoring ($n = 24$, 6.4 years $\pm$ 2.2; 15 males). Non-snoring controls were aged 7.8 years $\pm$ 2.6 ($n = 47$, 21 males). At baseline, significant reductions in IQ (9.1%), general knowledge (9.3%), executive functions of planning (20.6%) and working memory (8.9%), visual attention (17.9%), language development (13.8%), and visuospatial function (12.8%) were observed amongst snoring children when compared to controls (all $P < 0.05$). Reductions were not found for declarative memory, sensorimotor function and quantitative reasoning. AT improved sleep and respiratory parameters in snoring children, however there was no relative improvement in neurocognitive measures at follow-up. Severity of apnoea and hypopnoea was only mildly predictive of neurocognitive performance at baseline, suggesting factors other than arousals and hypoxia due to obstruction during sleep at the time of testing are important in determining neurocognitive performance amongst children.

Conclusion: These results suggest that neurocognitive deficits in children with obstructive sleep disordered breathing relative to controls do not improve during the first 6 months following treatment. Long-term follow-up of these children is now underway to determine whether the deficits are likely to be permanent.

O76

Obesity and severity of nocturnal desaturation have synergistic effects on the increased urinary excretion of leukotriene e4 in sleep apnea syndrome

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Introduction: Obstructive sleep apnea syndrome (OSA) is associated with underlying systemic inflammation and cardiovascular diseases. However, since OSA is also often associated with obesity, the link between OSA and surrogate markers of inflammation remains unclear. Among inflammatory mediators, leukotriene (LTs) pathway is activated in OSA. LTE_4 is the major urinary metabolite of cysteinyl LTs and provides the best marker of *in vivo* CysLT production.

Objectives: We measured urinary LTE_4 excretion of 98 OSA patients and 31 healthy subjects. Then, we investigated the influence of CPAP treatment for at least 3 months on LTE_4 urinary excretion in a subset group of 24 OSA patients. LTE_4 urinary excretion was quantified by liquid chromatography tandem mass spectrometry.

Results: LTE_4 urinary excretion was increased ($P = 0.009$) in OSA patients (68.5 ± 4.1 pg mg^{-1} creatinine) compared to control subjects (48.6 ± 5.1 pg mg^{-1} creatinine). A stepwise multiple-linear regression analysis was performed in the whole population to evaluate the impact of age, BMI, systolic, diastolic blood pressure, plasma insulin, glycemia and polysomnographic data (minimal SaO_2, mean SaO_2, AHI, RDI and percentage of time spent with a $SaO_2 < 90\%$). BMI ($P = 0.003$) and percentage of time spent with $SaO_2 < 90\%$ ($P = 0.007$) were independent predictors of LTE_4 urinary excretion. LTE_4 increased by 2.6 pg mg^{-1} creatinine per 1-point increase in BMI and by 0.9 pg mg^{-1} creatinine for each increase of 1% of nocturnal time spent with SaO_2 below 90%. No significant change occurred in BMI and LTE_4 urinary excretion after treatment with CPAP for at least 3 months.

Conclusion: BMI influences LTE_4 production three fold much more than hypoxia severity but both appear to be significant factors for the increased urinary excretion of LTE_4 in OSA patients.

O77

Sleep disordered breathing in patients with acute myocardial infarction

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Sleep disordered breathing (SDB) is a well established risk factor for cardiovascular morbidity. SDB is more common in patients with ischemic heart disease and may be associated with worse outcome after myocardial infarction. Therefore, it is important to identify SDB in patients with acute myocardial infarction. We studied patients without a previous diagnosis of SDB who were admitted for acute myocardial infarction. Sleep studies were done in the intermediate care unit when the patients were clinically stable. For the sleep studies we used the Watch-PAT100 which uses peripheral arterial tonometry, oxymetry and actigraphy in order to detect respiratory events. Patients were divided into 3 groups with no or mild (AHI <20), moderate ($40 >$AHI >20) and severe (AHI >40) SDB. Demographic and clinical data were compared among the three groups. Eighty four patients (21% female) with a recent myocardial infarction were studied. Forty four (52.4%) had no or mild SDB, 21 (25%) had moderate and 19 (22.6%) had severe. Age (no-mild: 55.6 ± 1.4, moderate: 61.2 ± 2.0 and severe: 60.8 ± 2.2, ns), BMI (28.5 ± 0.8, 26.9 ± 1.1, 29.4 ± 1.4, ns), and % males (76.2%, 81.8%, 78.9%, ns) were comparable among groups. Likewise, there were no differences in the rates of hypertension (43.2%, 47.6%, 63.2%) and diabetes (34.1%, 28.6%, 36.8%) but the severe SDB had significantly higher rate of CHF (11.4%, 19%, 42.1%), and previous MIs (9.1%, 28.6%, 31.6%, $P<0.05$). In addition, a high AHI correlated with elevated C-reactive protein levels (21.9, 21.2, and 42.8 mg L^{-1} in patients with AHI <20, AHI 20–40 and AHI >40, respectively; $P = 0.03$). We conclude that SDB is common among patients with recent acute myocardial infarction. The significant association between CRP levels and SDB may have an effect on recovery from MI and future prognosis

O78

Rantes is specifically elevated in obesity hypoventilation syndrome

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Background: Obesity hypoventilation syndrome (OHS) is defined by a body mass index (BMI) above 30 kgm^{-2} and daytime hypercapnia (>6kPa). We hypothesized that, compared to uncomplicated obese, OHS patients exhibit a specific inflammatory response that may participate to additional cardiovascular morbidity.

Aim: To compare inflammatory status and endothelial function, in OHS versus obese patients, matched for BMI, age and sex.

Methods: Sleep, blood gazes and endothelial function, measured by peripheral arterial tonometry (PAT) were analyzed in all included patients. Inflammatory (TNFα, IL-6, IL-8, IL-10, Leptin, MCP-1, RANTES) and anti-inflammatory (adiponectin and IL1-RA) parameters were also determined.

Results: Fourteen OHS patients (BMI: 40.5 ± 5 kgm^{-2}, age: 57 ± 12 years) and 22 matched obeses (BMI: 41.7 ± 5.4 kgm^{-2}, age: 56 ± 10 years) were included. $PaCO_2$ was increased in OHS versus obese patients (6.2 ± 0.5 versus 5.1 ± 0.4 kPa, respectively), whereas pH was decreased (7.39 ± 0.2 in OHS versus 7.43 ± 0.2 in obese controls). OHS exhibited a higher Homa-index and hypertension was more prevalent in this population. Serum levels of RANTES were increased in OHS compared to obese patients (58.8 ± 55.6 versus 13.4 ± 8.2 ng mL^{-1}, respectively ($P = 0.01$) whereas adiponectin levels were lower in the same patients (11.9 ± 9.3 versus 14.5 ± 6.7 µg ml^{-1}, respectively ($P = 0.05$). Others cytokines level were not different between the two groups. Finally, PAT correlated significantly with RANTES ($r = -0.6$ $P = 0.03$) and adiponectin ($r = 0.61$, $P = 0.03$) in OHS.

Conclusion: Compared to control obese patients, OHS is associated with a specific increase in the pro-atherosclerotic RANTES chemokine and a decrease in adiponectin, both patterns widely associated with increased cardiovascular risk.

O79

Long term compliance with Continuous Positive Airway Pressure (CPAP) for Obstructive Sleep Apnea (OSA)

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Introduction: CPAP is the treatment of choice for moderate to severe OSA. Treatment is usually life long but there are few published studies for compliance past 1–2 years. In the one series we identified long term compliance at 8 years was 33% (1).

Methods: We retrospectively reviewed hospital notes for all the patients who were started on CPAP for OSA during 1995–1998. Last measured compliance from an internal clock on CPAP was recorded as representative of long term compliance.

Results: We offered 339 patients CPAP, of whom 298 (88%) accepted treatment (36 did not tolerate, while 5 reported no benefit and hence stopped CPAP). Fifty were excluded from the final analysis (treatment was stopped in 19 as their condition improved, 24 moved to a different hospital so that their data were not available and another 7 were switched to bi-level ventilation). Out of 248 who remained on CPAP at our centre 13 patients were lost to follow-up (we assume they are not using CPAP). Excluding the 50 patients detailed above 81% (235/289) continued on long term CPAP. Of these 235 patients, completed compliance data was available for 221. Of these 196 were males and 25 females. At baseline the mean age was 55 (SD 6.9) years, Epworth sleepiness score 15.7 (SD 4.5), BMI 34.6 (SD 7.9) and 4% desaturation index 25.6 (SD 18.5)/h. The mean follow-up from the date CPAP was started was 7 (SD1.2) years. Mean hours of use was 6.4 (SD 2.0) hours/night with 193 (87% of those with known hours of use) using for more than 4 h/night.

Conclusion: Our data demonstrates that with careful patient selection, treatment titration and ongoing support good level of long standing compliance with CPAP can be achieved. This is important as cost effectiveness analysis such as those quoted in the NICE (national institute of clinical excellence) technology assessment depend on adequate initial acceptance and subsequent compliance.

Reference: 1. CPAP- an 8 year follow-up on acceptance, dropout and compliance on OSAS patients. H Cecilia, PO Haraldsson. Sleep Medicine, supplement-7 (2006), S15–16.

O80

Amplified neutrophil function in intermittent hypoxia/reoxygenation *in-vitro* mimicking sleep apnea

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Obstructive sleep apnea (OSA), characterized by Intermittent Hypoxia/Reoxygenation (IHR), is associated with atherosclerosis. Neutrophils are implicated in atherogenesis by producing

toxic molecules and enhanced neutrophils/endothelium interactions. Neutrophil apoptosis (NA) is an injury-limiting mechanism and its suppression may exacerbate inflammation and induce vascular damage. OSA as well as IHR *in-vitro*, profoundly suppress NA, whereas TNF-a has bi-modal effects, causing early acceleration and late inhibition of NA. The effects of TNF-a and the expression of the survival neutrophil regulator interleukin-8 (IL-8) on NA were investigated under IHR *in-vitro*. Whole blood or purified neutrophils from 8 healthy subjects (AHI = 2.7 ± 2.4; BMI = 24.9 ± 4.2; age = 34.3 ± 11.5) were exposed to IHR, sustained hypoxia (SH) or normoxia (NOX) *in-vitro* using BioSpherix OxyCycler C42 system (3 or 6 IHR periods, O2 saturation at 2%, for 6.6 ± 3.6 min h^{-1}, followed by reoxygenation). NOX and SH were employed for the same durations. NA was determined by nuclear and chromatin condensation (Giemsa and Hoechst 33342 staining), "low-CD16" appearance, and caspase-3 activity. Intracellular IL-8 was assessed by flow cytometry. By nuclear morphology, NA was attenuated by 73% under IHR compared to NOX. The suppressed NA by IHR depended on the intensity of the hypoxia and was more effective then SH (4.97 ± 1.7% at IHR versus 8.5 ± 3.1% at SH, $P<0.05$, compared with 11.45 ± 3.3% at NOX, NOX versus SH $P<0.01$, and versus IHR, $P<0.005$). Treatment with TNF-a (0.1–50 ng mL^{-1}) attenuated NA in doze- and time-dependent manner in NOX, IHR and SH. IHR suppressed NA via decreased caspase-3 activity (42.05 ± 11.3% at NOX, 16.04 ± 8.9% at IHR, $P<0.0001$), and increased IL-8 (17.9 ± 11.5% at NOX, 28.2 ± 17.6% at IHR, $P<0.01$). IHR in-vitro profoundly inhibited NA in healthy subjects as previously seen in OSA patients undergoing IHR in-vivo. Suppression of NA under IHR conditions was amplified by TNF-a and was mediated by caspase-3 and upregulation of the survival neutrophil regulator IL-8, thus supporting exaggerated inflammation under IHR. These data further support suppressed NA in OSA, and possibly delineate some of the mechanisms responsible for the suppressed NA and exaggerated inflammation in OSA.

Sleep in Little People

O81

NREM sleep dependent EEG features in children with Asperger syndrome

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We performed a two consecutive night polysomnographic and a complex neuropsychological examination of 10 children with Asperger syndrome (AS) and 14 healthy controls matched in age, gender and lateralization. We computed relative spectral power and phase coherence analyses for the all night NREM sleep period with respect to the following bandwidths: delta (0.5–4 Hz), theta (4.–8 Hz), alpha (8–11 Hz), sigma (11–15 Hz), beta (15–25 Hz); gamma1 (25–35 Hz) and gamma2 (35–45 Hz); Age controlled and Bonferroni corrected results showed in the AS group significantly increased relative power spectra activity in the delta frequency range over the left frontal (F3), central (C3) and bitemporal (T3,T4) areas, while significantly decreased values occurred mainly over the right frontal (F4) area in alpha frequency range. Phase coherence analyses revealed significantly decreased intrahemispheric values in AS group over the right fronto-central (F4-C4) areas in delta, theta and sigma frequency bands, and over the left fronto-central (F3-C3) areas in alpha and sigma frequency ranges. Relative delta activity over F3 area showed significant ($P<0.05$) positive correlation with the thought problems subscale of the CBCL (Child Behaviour Checklist), several verbal and visual short term memory performances, and negative correlation with certain executive functions, while relative alpha activity over right temporal area (F4) correlated negatively with CBCL internalization subscale, and verbal short term memory performance. Right fronto-central (F4-C4) coherence values correlated positively with certain executive functions and negatively with social behaviour and anxiety problems measured by CBCL. Left fronto-central (F4-C4) coherence correlated with executive performances (WCST) and with attentional problems. Our data reveal a possible local sleep regulation effect over the left cortical areas and a possible cortical dysconnectivity dominating over the frontal regions underlying the theorized executive dysfunction in autism spectrum disorders.

O82

Sleep and circadian rest activity cyles in infancy: the role of maternal depression

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Introduction: Major depressive disorder (MDD) is associated with sleep disturbances, abnormalities in the timing of REM and NREM sleep and with damped amplitude circadian rhythms. These findings are evident in both children and adults with MDD and in those at high-risk, who have depressed mothers. Damped amplitude rest activity cycles have also been reported in very young children with MDD, girls in particular. These findings raise the possibility that the initial entrainment period in infancy may play an important role. The present study compared developmental changes in sleep and rest activity cycles in infants at high and low risk for MDD, based on maternal history.

Methods: Fifteen infants participated in study, 4 with no maternal history of depression (low risk) and 11 infants with past or current maternal MDD (high risk). Sleep and circadian rest activity cycles were measured from light and motion-sensing actigraphs for 1 week every month starting at 2 weeks post partum, and continuing until 30 weeks post partum. Data were coded by group and total nocturnal sleep time, sleep latency, sleep efficiency, the number of day sleep episodes, their durations, and the strength of circadian rest activity cycles were compared at 2 and at 30 weeks, using repeated-measures MANOVA.

Results: The high-risk infants had significantly longer nocturnal sleep latency, lower sleep efficiency, and more daytime sleep than did low-risk infants at 2 and 30 weeks post partum. Circadian rest activity cycles were not evident in the high risk group at 2 weeks, and the remained significantly lower amplitude than the low risk infants at 30 weeks of age.

Conclusions: These findings suggest that sleep and rest activity cycles are poorly entrained in infants with depressed mothers. Our goal is to follow these infants longitudinally to further define sleep as a subsequent risk for their development of depression.

O83

Prone sleeping impairs circulatory control in sleeping infants

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Prone sleeping is the major risk factor for the Sudden Infant Death Syndrome (SIDS). We aimed to determine the effects of sleeping position on the development of circulatory control in infants over the first 6 months of postnatal age (PNA). Daytime polysomnography was performed on 20 full term infants (12F/8M) and mean arterial pressure (MAP) was recorded continuously and non-invasively (FinometerTM). Effects of sleeping position, sleep state and PNA on beat-beat heart rate (HR) and MAP responses to a 15 degree head-up tilt (HUT) were assessed during active sleep (AS) and quiet sleep (QS) in infants at 2–4 wks, 2–3 month and 5–6 month PNA. MAP and HR data were expressed as % change from baseline and responses divided into initial, middle and late phases. In the supine position a HUT usually resulted in an initial increase ($P<0.05$) in HR and MAP, followed by decreases ($P<0.05$) in HR and MAP in the middle phase; subsequently HR and MAP returned to baseline in the late phase. By contrast, in the prone position the initial HUT-induced rises in HR and MAP were usually absent, and at 2–3 month MAP actually decreased ($P<0.05$); subsequently HR but not MAP returned to baseline. At 2–3 month, MAP was lower ($P<0.05$) in prone than supine sleeping throughout the HUT. In conclusion, prone sleeping alters MAP responses to a HUT during QS at 2–3 month PNA. Decreased autonomic responsiveness may contribute to the increased risk for SIDS of infants sleeping in the prone position.

O84

Kiss: a multimodal therapy for children 5–10 years with insomnia

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Objectives: The rate of children with sleep disorders is high. Mindell (1993) suggests about 25% for preschool age children, Kahn et al. (1989) reported that 43% of 8–10 years-old had experienced a sleep problem for more than 6 months. Treatment for those children is necessary. The objective of the study was to assess a multimodal therapy program for children between 5 and 10 years with behavioural insomnia of childhood with a three months follow up.

Study Design: Twenty-three physical healthy 5 to 10 year old children and their parents participated. We used the Childrens

Sleep habits Questionnaire (CSHQ) and the Sleep Disturbance Index (SDI) in a german version to assess childrens sleep patterns and sleep problems as reported by parents. After 2 weeks sleeping diary a psychological behaviour and hypnotherapy training followed. In this training the children became 3 sessions in group therapy and so did the parents. After the treatment and 3 months later the children and parents were tested again.

Results: As expected, after the training the scores of the CSHQ were significantly reduced in the Wilcoxon-Test ($Z = -3.83$, $P < 0.001$) and after three moths the effect was similar ($Z = -2.67$, $P = 0.008$). All subscores of the CSHQ showed a significant reduction after the training and 3 months later. Looking at the SDI we can find a tendency of reducing the difficulties to fall in sleep. The sumscore shows although a significant reduction ($Z = -2.99$; $P = 0.003$). Those effects were still significant three months later. Looking at the sleep diary we found a significant reduction in falling asleep. The real sleeptime raised from 599.89 min during one night to 611.04 after the training and showed a significant effect three months after the training (642.46 min; $Z = -1.96$, $P = 0.050$).

Conclusions: The multimodal training program for children with behavioural difficulties is effectful. The program can decrease the symptoms of sleep disorders of children in age of 5 to 10 years. Looking at the daily effects of these problems such as difficulties to concentrate and behavioural problems as aggression it is important to reduce these symptoms in the early years. In further studies the school grades should be included and also the effect of the program on medical and physical health.

O85

Sleep dependent procedural learning in children

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Research evidence has shown that a night of sleep in adults can lead to procedural task performance improvements that are not matched during similar periods awake. This study examines the relationship between sleep and procedural learning in children, and assesses the role of sleep in the consolidation of procedural memory. Twenty healthy children (mean age = 8.85 years) were trained and subsequently re-tested on a finger thumb opposition task, involving repeated performances of a specific sequence. Participants were tested both before and after a period of sleep, and before and after a similar period of wake. Parents of children also completed the Paediatric Sleep Questionnaire (Gianotti et al. 1995), and participants completed a short form measure of IQ. Practice on the procedural task improved significantly with repeated performances over the initial training session, in addition participants also went on to demonstrate a subsequent time-delayed improvement, independent of any further intervening training. The extent of the subsequent improvement was specifically dependent on sleep, with participants showing a significantly greater improvement after a period of sleep, than after a similar period awake. A significant positive correlation was also observed between IQ and the degree of sleep dependent improvement on the task. Sleep dependent procedural skill learning in adults is relatively well defined, however research in children is lacking. This study confirms that sleep dependent learning occurs in children, with improvements on a procedural task specifically dependent on periods containing sleep. These findings indicate that sleep may have an important role in the development of learning in children, the correlation between IQ and sleep dependent improvement provides further evidence that sleep and learning are closely related. Further research involving sleep staging is necessary to provide more detailed information relating to the specific mechanisms involved in sleep dependent learning in children.

O86

Sleep quality and cognitive performance in healthy 7–8-year-old children

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Study objective: Among adults, sleep deprivation impairs cognitive performance. Some experimental studies in child populations have also shown mild effects of experimental short-term sleep restriction on cognitive performance. However, studies based on epidemiological samples are a few. The objective of the present study was to evaluate whether poor sleep quality is associated with cognitive performance in 7–8-year-old children.

Design and Setting: Cross-sectional study of children born in 1998 in Helsinki, Finland.

Participants: Two hundred and sixty-six (143 girls, 123 boys) children aged 8.1 (SD 0.3, range 7.4–8.8) years.

Interventions: N/A. Measurements: 7-day actigraph recording was performed to measure sleep duration and quality. The Sleep Disturbance Scale for Children was administered to parents. A neurocognitive test battery was performed.

Results: Longer sleep duration during the weekends correlated with better performance in symbol search ($r = 0.13$, $P = 0.04$) and visuomotor integration ($r = 0.17$, $P = 0.005$), but there were no other crude associations between sleep quality and cognitive performance. However, when controlling for confounding factors (age, sex, maternal education, and the study setting) in multivariate statistical models, average sleep duration as a continuous variable was linearly and positively associated with performance in block design ($P = 0.025$). Poor sleep efficiency was related to worse performance in similarities task ($P = 0.005$) and sleeping difficulties with impaired performance in symbol search ($P = 0.037$). Finally, long sleep duration was related to better performance in visuomotor integration task ($P = 0.012$).

Conclusions: Both sleep duration and sleep quality are related to cognitive performance in healthy children.

O87

Sleep disturbances in children with attention-deficit/hyperactivity disorder

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Several symptoms of Attention-Deficit/Hyperactivity Disorder (ADHD), such as inattention and motor restlessness, overlap with those associated with sleep disturbances. However, previous studies have not consistently shown that children with ADHD have more sleep disturbances. The objective of this study was to investigate sleep characteristics in children with ADHD compared to healthy controls and to examine associated behavioral and cognitive factors. Children with ADHD (9 boys, 13 girls; mean age = 9.5 years) were recruited through a university-based psychological clinic. ADHD diagnosis was based on DSM-IV criteria and ascertained by trained clinicians. Parents completed the Conners' Rating Scales-Revised (CRS-R), the Children's Sleep Habits Questionnaire (CSHQ), and Insomnia Severity Index for Children (ISI-C). Children wore an actigraph (Actiwatch, Mini-Mitter) during seven consecutive days after which they were administered the Conners' Continuous Performance Test (CPT). Parents and children from the control group (11 boys, 12 girls; mean age = 10.9 years) were administered the same measures except the CPT. Groups were compared on sleep measures using ANCOVAs controlling for age. No significant difference was found on CSHQ total score. However, ADHD children had higher scores on the sleep anxiety subscale of the CSHQ and on the ISI-C

($F = 7.20$, $P = 0.010$ and $F = 12.83$, $P = 0.001$, respectively), reflecting a more disturbed sleep compared to controls. On actigraphic measures, ADHD children showed less total sleep time ($F = 8.03$, $P = 0.007$), longer wake bouts ($F = 6.94$, $P = 0.012$), and increased nighttime activity ($F = 7.23$, $P = 0.010$). Pearson's correlations in the ADHD sample were computed between sleep measures and CRS-R and CPT scores. Lower actigraphic total sleep time was associated with higher scores on CRS-R subscales of Hyperactivity ($r = -0.61$, $P = 0.003$) and Anxious/shy ($r = -0.48$, $P = 0.028$). Higher nighttime activity was associated with higher variability of CPT reaction time ($r = 0.45$, $P = 0.041$). These results suggest that children with ADHD have poorer sleep as defined by parental reports and actigraphy. Actigraphic sleep parameters in ADHD children are also associated with symptoms of hyperactivity, but not with symptoms of inattention.

O88

Family environment and sleep quality in children

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Family environment is an important predictor of sleep quality in children. This work was aimed to evaluate sleep habits and sleep quality in children who are not refugees themselves but who grew up in refugee families adapting to life in Tbilisi after escaping from Abkhazia and compare it to the sleep of children of non-refugee families. We addressed the question: how much the family status may affect sleep of children during their early maturation. 60 children (7 to 11 years old) were studied in each group. Children completed Epworth sleepiness scale, Child Depression Inventory (CDI) and were interviewed regarding the main sleep-wake characteristics. General information about sleep behavior in children was collected from their parents as well. Parents were asked to evaluate children's behavioral sleep quality and fill 15 items questionnaire that was generated based upon the relevant literature. Parents were administrated the Perceived Stress Scale (PSS). Chi-square analysis and ANOVA with repeated measures were performed. Total sleep time was nearly identical in both groups of children. Significant difference between sleep time on week and weekend nights was found only for children from refugee families; they slept 1.2 h more on weekend nights ($P < 0.05$). Non-refugee parents reported better sleep hygiene and quality compared to the other group. Children of refugee families were rated as having problems with going to bed and maintaining sleep, and they had higher rate of sleepiness during the day (51% versus 34%; $P < 0.001$). Significant difference in the mean total CDI scores between non-refugee and refugee groups were also revealed (7.4 versus 9.7). Mean score for PSS was higher for refuge parents (23.9 versus 18.7; $P < 0.05$) appraising life situations as more unpredictable and stressful. Findings of this study suggest that stressful family situation is a risk factor for developing behavioral problems and sleep disturbances in children.

O89

Effects of parental evening interventions on stress, sleep, and school performance

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Poor school achievement performance and impaired attention as well as behaviour and emotional problems have been shown to be highly correlated with sleep difficulties in children and adolescents. Recent research has been shown that sleep may improve memory functions. We therefore investigate whether structured evening face-to-face interactions between parents and children including reading out and short recalls of school lessons will improve general learning and memory functions, stress coping, emotional competence, and will also manifest itself in functional neuroimaging, actigraphy, and in nocturnal cortisol excretion as a measure of stress. The study was performed in 4th grade pupils divided into an intervention and a control group; 21 out of 30 families finished the study. At baseline nocturnal cortisol excretion was significantly higher in boys than in girls. In general, cortisol excretion was the higher the earlier the pupils had to rise at school days. Sleep did not differ between sexes excluding a larger standard deviation in boys concerning sleep latency and sleep onset time. Sleep parameters correlated significantly to the math test in boys, while girls showed strong correlations between e. g. delayed sleep and negative stress coping and problem solving behaviour. The general delay of sleep at the end of the study seems to be an effect of the last days of the school year. No other effects of were seen in the control group, while within the intervention group these delays were less pronounced in children with a high rate of evening parental intervention. Although the delay of the rising up time was small, the delay of rising times was associated with a decrease in negative stress coping. In addition, decreased cortisol excretion correlated with an increase in text comprehension. In summary, the influence of parental evening intervention was negotiable, if it was done irregularly. At school, interactions between gender, nocturnal cortisol excretion, math performance, stress coping and sleeping times should be considered even in 4th grade pupils. Text comprehension could to be enhanced if stress was reduced.

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O90

Chronic sleep reduction, functioning at school and school performance in adolescents

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This study aimed to investigate the relationship between chronic sleep reduction, functioning at school and school performance. The sample consisted of 308 adolescents, aged 12.5–19 years (mean age = 14.6 years) in the first to fourth grades of two high schools. To measure chronic sleep reduction a questionnaire has been used with items referring to effects of chronic sleep reduction, such as emotional instability, irritability, loss of energy, sleepiness, and difficulty to get up. Cronbach's alpha of this questionnaire was .83. Correlations with insomnia and time in bed from light off were respectively 0.56 and -0.31. Functioning at school was measured with the School Perception Questionnaire, consisting of perception of teacher's behaviour, self-image concerning school performance, and achievement motivation. Cronbach's alpha's of these scales were 0.80, 0.89, and 0.79. School performance consisted of children's self reported marks at school. Real school marks were available for half of the participants. Mean self reported marks and Mean real marks were positively correlated ($r = 0.49$). Preliminary results showed that chronic sleep reduction and functioning at school were highly related ($r = -0.36$ to $r = -0.52$). Chronic sleep reduction and school performance appeared to have a significant negative correlation ($r = -0.30$). Relations between functioning at school and school performance varied from 0.26 to 0.68.

The Big Sleep

O91

Self-reported sleep duration and cognitive functioning in a general population

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Objectives: To explore the relationship between self-reported sleep duration and both objective and subjective cognitive functioning. According to previous studies indicating increased health risks in both short and long sleepers when compared with midrange-sleepers, we hypothesized a U-shaped association between sleep duration and cognitive functioning, and explored how the association was moderated by insomnia symptoms, sleep-disordered breathing, depression, alcohol consumption, drug use, and socio-demographic factors.

Design: A cross-sectional representative sample of the Finnish adult population.

Participants: Five thousand nine hundred and seventy-nine persons aged 30 years or older were interviewed and tested for cognitive functioning, and responded to the questionnaires.

Measurements: Objective cognitive functioning was assessed with tasks from the CERAD test battery (verbal fluency, encoding and retaining verbal material). In addition, an abbreviated version of the Mini-Mental State Examination (MMSE) was administered to participants aged 55 or over. Subjective cognitive functioning, self-reported sleep duration and other sleep-related factors were assessed with questionnaires. Depressive and alcohol use disorders were assessed with the M-CIDI interview. Medication was recorded in health examination.

Results: Both short and long sleepers had lower or at best equal cognitive functioning compared with midrange-sleepers. In multivariable models, the association was moderated by health-related and demographic factors and 29 of the 39 significant associations between the deviant sleep duration and objective cognitive functioning turned into non-significant ones. Among those having a basic education, both the short and long sleep durations were associated with impaired immediate recall. Verbal fluency was affected more by long than by short sleep durations. The association of long sleep duration with impaired cognitive functions was evident in the MMSE among participants 55 years of age or older.

Conclusions: Our study shows that the self-reported short and long habitual sleep durations were associated with cognitive impairments. This finding indicates that not only short sleepers but also long sleepers may be exposed to sleep deprivation, or to a failure in restorative function of sleep.

O92

Sleep habits of the general population in Austria: self reported data on sleeping behaviour, sleeping problems and treatment

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Introduction: Epidemiological studies show that the prevalence of sleep disturbances lies between 20% and 30% and increases with age. This study was performed to acquire up to date information about sleeping habits, sleep disturbances and treatment facilities in the adult population of Austria.

Method: In February/March 2007, a representative sample of the Austrian population (1000 participants, 478 men, 522 women aged over 14 years) was investigated for sleep habits and sleep disorders by face to face interviews. The pool was taken by random sampling from electoral rolls. Randomisation and the interviews were carried out by ''Karmasin Marktforschung'', the ''Austrian Gallup Institute''.

Results: A. Sleeping habits: Sleep duration between 6 to 8 h day^{-1} was reported by 75% of the Austrians, 15% need less, and 10% more sleep. Normal sleep latency (<30 min) were reported by 76%, whereas 6% had a longer one (18% did not give any answer). Problems with maintaining sleep had 26%, increasing with age (−30 year: 15%; 30–50 year: 21%, over 50 year: 38%). B. Sleep disturbances: Eighteen percent of the sample reported to suffer from non recuperative sleep. A majority of them (72%) had problems with falling and maintaining sleep for more than 6 months. A prolonged sleep latency (longer than 30 min) was reported by 6% of the sample; 26% complained about sleep disruption (1–3 times/night: 76%; 4–6 times/night: 4%) during the last months. Among these, the majority met the criteria of psychophysiological insomnia. Spontaneously nominated were snoring and apneas (22%), sleep terrors (22%), restless legs (21%), somniloquie (15%) and sleep paralysis (12%), followed by bruxismus (8%) and sleep walking (2%). C. Treatment: From the total sample of sleep disturbed subjects only 7% were treated: 96% of them consulted their doctor, 47% had taken a remedial action (changing of eating/drinking behaviour, change of sleeping place, etc.). 34% tried psychological therapy, 6% a CPAP mask and 4% an anti-snoring device.7% of the sample had taken sleeping drugs within the last 4 weeks.

Conclusion: In general, sleeping behaviour in Austria did not change very much from 1992–2007. Considering sleep duration, a trend towards ''short sleepers'' could be observed.

O93

Cost of insomnia in the UK

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The objective of this analysis was to determine the cost of insomnia in the United Kingdom based on the General Practitioner Research Database (GPRD). Incremental annual direct medical costs for insomnia patients were estimated by comparing to a random control sample from the general population without insomnia. The most prominent codes for insomnia were ''insomnia'', ''late insomnia'', ''persistent insomnia'', and ''insomnia not otherwise specificied''. Other sleep disorders such as sleep breathing disorders and parasomnias were excluded from the sample. A total of approximately 63,000 insomnia patients were identified from 2004–2006 and UK unit costs were applied to insomnia-related resource use for the 12 months post the index date period (defined as either the first insomnia prescription record or first diagnosis). Insomnia related costs included hip fractures, motor vehicle accidents, benzodiazepine abuse or toxicity, GP visits, nurse or nurse practitioner visit, specialist visits, and hospital visit. All of these aforementioned costs were controlled for within the framework of a generalized linear

statistical model (GLM). Due to the skewed nature of cost data, both *t*-test and bootstrapped confidence interval methods were performed and resulted in virtually identical results. Total per-patient medical costs in the insomnia group were £53.16 versus £21.36 for controls (*t*-test, $P<0.0001$) [CI: £24.17, £39.44]. In addition, insomnia patients were three times more likely to incur a cost (OR = 3.03, CI = 2.73–3.36) relative to controls. Bootstrap methods confirmed these findings. If the per-patient costs are projected to the national level assuming a 22% prevalence rate (NICE report on z-drugs), the direct cost of insomnia is estimated at £796 million. Therefore insomnia is of significant burden to the NHS in the United Kingdom.

O94

Day-after consequences of insomnia characterized by night-time awakenings in PCPS patients: results of the EQUINOX international survey

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Introduction: A cross-sectional survey, EQUINOX (Evaluation of daytime QUality Impairment by Nocturnal awakenings in Outpatient's eXperience), of patients visiting Primary Care Physicians' (PCPs) offices was conducted in 10 countries to determine the frequency of insomnia symptoms and their day-after consequences in patients complaining of these symptom (s) according to DSM-IV and ICSD criteria.

Methods: The survey included Finland, Greece, Jordan, Lebanon, Mexico, Morocco, the Philippines, Portugal, Sweden and Switzerland. Patients >18 years old having any insomnia symptom who were not on hypnotics in the previous four weeks were enrolled by PCPs over a 2-day period. One of the objectives of the survey was to compare the day-after consequences between subgroups of subjects reporting Difficulty Initiating Sleep, Difficulty Maintaining Sleep characterized by night-time awakenings, Early Morning Awakenings, and Non-Restorative Sleep. The impact of sleep problems on day-after activities including daily work and leisure activities, memory, concentration and mood was assessed via a 6-point categorical scale (0 = None, 5 = very high with 4–5 rated as severe). Number of hospitalizations, doctor visits, sick days, car, home and work accidents related to sleep problems according to the patients, over the last 6–12 months were assessed.

Results: A total of 5293 subjects (63.9% females; mean age 47.9 ± 15.3 years) were included in the analysis. When considering all day-after activities, 20–32% of patients with sleep disturbances had a severe impact. Within the past 6 months, 3.8% of patients reported a hospitalization, 39.3% had at least one doctor visit and 25.1% reported sick days that the patients considered related to sleep problems. Within the past 12 months, 9.0% of patients reported falling asleep while driving, 4.1% reported a car accident, 20.1% home accidents and 10.0% work accidents that the patients considered related to their sleep problems. These effects were observed with all symptoms of insomnia and were more frequent in patients suffering from a combination of all symptoms.

Conclusions: PCPs patients report a significant amount of severe impact on their day-after activities, health care consumption and accidents, that they consider related to sleep problems.

O95

Gender differences in the cross-sectional relationships between sleep duration, interleukin 6 and high sensitive C-reactive protein: the Whitehall II study

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Background: Emerging evidence suggests that disturbances in sleep and sleep disorders play a role in the morbidity of chronic conditions, including the development of cardiovascular disease for which an underlying inflammatory component has been proposed.

Methods and Results: The relationship between sleep duration and two markers of inflammation, interleukin-6 (IL-6) and high-sensitivity C-reactive protein (hs-CRP) was examined in white-collar British civil servants (all white individuals) from the Whitehall II study ($n = 4642$ for IL-6; $n = 4677$ for hs-CRP). The associations of sleep with IL-6 and hs-CRP are different and depend on gender (p for interaction <0.05). Following multiple adjustments for demographic characteristics and cardiovascular risk factors, in men and women there were no linear or non-linear trends between sleep and IL-6. However, in women but not men, levels of IL-6 were consistently lower in individuals who slept 8 h as compared to 7 h ($P = <0.05$). With hs-CRP, in the adjusted model, there was no association between hs-CRP and sleep duration in men. However, there was a significant non-linear association in women, the level of hs-CRP being significantly higher in short sleepers after multiple adjustments ($P = 0.04$).

Conclusions: No significant variation in inflammatory markers with sleep duration was observed in men. By contrast, both IL-6 and hs-CRP levels vary with sleep duration in women. The observed pattern of variation was different according to the inflammatory marker observed. Further studies are required to see if there is a temporal relationship between short sleep and markers of inflammation to support causality.

O96

Short sleep duration is associated with hypertension only among women: a population-based study

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Objectives: Sleep deprivation has been increasingly associated with a number of cardiovascular outcomes in epidemiologic studies. In particular, recent evidence suggests that short sleep duration may be associated with an increased risk of hypertension with possibly stronger effects among women than men. We sought to examine the cross-sectional gender-specific associations of sleep duration with hypertension in a large population-based sample from the Western New York Health Study (1996–2001).

Methods: Participants were 3,027 white men and women (43.5 versus 56.5%) without prevalent cardiovascular disease (median age: 56 years). Hypertension was defined as blood pressure $\geq$ 140/90 mmHg or regular use of antihypertensive medications. Multivariable logistic regression analyses were performed to calculate odds ratios of hypertension comparing short (<6 h) duration of sleep versus the midrange category (6–8 h), while accounting for a

number of potential confounders [i.e., age, marital status, annual household income, education, body mass index, waist circumference, physical activity, alcohol consumption, smoking habits, SF-36 mental and physical scores, and depressive symptoms).

Results: In both unadjusted and adjusted analyses, short duration of sleep was associated with a significant increased risk of hypertension compared to sleeping 6–8 h, only among women (ORunadjusted = 1.83, 95% CI: 1.36 to 2.45; ORadjusted = 1.61, 95% CI: 1.08 to 2.41). No significant associations were found among men (ORunadjusted = 0.81, 95% CI: 0.58 to 1.12; ORadjusted = 0.88, 95% CI: 0.59 to 1.32).

Conclusion: These findings corroborate the notion that sleep deprivation may produce more detrimental cardiovascular effects among women, likely by increasing the risk of hypertension. This association is independent of socioeconomic status, traditional cardiovascular risk factors, and psychiatric co-morbidities. However, prospective and laboratory evidence is necessary to support causality.

O97

Sleep disorders and behavioural effects in a community sample of Australian children aged 5–10 years: the South Australian Paediatric Sleep Survey (SAPSS)

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Introduction: The association between diagnosed sleep breathing disorders and behaviour in children is well documented. However, information pertaining to sleep disorders and associated behavioural effects in large community samples is limited, especially in Australia. This study aimed to address this limitation.

Methods: In 2007, the South Australian Paediatric Sleep Survey was conducted to gather information on sleep and daytime functioning in children aged 5–10 years ($N = 1845$). Sleep characteristics were measured using a combination of previously validated parent-report questionnaires. The Strengths and Difficulties Questionnaire (SDQ) measured behaviour. Sleep disorder subcategories were developed using principle axis factor analysis. Regression analysis using standard error estimates to control for heteroscedasticity was used to determine the relationship between sleep disorders and behaviour.

Results: Cohort demographics showed an even distribution of gender (48.1% male), age (mean 7.66 years: SD 1.67 years) and socio-economic index (mean 993.58: SD 77.72). 81.6% identified as Caucasian. A rotated factor analysis revealed 12 distinct factors pertaining to sleep disorders and daytime sleepiness. Regression analysis revealed sleep inertia (difficulty getting up) as the strongest variable ($P < 0.0001$) associated with emotional symptoms ($r^2 = 0.13$), conduct problems ($r^2 = 0.10$), hyperactivity ($r^2 = 0.08$), peer ($r^2 = 0.06$), and prosocial problems ($r^2 = 0.04$). Sleep duration was also significantly related to all SDQ domains and explained 22% of the variance of sleep inertia ($P < 0.0001$). Reported sleep disordered breathing was related to emotional symptoms and peer problems ($P < 0.05$) but unexpectedly, not to hyperactivity or conduct problems.

Discussion: Acknowledging the limitations of parent-report, these results show that sleep duration, rather than behavioural or sleep breathing disorders, has the greatest effect on daytime behaviour. Previous sleep and behaviour research has predominantly focused on sleep quality, however reduced sleep quantity may have as serious an impact on daytime functioning in children. As children are progressively sleeping less, these results highlight the ever-increasing need for sleep education in the community.

O98

Shift work and subclinical atherosclerosis. The Cardiovascular Risk in Young Finns Study

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Shift work is associated with an elevated risk of cardiovascular disease, but the mechanisms of this association are not yet clear. This study examined the relationship between shift work and subclinical atherosclerosis in 1543 (712 men and 831 women, 24 to 39 years old) young adults as part of the ongoing population-based Cardiovascular Risk in Young Finns Study. Carotid atherosclerosis was assessed by measuring the thickness of the common carotid artery intima-media complex with ultrasound. Working schedules were categorized as day work or shift work (2- or 3- shift work, regular evening or night work). In men, shift work was associated with higher carotid artery intima-media thickness ($B = 0.023$, $P = 0.011$), and compared to day workers, shift working men had a 1.9-fold risk of having plaque on their carotid arteries (95% CI, 1.20–3.07). These relationships persisted after adjustment for age and other risk factors. In women, no association was found between shift work and intima-media measures. Our results suggest that shift work accelerates the atherosclerotic process and that the effects of shift work on subclinical atherosclerosis can be observed at a relatively early age, especially in men.

O99

Sleep schedules and academic success in Technical University students

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Sleep reduction in university students is an increasing problem. The cultural influences and the increased competitive pressure imposed upon young generations induce work schedules similar to adults. The Portuguese population, in line with these trends, has a late bedtime (74% go to bed after midnight) associated with early awakening. The purpose of this work was to evaluate the prevalence of sleep disturbances in students of the Technical University (IST) and to correlate them with daily habits, academic success and load and sleep quality measures. An internet questionnaire was send to the 8000 IST students; 924 answers were obtained (rate 11.6%). It had standard questions: sleep habits, the Pittsburgh Sleep Quality Index (PSQI), the Epworth Sleepiness Scale (ESS), academic success and overload, eating and sport habits, alcohol, tobacco and drug consumptions.

Statistics: Descriptive, ANOVA1 and multivariate. The responders were equally distributed by the different IST courses and by the academic year. There was a preponderance of males (15.8% females) typical of IST. The PSQI was abnormal in 88.1%, ESS in 55.6%. Students slept on average 6.7 h during the week and 8 h in the weekend. PSQI >5 had significantly higher ESS score, slept significantly less during the week and the weekend, had more classes, tests and exams at earlier hours, had poorer eating habits, more coffee per day and a lower sports practise. The correlates for abnormal ESS were the hours of sleep, the early classes and coffee consumption. The academic success was correlated with the hours of sleep (best students 8.8, worse 7.9 h day^{-1}), PSQI and ESS scores, number of tests done, tests, classes and exams at too early hours (all lower in best students); best students had more pleasurable activities going to bed latter in the week end and using the computer for fun longer. Excessive academic load and poor Eating contributed further to the negative results already described.

Conclusions: A cluster of factors including sleep duration, excessive academic load, academic schedules starting too early or ending too late, sleep, eating and other daily habits influence academic success, sleep quality and daytime vigilance in University Students Sleep habits, University Students, Academic results.

O100

Sleep problems are independently associated with well-being in the elderly population – a nationally representative survey

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Background: Sleep related complaints are frequently reported by elderly individuals. Here we report the prevalence of loud snoring with breathing pauses, insomnia and short sleep (<6 h night^{-1}) in elderly individuals (>65 years of age) from a representative sample of the Hungarian adult populations. Furthermore we analyze the association of sleep problems with depression and quality of life in the elderly population.

Subjects and Methods: Hungarostudy 2002 was a nationally representative door-to-door cross-sectional survey involving 12000 adult subjects in Hungary. In addition to questions about socio-demographic characteristics, sleep- and health-related issues, the study questionnaire also included the Athens Insomnia Scale (AIS), the Beck Depression Inventory (BDI), the illness intrusiveness rating scale (IIRS) and the WHO-well being scale (WHO).

Results: The prevalence of loud snoring with breathing pauses in individuals 18–45, 45–65 and >65 year of age was 19, 39 and 31%, respectively ($P<0.001$). The prevalence of insomnia (AIS >10 points) in those age categories was 5, 11 and 16%, respectively ($P<0.001$). Seven, 12 and 15% of the elderly respondents, respectively, reported less than 6 h of sleep ($P<0.001$). In the elderly group snoring was more frequent in males, whereas women had an almost twofold greater odds (OR 1.9, 95% CI 1.4–2.7) for having insomnia and also for sleep deprivation (OR 1.5, 95% CI 1.1–1.9). In multivariate analysis short sleep, loud snoring and the presence of insomnia were all independently associated with "feeling tired in the morning" after statistical adjustment for age, gender, socio-economic status, the Beck Depression score and comorbidity in the elderly population ($n=2408$). In multivariate models both the BDI score and the WHO well being score was predicted by all three sleep problems (snoring, short sleep and insomnia) independently from socio-demographic characteristics and co-morbidity. Illness intrusiveness, on the other hand was predicted by insomnia, but not by the presence of snoring or short sleep in this age group in similar multivariate models.

Conclusion: Sleep problems are common in elderly individuals and are associated with depression and impaired well-being.

Sleep and Memory Processing in Children

S39

High-density sleep EEG recordings during adolescence

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The increased sleep need in children and adolescents (Iglowstein et al. 2003) is accompanied by extensive learning processes during the day. Because of the intertwined relationship between sleep and wakefulness (Borbély 1982; Jenni and LeBourgeois 2006) the question arises whether sleep and learning share common mechanisms in developmental processes of the brain. In adults, evidence is accumulating that sleep plays an important role in brain plasticity, i.e. the remodelling of neuronal connections in the brain after learning (Tononi and Cirelli 2006). Recently, the major electrophysiological marker of the homeostatic regulation of sleep-sleep slow wave activity (SWA, <4 Hz)-was shown to be closely related to such remodelling processes (e.g. Huber et al. 2004). Interestingly, SWA experiences a dramatic decline from childhood to adolescence (e.g. Jenni and Carskadon 2004). We make use of the high temporal and spatial resolution of high-density sleep EEG recordings to investigate local changes of SWA in the course of brain maturation. Changes in this electrophysiological marker of sleep homeostasis are combined with novel analysis techniques based on the morphological characterization and description of the spatiotemporal dynamics of sleep slow waves, which potentially reflect changes in cortical connectivity and excitability (Riedner et al. 2007; Massimini et al. 2004). Thus, our recent studies investigate the relationship between changes in cortical connectivity and excitability and sleep SWA during development. An example of such a relationship might be found in the observed lower frontal predominance of sleep SWA in all of our children and adolescents as compared to adults. This might be of interest given the late maturation of the frontal cortex (Giedd 2004). If indeed sleep plays an important role in brain plasticity, the knowledge about the relationship between sleep and brain plasticity during childhood and adolescence is clinically relevant because many children suffer from sleep disturbances and learning disabilities.

S40

The role of sleep in cognitive performance at the age of 11: results from the great sleep experiment for children

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During the last decades, it has become evident that sleep plays a role in cognitive processing, and most notable so in memory and executive functioning. However, the majority of the studies has been performed in adults; very little is known about developmental aspects of the relation between sleep and cognition. There is a need to extend the focus of the ongoing research to include schoolchildren. Similarities and differences in the relation of sleep to cognition as compared with adults may provide developmental clues to the mechanisms involved. This presentation will account of an educational and research event for Dutch elementary school children aged 10 to 12 years called 'The Great Experiment' During this event data were collected that allowed us to investigate the relation of sleep and cognition in healthy children. Thirty children participated in repeated, computerized, learning and testing tasks both before and after their sleep was polysomnographically recorded. Tasks included a prefrontal tasks, the tower of Hanoi, and four memory tasks, addressing visual, motor and visuomotor skill learning as well as executive learning. Sleep was analyzed qualitatively according to Rechtschaffen and Kales and quantitatively using power spectra and spindle and slow oscillation detection algorithms. An overview of findings will be presented. Detailed information on motor skill learning is provided as well in the abstract and presentation of R. Schutte et al. (ESRS 2008).

S41

Procedural and declarative memory consolidation in children

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Sleep is known to support memory consolidation in adults. We investigated in three studies whether sleep benefits declarative and procedural memory consolidation also in children. In Study I, healthy children (7–11 years, $n = 14$) and adults (20–30 years, $n = 12$) were tested on a procedural serial reaction time task (SRTT) before and after retention periods spent either sleeping or awake. Contrary to the finding in adults, in children sleep did not increase, but rather decreased implicit sequence knowledge ($P < 0.01$). In Study II, consolidation of declarative (word-pair associates, 2D-object location) and procedural memories (finger sequence tapping) during sleep was assessed in children (6–8 years, $n = 15$) and adults (20–35 years, $n = 15$). Sleep in children as well as in adults strongly improved declarative memory consolidation whereas procedural memory benefited from sleep in adults only, but not in children. We hypothesized that the lack of sleep-dependent gains in procedural memory performance in the children reflects a preferential contribution of sleep to the consolidation of explicit, i.e., declarative aspects of the task interfering with the consolidation of purely procedural, i.e., implicit contents. To test whether sleep in children benefits explicit aspects of procedural memory thereby hampering consolidation of implicit aspects, Study III aimed to dissociate effects of post-training sleep on explicit and implicit aspects of memory in one and the same motor task. Preliminary results support our notion of a competitive interaction between both types of memory. Explicit sequence knowledge was enhanced by sleep whereas implicit knowledge, i.e., motor speed did not benefit. Together, our results point to strikingly different dynamics of sleep-dependent consolidation of explicit and implicit memory traces in children compared with adults.

S42

The cost of sleep deprivation for adolescents: cognitive, psychometric and physiological effects after sleep curtailment

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Sleep enhances procedural and declarative memory consolidation. However, little research has been done in children and adolescents despite the high relevance of providing favourable conditions for learning at this developmental stage. Initial findings on the consolidation of declarative and non-declarative memory in children (e.g. Backhaus et al. 2007; Fischer et al. 2007) yielded contradictory results indicating the need for additional studies. Our research group has conducted a variety of projects on adolescent sleep patterns, learning and memory consolidation. A survey ('School Sleep Habits Survey' questionnaire and two weeks of sleep logs) of 601 students (12 to 18 years) showed that the majority of students (91.6%) slept less than the recommended 9.2 h with 7% sleeping below 7 h. Data from sleep logs demonstrated an even lower sleep duration for school nights. A second project examined the effects of partial sleep deprivation on cognitive performance

and physiological parameters in a randomised, cross-over study (22 subjects, 14 to 16 years). An adaptation night in the sleep laboratory was followed by either a normal night (9 h) or a four-hour sleep-restriction night, and a recovery night. Learning took place before the experimental night, general cognitive and memory retrieval were examined after the recovery night. No statistically significant difference between the groups was found. After sleep deprivation subjects had significantly higher saliva cortisol levels and tended to show increased interleukin-6 (IL-6) serum levels in the morning. In our latest project, 85 adolescents from 14 to 16 years were investigated with different sleep protocols for four consecutive nights (5, 6, 7, 8 or 9 h of sleep), under rigorously controlled conditions. The fourth experimental night and the adaptation night were monitored polysomnographically. Physiological measurements (saliva and urine cortisol; plasma levels of leptin, ghrelin, IL-6 and orexin), a neuropsychological test battery (e.g. word pair associate task) and different learning paradigms (e.g. Turkish vocabulary) were conducted repeatedly. Preliminary analyses indicate 1) elevated saliva cortisol levels on the sixth morning in the short sleep groups; 2) a significantly higher subjective tiredness throughout the days for the 5- and 6-h sleepers; and 3) little impairment of neuropsychological functions despite cumulative sleep curtailment. This implies a high capacity in adolescents to compensate for sleep loss.

Circadian Sleep-wake Cycle Disorders in Psychiatry

S43

Circadian disturbances in psychiatric disorders

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Numerous lines of evidence suggest that disturbed circadian rhythms and/or sleep-wake cycle contribute to the clinical status of patients suffering from psychiatric conditions such as major affective disorder, chronic schizophrenia, and premenstrual dysphoric disorder. In bipolar affective disorder, sleep disturbances often precede relapses into depression or mania. Sleep-wake cycles of schizophrenic patients are often disrupted, showing either phase delays, longer periods of activity, or circabidian rest-activity patterns. Women suffering from premenstrual dysphoric disorder often present sleep disturbances that could contribute to symptoms production and/or exacerbation. The aim of the present studies is to evaluate the participation of the endogenous circadian system to these psychiatric conditions. Four bipolar patients underwent a 48-h ultra-rapid sleep-wake cycle procedure designed to unmask the circadian variation of sleep propensity and consisting of 24 cycles of 60-min waking periods alternating with 60-min nap opportunities. Throughout this protocol, sleep was polysomnographically recorded and mood assessed by visual analogue scales. These studies suggest that the circadian variation of mood and/or sleep is disturbed in bipolar patients. Two patients with chronic schizophrenia participated to a 2-/3-week long forced desynchrony protocol using 30-hour days. These studies revealed an abnormal circadian variation of sleep propensity and especially REM sleep propensity. Finally, eight women suffering from premenstrual dysphoric disorder underwent a systematic assessment of sleep and circadian rhythms across their menstrual cycle by sleeping in the laboratory every third night for a full menstrual cycle and undergoing 24-h blood sampling assessments during the mid-follicular and mid-luteal phases of their menstrual cycle. Data from these studies indicate an interaction between circadian and menstrual processes in the regulation of body temperature and sleep in women. Altogether, these studies support a role for circadian and/or homeostatic processes in the expression of mood and sleep disturbances that characterize psychiatric conditions such as chronic schizophrenia, bipolar affective disorder, and premenstrual dysphoric disorder.

S44

Circadian rhythm disorders and innovative therapies

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In our 24-h society, there has been an increasing awareness of persistent circadian rhythm sleep disorders (CRSD). In CRSD, delayed sleep phase type and free-running type are common in young adults. Most patients have difficulty adjusting to school/social life. The syndrome is thought to be multifactorial: social, psychological, and environmental factors as well as biological factors have all been proposed to play important roles in the onset and development of symptoms, but no single factor is sufficient to explain it. In our cohort study of 150 consecutive cases, 70% were diagnosed as primary CRSD and the remaining 30% as psychiatric diseases (depression, personality disorders, anxiety disorders, or schizophrenia). We usually treat these patients in outpatient clinic with several treatments by instruction to regular day-night life, exposure of bright light, and/or melatonin. Sometimes, these treatments are not successful. Recently we have proposed hospitalization treatment for re-entrainment of the sleep-wake schedule in CRSD patients who do not show improvement by usual chronotherapy. The patients stay in hospital for about a month with a combination of several treatment strategies. We have confirmed the hospitalization is effective for the re-entrainment of irregular daily-life style. Most of patients returned to their social lives. After patients obtain normal sleep-wake schedule, there is a need for rigid adherence to the new schedule. Although the impact of specific differential mechanism of phase re-setting could not be adequately delineated, increase of physical activity, regular meals on time, and the preference to routine hospital schedule might have substantially contributed to the adequate phase reset. These strategies have been considered from several aspects; psychological and clinical characteristics. Although patients with CRSD who need therapy have multiple factors in pathogenesis and development of symptoms, we should treat them and solve their problems.

S45

Delayed sleep phase disorder: psychiatric disturbances

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Recent evidence indicates a bi-directional association between disturbances of circadian rhythms and psychiatric disorders, so that alteration in circadian rhythms are common among patients with mood disorders and patients with circadian rhythm sleep disorders appear to have a high prevalence of psychiatric conditions. For example, using structured clinical interviews, our data indicate that the prevalence of Axis 1 disorders was significantly higher in patients with delayed sleep phase disorder (DSPD) than controls. The most prevalent disorders recorded for subjects with DSPS were substance use disorders, mood disorders and anxiety disorders. The mechanism that link circadian rhythm disorders, such as delayed sleep phase with psychiatric disease is unknown. Circadian desynchronization due to intrinsic changes in biological timing and sleep or environmental and societal factors, such as light exposure can all contribute to the development of mood disorders. Recent studies on the interaction between circadian clock genes and mood disorders are beginning to shed light on the role of the circadian regulation in psychophysiological and pathological brain functions. For example, polymorphisms of the hper3 gene has been shown to be associated with DSPD and extreme evening preference and weakly associated with mood disorder phenotypes.

S46

Molecular interaction between circadian rhythm and mood disorder

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Our biological clock counts daily rhythms with approximately 24 h called circadian rhythm in our body. The mammalian circadian system consists of three components: input, pacemaker, and output. Almost all physiological phenomena including mental states, in addition to sleep-wake cycles, can be considered as circadian outputs. The recent molecular advances revealed that molecular clocks were located not only in the central oscillator, suprachiasmatic nuclei (SCN), but also in peripheral tissues, even in cultured cells. We established both *in vivo* and *in vitro* rhythm monitoring system. To understand molecular interaction between circadian rhythm and depression or mood disorders, we investigated circadian rhythm of the learned helplessness (LH) rat, an animal model of depression, at the behavioral and cellular level. The locomotor activity rhythm *in vivo* and circadian transcriptional rhythm in vitro seemed to be correlated with each other. The phosphorylated glycogen synthase kinase-3β (pGSK-3β) was likely to be the key molecule that connects behavioral rhythm with cellular ones. Clock genes were included in the downstream targets of GSK3β. The phenotypes including circadian rhythm in fibroblasts correlate to those in vivo, suggesting that the fibroblasts from the patients can be used as a diagnostic material and a therapeutic tool.

New Insights into Sleep and Breathing from Top to Bottom

S47

Functional and structural imaging of opioid effects on respiratory control

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Opioid drugs are a mainstay for the treatment of acute and chronic pain, however their use is limited by potentially fatal depression of respiration. Opioids interfere with sleep, and are associated with an increased incidence of sleep disordered breathing through their actions in the pontine reticular formation. I have used novel functional and structural magnetic resonance imaging techniques to examine the respiratory control system in healthy human volunteers, and its modulation by opioid analgesics. Imaging the brainstem has proven technically challenging, but necessary for such studies. I shall discuss the techniques that are currently available, and how such methodology could advance the understanding of sleep disordered breathing. A fuller understanding of opioid action on respiratory control may help develop novel therapies that could combat opioid-induced respiratory depression whilst maintaining analgesia. Such understanding could also be crucial in understanding mechanisms of sleep disordered breathing and dyspnea. My work with opioids confirms the importance of higher cortical centres (and by extension arousal state) for the effects of opioid drugs on respiration.

S48

Imaging the whole brain in obstructive sleep apnoea syndrome

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People with obstructive sleep apnoea (OSA) exhibit neural changes which likely influence comorbidities and possibly progression of the syndrome. Neuroimaging has shown structural and metabolic changes to the brain in OSA patients, as well as functional alterations in a number of areas. Recent magnetic resonance imaging (MRI) techniques have allowed detection of subtle but extensive neural injury in gray and especially white matter regions, including limbic, cerebellar, and cortical areas, and axonal groups connecting these regions. Consequences of such injury likely include altered function within damaged structures. Indeed, functional MRI studies show abnormal responses to physiologic (pressor and respiratory) challenges, and to cognitive tasks. The affected brain structures have roles in cognitive function and emotional regulation, as well as cardiovascular and respiratory control (also demonstrated with functional MRI). Although improvements in some cognitive functions and mood are seen following CPAP treatment, reflecting shorter-term functional brain alterations, other neuropsychological deficits remain after such intervention, perhaps reflecting injury-related alterations. The functional changes could also contribute to physiologic comorbidities and perhaps exacerbate the disorder through weakening respiratory regulation. More recently, the neural injury in OSA has been shown to be influenced by several factors, including age, gender, mood, and sleep state, so the relationship between the disorder and brain alterations is complex. The processes contributing to these deficits likely arise in part from physiological consequences of apnea, including hypoxia and hypercapnia; animal models simulating one characteristic of OSA, intermittent hypoxia, demonstrate cell injury and apoptosis. Additionally, injury is suspected from comorbidities independently associated with brain damage, notably depression and hypertension. Relative protection in females is also apparent, a finding consistent with animal models of hypoxia. In summary, brain structure and function are affected in OSA, and these neural changes likely result from a combination of syndrome characteristics, comorbidities and, possibly, prior damage. The neural deficits appear to contribute to poor cognitive and affective functioning, and interfere with autonomic and respiratory regulation.

S49

Sleep apnoea syndrome: future clinical and research directions

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Obstructive sleep apnoea (OSA) syndrome corresponds to recurrent episodes of partial or complete pharyngeal collapse occurring during sleep. It is a growing health concern affecting up to 5% of middle-aged men and women in the general population. Sleep apnoea is a major cause of excessive daytime sleepiness, resulting in impairment in driving ability and increase in traffic accidents. Sleep apnoea is also a serious health hazard being recognized as an independent risk factor for hypertension, arrhythmias stroke and coronary heart disease. People with obstructive sleep apnoea have a peak in sudden death during night-time and an increased rate of cardiovascular morbidity and mortality. Sleep apnoea is also associated with several cardiovascular sub-clinical or clinical conditions including diastolic hypertension, diastolic ventricular dysfunction, early atherosclerosis as well as conditions leading to long-term cardiac pacing. Lastly, OSA metabolic consequences are currently under investigation. A number of reports found increased insulin resistance and impaired glucose tolerance in OSAS patients, independent of body weight, and a worsening of insulin resistance with increasing AHI. However, other studies failed to demonstrate an independent effect of AHI owing to the major impact of obesity. In cohorts of the general population, both the Sleep Heart Health Study and the Wisconsin Cohort Study have identified OSA as an independent risk factor for insulin resistance, after adjustment for potential confounding variables such as age, sex and BMI. It should be mentioned however, that treating OSA in obese subjects seems to be of little impact on metabolic dysfunction. Clinical challenges Sleepiness (EDS) is indeed a major symptom in OSA. The difficulty particularly in moderate sleep apnoea patients is to identify EDS resulting from other causes than sleep apnoea. In general population cohorts, depression is a major confounding factor. Obesity alone may also interfere specifically through adipokines and chemokines being activated even in the absence of apnoea. An extreme example is obesity-hypoventilation syndrome (OHS). In OHS, leptin and other adipokines seem to be strongly activated which could produce both EDS and systemic inflammation. In OSA, stress activation involving both the HPA axis and the sympathetic system may also play a role. It is now well established that cognitive and attentional deficits may occur in OSA in the absence of perceived subjective EDS. This questions the sensitivity of the tools used for evaluating EDS i.e. Epworth Sleepiness Score. Also, attentional deficits may occur without objective EDS. Reaction time, sustained and divided attention tasks may be altered in the absence of EDS. It should be further studied whether these attentional deficits may impair driving ability and other social and professional abilities. If confirmed, this raises the difficult questions of who should be treated since the absence of perceived EDS would not be required for treating OSA. Another big clinical challenge is treatment of non-symptomatic OSA as regards to cardiovascular risk. This is still a controversial area besides the feasibility of treating non-sleepy patients with CPAP. Whether EDS is linked to OSA cardiovascular morbidity is still unclear as well as whether the cardiovascular response to CPAP in OSA is dependant on the presence of EDS. In any case, there is a need to find biological markers that could help to make a decision treatment whatever the symptoms are. Until now, the complex relationship between OSA, the genetic background and the associated cardiovascular and metabolic morbidities have made very complex the identification of vulnerability indicators. This is

however required since exposure to sleep apnoea and intermittent hypoxia results in different phenotypes. The last clinical challenge is access to diagnosis. There is compelling evidence that several clinical sub-groups are at risks. This is the case for instance for refractory hypertension, obesity and type II diabetes, heart failure, arrhythmias and stroke. It is thus required to have different strategies for detection and diagnosis in these sub-groups. Polysomnography (PSG) is mainly adapted to search for a specific cause for a given symptom (e.g. EDS) and particularly in case of low pre-test probability. Conversely, PSG is not at all adapted to diagnosis in at-risk specific sub-groups owing to the epidemiological needs. This is more and more recognised, even in the US. Several international task forces are currently working on proposals. Importantly, it is required to validate new pathways for management of OSA rather to simply validate specific tools versus PSG. Research perspectives In heart failure patients presenting with sleep-disordered breathing, on-going long-term trials evaluating morbidity and mortality with assisted-servo ventilation devices are starting in 2008. One of the major questions in OSA is whether treating sleep apnoea results in larger improvement than using usual cardiovascular drugs for lowering blood pressure, reducing inflammation or preventing cardiovascular morbidity. Although a reduction in cardiovascular morbidity has been established in observational cohorts, there is a need to evaluate CPAP effects in large randomised-controlled trials. However, ethical issues limit the period of observation, at least in moderate to severe apnoeic patients. There are however on-going 6-month trials (Apples Trial, C Kushida) or even longer trials in mild to moderate OSA (Mosaic trial, J Stradling) comparing active CPAP versus sham-CPAP. There are also starting phase I and II drug trials directed towards preventing upper airway collapse. This is supposed to be obtained either by stabilising ventilation or by increasing upper airway tone. One of the recent major clinical findings of the past years is the occurrence of atherosclerosis in OSA patients free of any cardiovascular morbidity otherwise and of other cardiovascular risk factors. This is part of the sub-clinical cardiovascular impairment described in OSA together with masked hypertension, increase in artery rigidity or diastolic dysfunction. Although it has been suggested that early atherosclerosis is correlated with systemic inflammation, molecular and cellular mechanisms remain largely unknown. Intermittent hypoxia (IH) is playing a major role. Sleep apnea leads to oxidative stress with production of reactive oxygen species (ROS). Numerous studies have shown an increased oxidative stress using various biological markers. The increased levels of reactive oxygen species contribute to generate adhesion molecules, to activate leucocytes, and to produce vascular and systemic inflammation. Recently, Lena Lavie and her group elegantly evidenced that neutrophils apoptosis is delayed in OSA patients. Conversely, endothelial cells apoptosis as measured by its circulating level seems to correlate to endothelial dysfunction in OSA. All these mechanisms are presumably responsible for vascular endothelium damage. IH has been extensively studied in rodents. It is now established that vascular inflammation, increase in adhesion molecules, activation of NFkB as well as hemodynamic changes in the vascular wall and increase in intima-media thickness occur after only several weeks of exposure to IH. On-going studies are evaluating specific conditions, particularly in genetically modified animals, in order to elucidate the cellular and molecular mechanisms and the synergistic effects of hypertension, obesity or dyslipidemia. Addressing these mechanisms, interventional studies in humans comparing CPAP with anti-inflammatory drugs such as statines are desirable. Specific medications for hypertension treatment in OSA, as HT *per se* contributes to vascular inflammation and atherosclerosis, remain to be designed. In the next years coming elucidating the cellular mechanisms underlying IH-related cardiovascular morbidity, may support innovative therapeutic strategy in OSA.

S50

Beyond sleep apnea syndrome: lessons from other sleep disorders

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There is ample scientific evidence to support that sleep is an essential physiological need state for general healthy functioning. Sleep deprivation associated with disease-related sleep fragmentation, such as sleep apnea and RLS, results in neurocognitive deficit apparently similar to those observed in sleep restriction/sleep loss studies. Individual variability in neurobehavioral responses to sleep restriction suggests a trait-like (possibly genetic) differential vulnerability or compensatory changes in the neurobiological system involved in cognition. Moreover, specific sleep disorders seem to cause different cognitive consequences. Pearson et al. (Sleep Med 2006; 7: 25–30). found in RLS patients compared to age-matched controls deficits in some cognitive tests related to pre-frontal cortical (PFC) functioning. However, more recent studies (Gamaldo CE et al.; Sleep Med, in press) showed that RLS patients performed better than sleep-restricted controls in some specific tasks and displayed greater sustained alertness: this suggests that RLS subjects may have a relative degree of sleep loss adaptation. In sleep apnea patients the same phenomenon cannot be observed. In a murine sleep apnea model, Zhu et al. (J Neurosci 2007; 27: 10060–71) found that select wake neurons can be rendered persistently impaired after long-term exposure to hypoxia/reoxygenation. In sleep apnea patients longitudinal neuropsychological evaluation showed a partial reversibility of cognitive deficit after CPAP treatment. Could this aspect be also related to an inadequate CPAP treatment (persistence of sleep fragmentation), reflecting the same phenomenon observed in treated insomniacs that show normalized sleep macrostructure but a persistence of abnormal sleep microstructure ? Several studies showed the importance of a full polysomnography in the evaluation of motor phenomena during sleep in patients with suspected sleep apneas. Nocturnal frontal lobe epilepsy may be misdiagnosed as sleep apnea syndrome, and severe sleep apnea syndrome may mimick REM sleep behaviour disorder. A large part of adult sleepwalkers seem to be affected by a sleep-disordered breathing, that causes a NREM sleep instability (Guilleminault et al. Brain 2005; 128: 1062–9 and Sleep Med 2006; 7: 163–70).

Why GABA and Its Receptors are Still Relevant for Sleep: from Physiology to Pharmacology

S51

The gamma-aminobutyric acid (GABA) transmitter pathway: its key-role in the regulation of NREM and REM sleep

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In the last forty years, the structures responsible for waking (W), slow wave sleep (SWS) and paradoxical sleep (PS) have been progressively identified. In that context, we showed in the last decade that several populations of GABAergic neurons from the forebrain to the medullay oblongata are key players in SWS but also PS control using our model of head-restrained rats, functional neuroanatomical studies and "*in vitro* recordings". We first demonstrated that the decrease of activity during SWS and the cessation of activity during PS of the wake-active locus coeruleus (LC) noradrenergic and dorsal raphe serotonergic (DRN) neurons is due to a tonic GABAergic inhibition. We further showed that the SWS-on GABAergic neurons responsible of the inhibition during SWS would be located in the ventrolateral preoptic area (VLPO) while the PS-on GABAergic neurons responsible for the complete inactivation during PS would be located in the ventrolateral periaqueductal gray (vlPAG) and the medullary dorsal (DPGi) and lateral paragigantocellular (LPGi) reticular nuclei. Then, we showed that the putative glutamatergic PS-on neurons responsible for the onset and maintenance of PS located in the pontine sublaterodorsal tegmental nucleus (SLD) are tonically inhibited during W and SWS by GABAergic PS-off neurons localized in the ventrolateral periaqueductal gray (vlPAG) and the dorsal part of the deep mesencephalic reticular nucleus immediately ventral to it (dDpMe). We further proposed that at the onset and during PS, these GABAergic PS-off neurons are tonically inhibited by the vlPAG, DPGi and LPGi GABAergic PS-on neurons. In this new model, the onset of PS is not possible directly from W because the wake-active hypothalamic hypocretinergic neurons and brainstem monoaminergic neurons tonically excite the vlPAG/dDpMe PS-off GABAergic neurons. The decrease or cessation of activity of these wake-active neurons during SWS and in narcoleptics weaken the activity of vlPAG/dDpMe PS-off GABAergic neurons inducing a desinhibition of the GABAergic PS-on neurons and by this way PS. In conclusion, our results indicate that multiple antagonistic populations of GABAergic neurons control SWS and PS. Based on these results, we propose a new model for SWS and PS onset and maintenance.

S52

New insights from basic animal research on GABAA receptor mediated inhibition to understand selective pharmacological profiles of hypnotics

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GABA, the predominant inhibitory transmitter in the brain, and its GABAA receptors play an important role in sleep regulation. Most hypnotics, including benzodiazepines, non-benzodiazepine drugs, as well as more recently developed compounds (e.g. THIP/Gaboxadol), target the GABAA receptors. Their pharmacological profile and selectivity underlie their distinct impacts on sleep and the electroencephalogram (EEG). GABAA-mediated inhibition usually refers to the "phasic" inhibition, arising from synaptic GABAA receptors, which transiently inhibit neurons. It is well-established that traditional hypnotics target the synaptic GABAA receptors. However, there is growing evidence that GABAA receptors located outside the synapse (i.e., peri- and extra-synaptic) are continuously activated by low GABA concentrations and mediate a "tonic" inhibition. This slower type of signaling may contribute to the regulation of the phasic inhibition and gives new perspectives to understand the actions of hypnotic drugs. The field of "tonic inhibition" is relatively young and its potential involvement in sleep and generation of brain activities has only just started to emerge. Recent *ex vivo* and *in vivo* animal data showed that tonic inhibition displays a very specific pharmacological profile. In particular, GABAA agonists such as THIP/Gaboxadol and muscimol, as well as the general anesthetic etomidate were recently shown to act on extrasynaptic GABAA receptors mediating tonic inhibition. These compounds all have sedative and/or hypnotic effects and induce profound changes in the EEG pattern which are distinct from those observed with benzodiazepine or non-benzodiazepine compounds such as diazepam and zolpidem. Taken together, characterizing the mechanism of action of these compounds in vivo, as well as deciphering their effects on sleep and the EEG, will provide further insight into the physiological significance of GABAA-mediated inhibition in sleep.

S53

Effects of GABAA hypnotics on EEG, sleep and performance in human subjects

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Abstract unavailable

S54

GABAA agents in insomnia pharmacotherapy: novel therapeutic targets

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The GABAA receptor complex has remained for decades the major therapeutic target for treatment of insomnia. GABA is the major inhibitory neurotransmitter of the CNS and some of the adverse effects of these medications can be attributed to their general CNS depression. Over the last two decades drug development has focused on improving the risk-benefit ratio for GABAA agents used as hypnotics. This presentation will discuss novel therapeutic targets in GABAA insomnia pharmacotherapy, including new pharmacologic, outcome, and patient targets. The classical benzodiazepines (Bz) act non-specifically at the benzodiazepine site on the GABAA receptor complex, while the newer non-benzodiazepine receptor agonists (BzRAs), zolpidem, zaleplon, and zopiclone (eszopiclone in the US) are more selective for those receptor subunits with sedative effects. New formulations, modified release and sub-lingual, have been developed to pattern drug pharmacokinetics to better fit the typical insomniac's hourly distribution of wake time across the night. A drug, gaboxadol, that acts at a different class of GABAA receptors, extra-synaptic GABAA receptors, is being investigated as a hypnotic, as is a drug, tiagabine, with a different mechanism of action, GABA reuptake inhibition. The traditional therapeutic outcome measures for insomnia pharmacotherapy have been latency to sleep onset, amount of wakefulness after sleep onset and total sleep time, measured by self-report or NPSG. The classic Bzs suppress stage 3 and 4 sleep, the newer BzRAs have no effect on stage 3 and 4 sleep, while the GABAA agonists, gaboxadol and tiagabine,

increase stage 3 and 4 sleep. The therapeutic significance of sleep staging, specifically stage 3 and 4 sleep versus stage 1 sleep, has been investigated as a new outcome measure. While insomnia is defined as a sleep complaint associated with impaired daytime function, studies rarely have shown improved sleep and improved daytime function. Recently, attention has turned to daytime function as a therapeutic outcome. Finally, as regards new patient targets, insomnia comorbid with depression or anxiety, with chronic pain, or associated with post-menopausal sleep disturbance has become a therapeutic target. Studies have now shown that conjunctive treatment with hypnotics is associated with improved sleep, as well as, greater improvement in depression or anxiety relative to conjunctive placebo treatment. Similarly, in comorbid chronic pain, hypnotic treatment improves both the sleep and pain, as does hypnotic treatment of post-menopausal sleep disturbance improve both the sleep and the post-menopausal symptoms.

BSS-ESRS Joint Symposium
Genotype and Phenotype of Obstructive Sleep Apnoea: What's New and Where Are We Going?

S55

The phenotype of obstructive sleep apnoea

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In all studies of OSA, upper body obesity (especially as characterised by the neck circumference) has consistently been the best predictor of the degree of OSA. Other factors relating to lower facial shape have been the next most obvious predictors of the degree of OSA. Upper body obesity probably produces upper airway loading, either by superficial compressive pressure from subcutaneous deposits, or by more deeply placed peri-pharyngeal fat pads. Upper body obesity may also influence pharyngeal muscles through fatty infiltration or, much more indirectly, through hormones released by fat cells. There is also clear evidence that upper body obesity correlates with vascular disease much better than general obesity (as characterised by the BMI). This link is assumed to be via visceral (intra-abdominal) fat and its predominant effects on insulin resistance and sympathetic output, as well as various changes in hormone levels such as leptin and adiponectin. In ours and others studies, neck circumference has been the best predictor of a number of vascular risk factors, even better than waist circumference, or waist to hip ratio. Thus OSA, upper body obesity and vascular risk (largely characterised via components of the 'metabolic' syndrome) are inextricably linked in a way that renders epidemiological association studies invalid as a way of proving cause and effect. Trying to control for upper body obesity is doomed to failure, since on the one hand we do not know the best way to measure such obesity (and OSA may always code for some residual effect) and, on the other hand, any upper body correction made may overcorrect and erroneously remove a true OSA effect. This means that randomised CPAP interventional trials, using robust control arms, are the only way forward. Studies using poor compliers as control subjects introduce large bias. There are also large non-specific 'trial effects' on relevant outcomes, as we have shown for aldosterone and alanine transferase levels, where highly significant effects were found in both treatment and control arms, but no difference between the two. Thus cross sectional studies, and non-randomised or uncontrolled interventional studies, are flawed as evidence of OSA effects.

S56

Is it really all about the upper airway?

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Sleep-disordered breathing (SDB) is a relatively common disorder, resulting in significant adverse health consequences. Sleep apnea is caused by a combination of breathing instability and upper airway predisposition to collapse. There is increasing evidence of instability of the ventilatory control system in patients with obstructive sleep apnea (OSA). One manifestation is the persistence of periodic breathing and repetitive central apnea following 'curative' tracheotomy in patients with OSA and the response of central apnea to nasal CPAP therapy. Although pure central apnea is perhaps the least common morphologic pattern of apnea, unlocking the underlying mechanisms may provide insight into the pathogenesis of sleep apnea as a whole. Apnea or hypopnea leading to asphyxia, and transient arousals from sleep may result in ventilatory overshoot, hypocapnia, and recurrent apnea. Central apnea may also influence the development of obstructive sleep apnea as upper airway narrowing or occlusion may occur at the nadir of ventilatory motor output. Restoration of ventilation must restore patency to a narrowed or occluded upper airway, overcoming tissue adhesion forces, and gravitational forces. Accordingly, susceptibility to the development of hypocapnic central apnea, as measured by the hypocapnic apneic threshold, may influence susceptibility to develop upper airway obstruction. Thus, factors that influence the susceptibility to central apnea may also influence the development of obstructive apnea. This presentation will address the following hypotheses: 1) Patients with sleep apnea are more susceptible to development of central apnea relative to healthy subjects? 2) The hypocapnic central apnea demonstrates substantial plasticity in response to episodic hypoxia. 3) Reduced ventilatory motor output compromises upper airway patency even in normal healthy subjects during NREM sleep.

S57

Genetics of obstructive sleep apnea

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Heritability of obstructive sleep apnea (OSA) has been shown in several populations. Sofar, no genes conferring risk for OSA have been identified. To address this, we are developing a large genetic study with the Icelandic Sleep Apnea Cohort (ISAC). Initially linkage approach was used in this project. We recruited 1,386 individuals previously diagnosed with OSA treated with CPAP who were related within 6 meioses. Available sleep studies were rescored and information about comorbidities, medication use, BMI, degree of sleepiness at diagnoses obtained. Patients newly diagnosed with OSA ($n = 434$) have been studied with a more complex phenotyping protocol that includes fasting blood sugar, insulin, cytokine levels, acoustic rhinometry and upper airway and abdominal MRI (for visceral fat). The approach to human genetic studies has moved from linkage to genome-wide association (GWA). We have 5,760 Icelandic individuals (71% males) diagnosed with OSA since 1987 with valid consent for genetic studies of OSA in the deCODE biobank. Efforts are currently underway to genotype the large Icelandic OSA cohort on the Illumina platform, using the 370K SNP Bead Chip. Over 35,000 Icelanders who have already been genotyped will serve as controls. Future studies will require large replication cohorts with in-depth standardised phenotyping for validation of genetic markers discovered to associate with OSA or the intermediate traits for OSA.

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S58

Prospects for new treatments

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Obstructive sleep apnea (OSA) is a common and serious breathing problem caused by effects of sleep on pharyngeal muscle tone in individuals with already narrow upper airways. There has been increasing focus on delineating the brain mechanisms modulating pharyngeal muscle activity awake and asleep to understand the pathogenesis of OSA and, potentially, to develop novel neurochemical treatments for this disorder. Determining the brain

mechanisms underlying the modulation of the respiratory network during sleep is relevant to understanding the increased upper airway resistance, airflow limitation and hypoventilation in normal sleeping individuals, as well as the airway obstruction underlying the pathogenesis of OSA. Determining the mechanisms underlying the control of the respiratory system during sleep is also relevant to the respiratory effects of commonly prescribed sedative-hypnotic agents and the attendant risk for sleep-disordered breathing in some individuals, as well as identifying potential targets for rational pharmacological strategies to increase pharyngeal muscle tone in sleep to prevent OSA. Accordingly, this presentation will summarize current concepts underlying the neurobiology of sleep and arousal states, and so identifies the rationale for focus on particular neuromodulators and their effects on the respiratory system.

Sleep Disturbances in Neurological Disease: Do Hypocretin (Orexin) Defects Play a Role?

S59

Central hypersomnias other than narcolepsy: is there hypocretin involvement?

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S60

Sleep disorders and hypocretin disturbances in traumatic brain injury

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Sleep-wake disorders are common after traumatic brain injury. Recent studies revealed that excessive daytime sleepiness, hypersomnia, and fatigue are particularly prevalent and negatively interfere with quality of life. Until now, however, the etiology of posttraumatic sleep-wake disorders remains unclear. Findings in clinical and preliminary autopsy studies suggest that the hypocretin system might play a role in the generation of posttraumatic excessive daytime sleepiness. In this talk, characteristics, prevalence and implications of posttraumatic sleep-wake disturbances will be reviewed, including their link to the hypocretin system.

S61

Excessive daytime sleepiness in myotonic dystrophy: the role of hypocretin

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Myotonic dystrophy (MD) type I is a progressive multisystem disease caused by an abnormal expansion of a CTG repeat in the 3′ untranslated region of the DMPK gene on chromosome 19 that interferes with mRNA splicing regulation. Excessive daytime sleepiness (EDS) is a common complaint in MD that may even precede the development of other systemic symptoms. Sleep breathing disturbances are a potential cause of ESD in MD. However, the correct treatment of the respiratory disturbances do not resolve hypersomnia in most patients. Nevertheless, the degree of muscle impairment is not related to the sleep disorders found in MD patients. The neurodegeneration process of MD may play a role in the development of sleep disorders due to involvement of the central regulation of the sleep-wake cycle. In this setting, MD may share with narcolepsy the presence of Sleep Onset REM periods in the MSLT. A deficient hypocretin neurotransmission, in analogy to narcolepsy, has been hypothesized as having a role in the sleep disorders in MD. Low levels of CSF hypocretin-1 may be found in a subset of MD patients with EDS. However, CSF hypocretin-1 levels were found mainly in an intermediate range between normal and narcolepsy, a value that is considered of doubtful clinical significance. Additionally, most MD patients with EDS studied have no abnormalities in CSF hypocretin levels. While waiting for pathological studies of MD brains analysing the hypocretinergic neuronal status in the hypothalamus, current clinical and laboratory evidence do not support selective hypocretin system impairment in MD. A partial deficient hypocretin neurotransmission, as assessed by CSF analysis, may be a non-specific finding that may also be found in other neurodegenerative disorders.

S62

Hypocretin defects in Parkinson's disease

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There is a growing interest in hypocretin function in Parkinson's disease (PD), given the high prevalence of non-motor symptoms such as sleep disturbances in this disorder. Excessive daytime sleepiness with frequent naps and so-called 'sleep-attacks' have been reported in 15–50% of patients. Furthermore, there are clear night time sleep disturbances, such as fragmented nocturnal sleep, REM-sleep behaviour disorder and periodic leg movements, as well as daytime sleep-onset REM periods. However, studies measuring CSF hypocretin levels have yielded contradictory results. In a post-mortem study, we found that the hypocretin-1 tissue concentrations in the prefrontal cortex were almost 40% lower in PD patients, while ventricular CSF levels were almost 25% reduced. The total number of hypocretin neurons was almost half compared with controls. Lewy bodies were abundantly present in the perifornical hypothalamus as a sign of an active disease process in that region. Hypocretin neurons that contained a Lewy body were discernable in every PD patient, but the majority of hypocretin neurons did not show this colocalization. Similar findings were described by Thannickal et al. who found an increasing loss of hypocretin cells with disease progression in PD. In that study an increased loss with disease severity of melanin concentrating hormone (MCH) cells was also described, which cell bodies are located in the same area. Hypocretin and MCH cells were lost throughout the anterior to posterior extent of their hypothalamic distributions. The hypocretin system is thus affected in PD. However, the question still remains whether partial hypocretin neuronal loss results in true hypocretin dysfunction and is responsible for at least part of the sleep disturbances in PD.

Ageing, Sleep and Daytime Sleepiness: Are Older People Less Alert Than Young Adults?

S63

Age-related changes in human sleep: homeostatic or circadian?

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The reduction of electroencephalographic (EEG) slow-wave activity (SWA) (EEG power density between 0.75–4.5 Hz) and spindle frequency activity, together with an increase in involuntary awakenings during sleep, represent the hallmarks of human sleep alterations with age. It has been assumed that this decrease in nonrapid eye movement (NREM) sleep consolidation reflects an age-related attenuation of the sleep homeostatic drive. To test this hypothesis, we measured sleep EEG characteristics (i.e., SWA, sleep spindles) in healthy older volunteers in response to high (sleep deprivation protocol) and low sleep pressure (nap protocol) conditions. Despite the fact that the older volunteers had impaired sleep consolidation and reduced SWA levels, their relative SWA response to both high and low sleep pressure conditions was similar to that of younger persons. Only in frontal brain regions did we find an age-related diminished SWA response to high sleep pressure. On the other hand, we have clear evidence that the circadian regulation of sleep during the 40 h nap protocol was changed such that the circadian arousal signal in the evening was weaker in the older study participants. More sleep occurred during the wake maintenance zone, and subjective sleepiness ratings in the late afternoon and evening were higher than in younger participants. This resulted in more intrusion of low-frequency waking EEG components during the wake maintenance zone in the elderly. In addition, we found a diminished melatonin secretion and a reduced circadian modulation of REM sleep and spindle frequency—the latter was phase-advanced relative to the circadian melatonin profile. Therefore, we favor the hypothesis that age-related changes in sleep are due to weaker circadian regulation of sleep and wakefulness. Our data suggest that manipulations of the circadian timing system may offer a potential strategy to alleviate age-related decrements in sleep and daytime alertness levels.

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Reduction in sleep propensity with ageing

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Key characteristics of sleep in older people include earlier wake-time, reduced slow wave sleep and increased number of awakenings. These changes are considered to reflect a reduction in the quality of sleep. Within the context of sleep as a recovery process this age-related reduction in nocturnal sleep quality is expected to be associated with increased daytime sleep propensity. A number of experiments were conducted to investigate daytime sleep propensity as well as sleep propensity across the circadian cycle and the association between nocturnal sleep, sleep disruption and daytime sleep propensity in young, middle-aged and older people. The habitual sleep-wake cycles of the participants were quantified prior to the laboratory experiments. The participants were healthy and did not suffer from sleep disordered breathing or periodic limb movement disorder which may lead to increased daytime sleep propensity. Sleep propensity was assessed by the multiple sleep latency test and total sleep time. The overall conclusion from these experiments is that healthy older people without sleep disorders are less sleepy than young people. The data will be discussed within the context of sleep as a recovery process, the age-related reduction in sleep need and the age-related increase in insomnia.

S65

Adenosinergic mechanisms of age-related changes in sleep-wake regulation

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A night without sleep is typically followed by enhanced daytime sleepiness, increased low-frequency activity in the waking electroencephalogram (EEG), and reduced performance on neurobehavioral tasks. The magnitude of these changes is highly variable among healthy individuals. Our findings in young men (20–30 years) of high and low subjective caffeine sensitivity suggest that adenosinergic mechanisms contribute to the inter-individual differences in sleep deprivation-induced changes in regional EEG theta (6–8 Hz) activity and optimal performance on the psychomotor vigilance task (PVT) (Rétey et al. J Neurosci, 2006). In comparison to young subjects, healthy men of older age (60–70 years) feel less sleepy after sleep deprivation, and show faster reaction times (RT), higher performance stability and fewer response lapses (RT >500 ms) on the PVT, especially in the morning after one night without sleep (Adam et al. Sleep, 2006). We hypothesized that age-related changes in adenosine signal transmission underlie the reduced vulnerability to sleep deprivation in older men. In accordance with this hypothesis, the effects of prolonged waking and the adenosine receptor antagonist, caffeine, on an antero-posterior power gradient in EEG theta activity are negatively correlated in young, as well as older age groups. This observation supports an inverse relationship between sleep loss- and caffeine-induced changes in waking EEG topography. Moreover, caffeine removes the age-related difference in RT on the PVT following prolonged waking. The blockade of adenosine receptors, however, does not abolish the difference between the age-groups in performance stability and response lapses. These findings indicate that apart from the adenosinergic system also other mechanisms contribute to age-related changes in vigilance during sleep deprivation. Normal aging may provide a useful model to investigate possible mechanisms underlying different outcome variables (e.g., sleepiness, EEG, performance) that are thought to reflect physiological sleep-wake regulation in humans.

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S66

Causes of daytime sleepiness and napping in older adults

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A commonly held assumption about sleep and aging is that, since complaints of nighttime sleep disturbances increase with advancing age, older adults are more likely to experience daytime sleepiness and to nap during the daytime relative to younger adults. However, emerging data support a more complex picture of disturbed nighttime sleep and related daytime behaviors in aging. For

example, a recent meta-analysis of sleep changes across the human lifespan indicates that most age-related changes in objectively measured nighttime sleep occur before age 60 and are minimal thereafter in healthy older adults. Further, several recent studies indicate that health older adults better tolerate acute and chronic sleep deprivation than do younger adults. We will examine the relationships among nighttime sleep complaints and daytime sleepiness and napping and their interactions with health in older adults, with particular attention to ''normative'' versus ''typical'' aging.

Neurophysiological Measures of Insomnia

S67

Assessing waking hyperarousal in poor sleepers using psychophysiological measures

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The etiology and pathophysiology of insomnia has been proposed to involve neurocognitive hyperarousal. Psychophysiological measures, such as EEG and ERPs, are ideal tools to index CNS arousal and attention. Research has shown that insomnia patients have greater high-frequency EEG in sleep and wakefulness, as well as larger waking P300s. However, results of such studies are mixed, as capturing the elusive hyperarousal is highly variable across studies and individuals. Two separate studies were designed to assess sensory and cognitive information processing at sleep onset and during sleep in good and poor sleepers. Waking EEG and ERP data were also collected in pre- and post-sleep recordings. Study1 investigated early sensory processing in 13 self-reported poor sleepers (M age = 20) and 13 good sleepers (M age = 22). A paired-click paradigm was administered during 30-min of wake and throughout the night (two 0.04 ms square-wave clicks presented binaurally at 95dB; ISI = 500 ms; ITI = 10s; sampling rate = 1000 Hz). A P50 wave was measured from successive stimuli (S1 and S2) at central sites in wake. There were no group differences for the suppression ratio (S2:S1), an index of sensory gating or blocking of repetitive, irrelevant stimuli. Study2 assessed cognitive information processing using a pitch odd-ball paradigm (70dB, 50 ms tones presented binaurally every 1–2 s at random; 1000 Hz Standard on 80%, 2000 Hz deviant on 20% of trials). Participants were 13 primary insomnia patients with sleep onset complaints (M age = 22) and 12 controls (M age = 23). N1-P2-P300 peaks were measured from 11 EEG sites during wake and sleep onset. Poor sleepers had smaller P2 amplitudes compared to controls, in wake recorded at sleep onset, at all 6 fronto-central sites. No group differences were apparent in Stage 1 or 2 sleep, nor pre- or post- alert waking recordings. The smaller P2 reflects hyperarousal or failure to inhibit stimuli during wakefulness immediately prior to sleep onset. No evidence for hyperarousal was apparent with N1 or P300 waves. Poor sleeper groups were consistently more variable on measures. Follow-up analyses will address the role of subjective and objective sleep quality in the lab, and the influence of affective state and level of sleepiness which may affect hyperarousal.

S68

ERP measures during wakefulness and sleep-onset in psychophysiological and paradoxical insomnia sufferers

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Introduction: QEEG studies suggest that individuals suffering from psychophysiological insomnia (Psy-I) display lower cortical arousal than those suffering from paradoxical insomnia (Para-I). Recently, our group showed both cortical arousal and inhibition deficits in Psy-I relative to GS (Bastien et al. Sleep). ERPs data in Para-I is still scarce. The aim of this study is to further circumscribe the neurophysiological basis of chronic insomnia in Psy-I and Para-I using ERPs.

Methods: Fifteen Psy-I, 15 Para-I and 15 GS were enrolled. Participants underwent four consecutive nights of PSG (N1 to N4). ERPs (N1, P2) in the evening and upon awakening were recorded on N3 and N4. Sleep-onset recordings were added on N4 (N1, P2 and N350). Auditory stimuli consisted of 'standard' (70 dB, 2000 Hz, probability 0.85) and 'deviant' (90 dB, 1500 Hz, probability 0.15). Participants were instructed to ignore stimulation at all times.

Results: Mixed model ANOVAs were used to test dependant variables (ERPs amplitudes and latencies) at each assessment (evening, sleep-onset, morning) for the two stimuli. In all groups, the amplitude of all components was greater for the deviant than for the standard stimulus. At sleep-onset, N350 was significantly smaller in both groups of INS than in GS. N350 amplitude was similar in Psy-I and Para-I. While N350 amplitude at sleep-onset in GS increased on successive trials, it did not in Psy-I and Para-I. On the other hand, the amplitude of P2 was greater in Para-I than in Psy-I and GS. Furthermore, ERPs latencies were shorter in Para-I compared to Psy-I and GS. Strangely, Para-I also displayed a N2 component during wake, component that was absent in Psy-I and GS.

Conclusion: These results suggest that paradoxical insomnia sufferers display greater arousal levels than psychophysiological insomnia sufferers and good sleepers. Furthermore, paradoxical insomnia sufferers are more much disturbed by the stimulation than psychophysiological insomnia sufferers.

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S69

The microstructure of sleep in insomnia

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In the last 15 years, quantification of arousals according to the AASM rules has been carried out in a number of sleep disorders as a translation of fragmented sleep. The concept of arousals as stage markers has been introduced in the recently published AASM scoring manual but no information on the new criteria is so far available. In the meanwhile, a number of experimental and clinical studies have confirmed the topical role of unstable sleep in insomniacs and established a significant correlation in these patients between CAP rate and the subjective estimates of sleep quality. Regardless of any other change in the conventional PSG measures, the higher CAP rate the poorer the quality of sleep. Accordingly, any sleep-improving treatment reduces the amount of CAP and potentiates sleep stability through the increase of non-CAP. PSG remains the "gold standard" for measuring sleep, and especially insomnia. PSG findings in subjectively defined insomniacs reveal more impairment of sleep continuity parameters (i.e., longer sleep latencies, more time awake after sleep onset, lower sleep efficiency) and reduced total sleep time compared to subjectively defined good sleepers. Also, insomniacs tend to spend more time in stage 1, less time in deep sleep, and display more frequent stage shifts through the night. There is, however, a significant overlap in the distribution of sleep recordings of subjectively defined insomniacs and good sleepers such that some individuals with insomnia complaints may show better conventional sleep measures than insomniacs. These overlaps might account for some of the discrepancies between conventional PSG data and subjective evaluation of sleep quality. The extension of conventional sleep measures to CAP variables may improve our knowledge on the diagnosis and management of insomnia. In particular, assessment of sleep quality by means of specific PSG measures including sleep efficiency, sleep depth and sleep stability could allow us to attribute a more objective identity to insomnia which risks otherwise to be considered as an inscrutable, unexplainable and immeasurable mental complaint.

S70

Recent fMRI data in chronic primary insomnia

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Research has shown that patients with insomnia often complain of impaired concentration, impaired memory, and decreased ability to accomplish daily tasks and that these factors worsen as their sleep problems increase in severity. Despite the evidence that insomnia exacts a significant toll on individuals, research has been unable to show consistent, reliable deficits when assessing cognition in insomnia via neuropsychological measures. This may be due to several factors, including: a) failing to find the cognitive domain most sensitive to insomnia; b) measuring the wrong aspect of cognition; and/or c) the cyclical nature of insomnia leading to assessments occurring after both ''good'' and ''bad'' nights, thereby minimizing the effect size related to insomnia. In this study, classic neuropsychologcal assessment is combined with functional MRI (FMRI) to investigate and assess cognitive performance in primary insomnia and address some of the issues related above. We are using FMRI to test the neurophysiological response to cognitive challenges in multiple domains: verbal encoding, updating of information in working memory, and response inhibition. Importantly, difficulty or load is parametrically manipulated in these tasks, so that we can identify contexts in which cognitive function and brain activation are similar in insomnia versus controls, and where insomnia patients show abnormalities. Furthermore, we are testing subjects on two consecutive nights to examine the impact of prior sleep, both within and between subjects, on performance and cerebral responses. Hypotheses include: 1) insomnia patients will show identical performance to the controls; and b) insomnia patients will show increased activation in task-related brain regions relative to the controls. These differences should be exacerbated after a poor sleep night in the patients relative to after a good sleep night.

Neurophysiology Never Sleeps

O101

Cholinergic basal forebrain structures are involved in the mediation of the arousal effect of noradrenalin

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The basal forebrain (BF) is involved in the regulation of sleep-wake activity. Cholinergic BF structures contribute to cortical activation. These cholinergic neurons receive noradrenergic input and noradrenalin (NA) excites them via alpha-1 receptors. NA microinjection into the BF enhances wakefulness. Cholinergic BF neurons may be involved in the mediation of the arousal effect of NA, but non-cholinergic ones may contribute as well and the relative role of cholinergic versus non-cholinergic neurons is unclear. In order to elucidate the role of cholinergic BF structures we have tested the arousal effect of methoxamine (MTX), an alpha-1-adrenergic agonist administered locally into the BF in intact animals and after selectively destroying BF cholinergic cells by immunotoxin 192 IgG-saporin microinjection. The experiments were carried out in 7 male Han-Wistar rats with implanted EEG/EMG electrodes and guide cannulae for microdialysis probes. A microdialysis probe targeted into the BF was perfused (1 μL min^{-1}) with artificial cerebrospinal fluid (CSF) for 6 h on the baseline day and with CSF in the 1st and MTX (20 mg mL^{-1}) in the 2nd 3-h period of the subsequent MTX day. Sleep-wake activity was recorded for 24 h on both days. Then 192 IgG-saporin (0.23 μg in 1 μl) was injected into the BF and 2 weeks later the same experimental schedule with CSF and MTX was repeated again. In intact animals MTX had a robust arousal effect. Non-REM sleep (NREMS) was suppressed significantly for 6 h (baseline day: 58.5 ± 1%, MTX day: 31.5 ± 2.9%). REM sleep (REMS) was decreased significantly for 9 h (baseline day: 13.1 ± 0.8%, MTX day: 1.1 ± 0.3%). Lesion of BF cholinergic structures by saporin diminished the NREMS suppressing effect of MTX in a great extent, only a tendency to a decrease in NREMS was noted (baseline day: 55.7 ± 2.2%, MTX day: 48.2 ± 2.9%). REMS suppressing action of MTX was not much influenced by saporin treatment (baseline day: 11.9 ± 0.8%, MTX day: 1.5 ± 0.5%). These findings indicate that BF cholinergic neurons may be involved in the mediation of the cortical activation induced by noradrenalin.

O102

The rat-psychomotor vigilance task: sleep disruption and basal forebrain adenosine dialysis

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In humans, sleep disruption from disease, vocational demands, or experimental manipulation markedly degrades performance in tasks requiring sustained attention. Recent work suggests that basal forebrain (BF) adenosine (AD) mediates the homeostatic sleep drive. We hypothesized that experimentally induced total sleep deprivation (SD), sleep fragmentation (SF), and AD dialysis in the BF would increase sleepiness and impair performance in an animal analogue of the human psychomotor vigilance task (PVT), widely used in human sleep research to assay sustained attention. Different schedules of movement of an activity wheel were used to produce 24 h SD (3s on: 12s) and SF (4s on: 56s off). An exercise control (EC) condition for both SD and SF provided the same overall amount of locomotor activity, while allowing long periods of uninterrupted sleep. A baseline condition (no wheel movement) was also used.Bilateral BF dialysis (via microdialysis) of either aCSF control, or 300 μM of AD, or 300 μM of AD co-perfused with 1 μM of the AD A1 antagonist 8-cyclopentyltheophylline (CPT) was performed continuously for 2 h immediately prior to the rPVT test. Response latencies (RL) increased after both SD and SF, but there was little difference between the effect of SF and SD. However, while both SD and SF increased the number of lapses (trials with RTs two-times greater-than basal RL) when compared to baseline and EC, rats made more lapses after 24 h of SF, than after 24 h of SD. Thus while SD and SI both produced vigilance impairments analogous to those seen in sleepy humans, SI produced a greater impairment. Similarly, during rPVT sessions immediately after AD dialysis RL slowed, and the number of lapses increased significantly when compared to baseline (no drug) or aCSF dialysis. However, this AD-induced vigilance impairment was blocked by co-dialysis with CPT. Thus the effect of 300 μM AD dialysis on rPVT performance resembled that of 24 h of SD or SF. In summary, sleep deprivation, sleep fragmentation, or elevation of AD in the BF of rats, induce reversible vigilance deficits similar to those induced by sleep disruption in humans. Furthermore, constant interruption during sleep had greater consequences for vigilance performance than did remaining awake for the same duration.

O103

Slow oscillations in the slow wave sleep EEG: redistribution with increased sleep pressure

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Slow oscillations (SO) represent the most prominent feature of the nonREM sleep EEG. At the cellular level, they are characterized by slow membrane potential fluctuations of cortical neurons, with depolarizing (up state) and hyperpolarizing (down state) components alternating with a frequency below 1 Hz. SO have a cortical origin and are hypothesized to synchronize other sleep rhythms. However, their role in sleep regulation is unclear. We investigated the behavior of SO under increased sleep pressure and their relationship with slow wave activity, a well-established marker of sleep homeostasis.<p>EEG recordings (C3A2 and F3A2) of baseline and recovery sleep after sleep deprivation (40 h of prolonged wakefulness) were analyzed (8 healthy males, mean age 23 years). Sleep stages were determined according to standard criteria. Analysis was restricted to slow wave sleep of the first sleep episode, where sleep pressure is highest. Half-waves were defined as positive or negative deflections between consecutive zero crossings (SO: 0.5–1 Hz; low delta activity: 1–2 Hz) in the band-pass filtered EEG (different filter settings). Power spectra were computed with 0.1 Hz resolution.<P>The typical increase in delta activity after sleep deprivation was not present in the power spectra below 1 Hz. However, analyses of the single waves indicated that sleep deprivation led to a lower number of waves per minute below 1 Hz, and a higher number above 1 Hz; the amplitude of waves was increased in the frequency range between 0.5 and 2 Hz. Analysis of the polarity of the waves revealed that the number of negative half-waves per minute was significantly affected by sleep deprivation, while the number of positive half-waves per minute remained unchanged. Filter settings were an important parameter influencing the results.<P>In conclusion, sleep deprivation led to a redistribution of oscillatory events in the EEG during slow wave sleep. Spectral power in the SO range did not reveal any change, probably due to the fact that the number of waves decreased but their amplitude increased resulting in similar power below 1 Hz.

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O104

Interleukin-1 microinjection into the rat laterodorsal tegmental nucleus inhibits REM sleep

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Interleukin-1 (IL-1) increases NREM sleep and inhibits REM sleep. Although much information is available with respect to the mechanisms by which IL-1 enhances NREM sleep, little effort has been expended to determine mechanisms mediating IL-1-induced REM sleep suppression. Cholinergic neurons in the laterodorsal and peduncolopontine tegmental nuclei (LDT/PPT) are part of the neuronal circuitry responsible for REM sleep generation. Because available data indicate that IL-1 inhibits the cholinergic system, the aim of this study was to test the hypothesis that IL-1, directly microinjected into the rat LDT nucleus will inhibit REM sleep. Male Sprague-Dawley rats ($n = 21$), maintained on a 12:12 h light:dark cycle at 22 °C, were instrumented for standard chronic polygraphic recordings of sleep-wake activity. A stainless steel guide cannula aimed at the LDT nucleus was also stereotaxically implanted. IL-1 was dissolved in pyrogen-free saline (PFS; 100 nl) and given at the beginning of the light phase of the light-dark cycle. Each animal received both vehicle (PFS) and IL-1, so each rat served as its own control. Animals were divided into two groups: rats in group 1 received 0.25 and 0.5 ng IL-1, whereas animals in group 2 received 1 and 4 ng IL-1. At the end of the experiments, location of injection sites was histologically verified. IL-1 (1 ng) microinjection into the LDT nucleus induced a significant and long lasting inhibition of REM sleep. In the first 12 post-injection hours REM sleep was reduced from $11.7 \pm 0.9\%$ of recording time in control condition (vehicle microinjection) to $8.6 \pm 0.9\%$ following IL-1 administration. IL-1-induced REM sleep inhibition was not followed in post-injection hour 13–24 by any rebound. Results of this study support the hypothesis that IL-1 can inhibit REM sleep by acting at the level of the LDT nucleus. In vitro data showing that IL-1 inhibits the firing rate of LDT cholinergic neurons suggest that REM sleep inhibition induced by IL-1 microinjection into the LDT may result from the IL-1-induced inhibition of cholinergic neurons.

O105

Processing of sounds during sleep spindles in humans: an EEG/fMRI study of auditory stimulation in non-REM sleep

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Introduction: Non-REM sleep (NREM) has classically been associated with isolation of the brain from the external world, due to the blockade of incoming stimuli at the thalamic level, in particular during sleep spindles. Although some data suggest that sounds are still processed during NREM, no neuroimaging study has assessed how spindles modulate the processing of auditory stimuli. Using simultaneous EEG/fMRI, this study aimed at describing the neural correlates of auditory information processing during NREM and spindles in humans.

Methods: In the experimental group (EG, $n = 13$), non-sleep deprived healthy young subjects were scanned during the night in a 3T fMRI device, with a continuous EEG recording. During this session, pure tones were presented (400 Hz, 300 ms, 70% probability during each scan). In the control group (CG, $n = 14$), subjects followed a similar protocol, but without sounds presentation. After artifacts removal, NREM (stages 2–3) and waking epochs, with corresponding fMRI images, were selected. Sleep spindles were automatically detected in NREM epochs. In the EG, tones were categorized in 3 types according to their occurrence during waking (TW), NREM but outside spindles (TN), or spindles (TS). We first assessed the brain responses to the 3 types of tones. Then we compared the brain responses to spindles between groups.

Results: TW were associated with activation of the thalamus and primary auditory cortex. TN induced activation of thalamus, primary auditory cortex, but also brainstem and posterior cingulate gyrus. TS were associated with activation of parahippocampal gyrus and brainstem. A higher activation of the hippocampus was found during spindles in the EG compared to the CG.

Conclusion: Sounds are processed in classical auditory circuits during NREM, but not during spindles. However, presentation of sounds during NREM affects the neural correlates of spindles, leading to increased activation of mesio-temporal areas in relation to spindles.

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O106

Local arousals during sleep

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Increasing evidence suggest that human sleep is a global phenomenon in which locally modulated behaviors occur. Topographic differences in the distribution of Slow Wave Activity (SWA), the marker of sleep homeostasis, are evident. Moreover experimental studies showed that SWA can be selectively enhanced or dimished in confined brain regions suggesting that certain brain regions may sleep "deeper" than others. Clinical observations also indicate that sleep and wakefulness could occur simultaneously in different parts of the brain. Here we show that two distinct region of the brain, the pre-frontal cortex and the motor cortex, though mantaining similar global dynamics of SWA during NREM sleep, can exhibit dissociated behaviors. We analysed sleep EEG in five drug resistant epileptic patients studied with intracerebral implanted electrodes during presurgical investigation. Each subject had at least two electrode contacts which could be localized unequivocally within the pre-frontal region and the motor cortex. Scalp EEG was recorded from Fz-Cz. The pre-frontal and motor cortex showed the expected cycle by cycle decreasing trend of SWA (as observed on scalp EEG). Nevertheless, expecially at sleep onset and during the transition towards REM sleep, an uncoupling of EEG rhythms could appear lasting till some minutes, with wakefulness-like EEG activity (alpha and beta waves) in the motor cortex and sleep activity (delta waves) in the pre-frontal cortex. Moreover both visual scoring analysis and wavelet transform analysis of the EEG showed that many brief arousals occurring at the level of the motor cortex, lasting less than 15 seconds and characterized by the occurrence of alpha and beta activity, were accompanied by an evident opposite increase in delta activity over the prefrontal cortex suggesting an anti-arousal reaction that may protect the continuity of sleep. These findings may give new insights for the comprehension of arousal regulation during NREM sleep and for the explanation of anomalous sleep/wake phenomena (sleep walking, misperception insomnia).

O107

Brain processing of nociceptive stimulation during sleep in humans: surface and intracortical responses

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Contrary to previous studies suggesting the absence of cortical evoked potentials to laser (LEPs) during light sleep (Beydoun et al. 93, Qiu et al. 02), we recently reported the persistence of attenuated nociceptive LEPs during all sleep stages with unusual topography (Bastuji et al. 08). During paradoxical sleep (PS), LEP components recorded over the frontal scalp virtually disappeared, while posterior components were preserved. This result suggests that the network of cortical activation could be different during sleep and wakefulness. Moreover, the amplitude of a late LEP component (350–450 ms) was shown to predict the incoming arousal. A possible explanation is that the periodic fluctuations in the thalamo-cortical coupling (Magnin et al. 04) within a given sleep stage might explain why stimulations of similar intensity may, or may not, awake the subject. In a second study, we recorded LEPs using intracerebral electrodes in epileptic patients scheduled for functional surgery. Sequences of 10- 30 thermal laser stimuli were delivered at pain threshold over the radial territory during all sleep stages. First results obtained in 8 patients demonstrate that the evoked responses persist during sleep in the usual nociceptive cortical network. The LEPs recorded in the insula (N180/P230) and in the suprasylvian opercular area (N140/P180) were present but attenuated at least during both stage 2 and PS. This preliminary result suggests that the cortical areas involved in the sensory-discriminative aspects of pain remain active during sleep. In 4 patients with contacts in the thalamus, we observed that the insular evoked responses were of smaller amplitude during the thalamo-cortical coupling periods of PS as compared to the decoupling ones.

O108

REM sleep homeostasis: a role for nonREM sleep

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Introduction: REM-sleep is homeostatically regulated and the homeostatic pressure for REM-sleep accumulates in its absence, during either nonREM-sleep and/or wakefulness.

Hypothesis: We hypothesize that REM-pressure accumulates during nonREM-sleep and that wakefulness prevents the build-up of REM-sleep pressure.

Experimental Paradigm: One group of Sprague-Dawley rats ($n = 4$) was REM-sleep deprived (RD) for 2-h by being subjected to brief (2–3 sec) arousing stimuli at the onset of each REM-episode (RD1). A second group of rats ($n = 4$) was REM-deprived for 2-h by being kept awake for 50–60 sec after each REM-entry (RD2). A third group of rats ($n = 4$) was subjected to 2-h RD by being kept awake for 90–120 sec after each REM interruption. A fourth group of rats ($n = 4$) was permitted 2-h spontaneous sleep. After the termination of RD protocols, all rats were permitted 2-h recovery sleep.

Results: Different groups of RD rats exhibited significantly different degrees of REM-sleep homeostatic pressure that was estimated by the number of attempts to enter into REM-sleep during the deprivation protocol. RD1 rats experienced the highest number of REM-attempts within the deprivation period (58.9 ± 2.3). RD2 rats exhibited 21.7 ± 1.7 entries into REM-sleep. RD3 rats had the lowest number of REM entries (9.7 ± 0.33) and this number was not significantly different from that in spontaneously sleeping rats (10.9 ± 0.9). Moreover, RD3 rats exhibited no REM-sleep rebound during the post-deprivation period ($15.4 \pm 1.1\%$) compared to control rats ($14.9 \pm 0.9\%$), while the other two groups of RD rats exhibited significant increases in the post-deprivation amount of REM-sleep ($20.6 \pm 0.6\%$ in RD1 and $18.5 \pm 1.2\%$ in RD2). Therefore, RD3 did not lead to an elevation of REM-sleep homeostatic pressure compared to spontaneously sleeping rats.

Conclusions: Findings of this study are consistent with the hypothesis that REM-sleep is functionally and homeostatically related to nonREM-sleep rather than to wakefulness. Wakefulness appears to prevent the buildup of REM-sleep homeostatic pressure.

O109

Shortened first nREM-REM cycle duration in women with vasospastic syndrome and difficulties initiating sleep

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Alterations in internal phase angles (e.g. between the circadian core body temperature rhythm and the sleep-wake cycle) have been reported in sleep onset insomniacs, depressed patients, and delayed sleep phase syndrome, exhibiting altered sleep patterns such as shorter REM sleep latencies (REML) or changes in NREM-REM sleep cycle durations. We have recently shown that women with a vasospastic syndrome and difficulties initiating sleep (WVD) exhibit a phase delay of the thermoregulatory system with respect to their habitual sleep-wake cycle in comparison to controls (CON). Therefore we examined whether WVD also show a different ultradian NREM-REM cycle duration. Seventeen healthy women ($N = 8$ WVD; 9 CON; luteal phase; age: 20–33 yr) performed a 40-hr constant routine protocol, with a baseline and a recovery 8-hr night before and after. Baseline and recovery nights yielded similar differences between WVD and CON (pooled data are given). ANOVAs were performed on log-transformed values. In comparison to CON, WVD exhibited a significant longer sleep onset latency (WVD 14.9 ± 2.4 min [mean $\pm$ SEM]; CON 7.1 ± 1.1 min; $P < 0.01$), a shorter first NREM-REM sleep cycle duration (WVD 68.9 ± 4.7 min; CON 90.2 ± 7.9 min; $P = 0.01$) and a shorter first NREM sleep episode duration (WVD 55.7 ± 3.7 min; CON 75.1 ± 7.4 min; $P = 0.01$). Additionally, WVD tended ($P = 0.09$) towards a shorter REML. In both groups, NREM EEG power spectra revealed a progressive decrease of EEG delta activity (0.75–2.0 Hz) across NREM-REM sleep cycles. In WVD this decrease was less pronounced from the first to the second sleep cycle. In comparison to CON, WVD showed a higher EEG delta activity in the second cycle relative to the first cycle ($P < 0.04$). We conclude that a change in internal phase of entrainment in WVD (i.e. phase delayed thermoregulatory heat loss with respect to the sleep-wake cycle) may contribute not only to the prolonged sleep onset latency but also to changes in ultradian sleep patterns.

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O110

Small-world network organization of different EEG bands during sleep

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The objective of this study was to analyze the functional connectivity patterns of the different EEG bands during wakefulness and sleep (different sleep stages and Cyclic Alternating Pattern (CAP) conditions), using concepts derived

from Graph Theory. We evaluated the spatial patterns of EEG band synchronization between all possible pairs of electrodes (19) placed over the scalp of 10 sleeping healthy young normal subjects using two graph theoretical measures: the clustering coefficient (Cp) and the characteristic path length (Lp). The measures were obtained during wakefulness and the different sleep stages and CAP conditions from the real EEG connectivity networks and randomized control (surrogate) networks (Cp-s and Lp-s). We found values of Cp/Cp-s clearly higher than 1 and the values of Lp/Lp-s very close to 1 in all sleep stages and for all EEG bands. All bands below 15 Hz showed an increase of these features during sleep (and during CAP A phases in particular), compared to wakefulness. The results of this study seem to confirm our initial hypothesis that during sleep there exists a clear trend for the functional connectivity of the EEG to move forward to an organization more similar to that of a small-world network, at least for the frequency bands lower than 15 Hz. Sleep network ''reconfiguration'' might be one of the key mechanisms for the understanding of the ''global'' and ''local'' neural plasticity taking place during sleep.

Sleep in Later Life

O111

Sleep-wake rhythm fragmentation predicts age-related medial temporal lobe atrophy

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What determines the marked individual differences in age-related medial temporal lobe (MTL) atrophy? Several findings suggest harmful effects of sleep deprivation and circadian rhythm fragmentation on the MTL [1–5]. In animal studies, the experimental prevention of an uninterrupted period of sleep reduced hippocampal cell proliferation [6] and induced several molecular and cellular level alterations that could inhibit hippocampal function [7]. These findings led us to investigate the relation between the typical age-related increase in sleep-wake rhythm fragmentation and MTL atrophy in 138 aged individuals (69.1 $\pm$ 8.5 mean $\pm$ sd years of age, 85 males and 53 females). The sleep-wake rhythm was assessed for seven days continuously using actigraphy and quantified with nonparametric variables reflecting different rhythm aspects [8], among which the intradaily variability (IV) which quantifies the fragmentation of the rhythm, i.e. the frequency and extent of transitions between periods of rest and activity. The participants underwent a brain MRI scan from which MTL atrophy was rated according to validated standard procedures [9]. Stepwise regression revealed that the most significant MTA predictors were age (beta = 0.28) and fragmentation of the sleep-wake rhythm (beta = 0.35); no other sleep-wake rhythm variables accounted for further variance. Together, age and fragmentation accounted for 26% of the variance in MTA, indicating that rhythm fragmentation has an important contribution to MTA on top of the well-described predictive value of age. In conclusion, the sleep-wake rhythm fragmentation that is most typical of aging [10] accounts for at least as much of the variance in MTL atrophy as aging per se does. 1.Science (1981) 211, 1056; 2.Neurobiol Learn Mem (2001) 75, 51; 3.Nat Neurosci (2001) 4, 567; 4.Nat Neurosci (2007) 10, 385; 5.PLoS medicine (2006) 3, e301; 6.J Physiol (2003) 549, 563; 7.J Neurosci (2003) 23, 9687; 8.Am J Geriatr Psychiatry (2007) 15, 92; 9.J Neurol Sci (1993) 114, 7. 10.Physiol Behav (2002) 76, 597.

O112

Evoked K-complex amplitude is a sensitive marker of adult brain aging

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The K-complex (KC) represents the occurrence of a single delta wave in the NREM sleep EEG, that can be evoked by the presentation of sub-arousal threshold stimuli. Its frequency characteristics and amplitude necessitate that it be produced by the synchronized burst firing of large numbers of cortical cells. We have previously reported a reduction in the amplitude of the averaged evoked KC in elderly subjects compared to young adults. The present study investigated subjects aged between 18 and 78 years to determine the nature of the age-related change. 62 subjects (32 women) received auditory tones (80 dB, 100 Hz, 50 ms) with a random ISI of between 15 and 30 seconds throughout NREM sleep. EEG was recorded from 5 midline electrodes (Fz, FCz, Cz, CPz, Pz). All evoked KCs from stage 2 sleep were averaged and the P2, N550 and P900 peaks measured from each site and entered into a regression analysis with age. The P2 and P900 components represent the start and end of the evoked KC. The amplitude of neither component demonstrated a significant linear relationship with age (R^2 values ranging from 0.02 to 0.08 across sites for each component. N550 amplitude reflects the magnitude of the evoked delta response in the averaged KC. N550 amplitude demonstrated highly significant linear decreases with age at all sites with R^2 values ranging from 0.43 to 0.63. The overall R^2 values for men after entering all sites was 0.68 ($P<0.001$) and for women was 0.66 ($P<0.001$). The slope of the regression relationships was steepest at Fz (1.58 m) and systematically decreased across the more posterior sites, being least steep at Pz (0.93 m). Normal aging is associated with linear reductions in cortical gray matter volume as measured with structural MRI, and with reduced integrity of white matter pathways as measured with diffusion tensor imaging (DTI). Both effects are more pronounced in frontal brain regions. Both of these phenomena may be contributing to the linear reduction in evoked KC amplitude with increasing age, and to the steeper regressions slopes seen over frontal relative to more posterior scalp regions. The data indicate that evoked KC amplitude is a good functional indicator of brain age in normal healthy men and women.

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O113

Are there age-related changes in dream recall?

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Background: The ultradian NREM-REM sleep cycle together with the circadian modulation of REM sleep generate the main characteristics of dreaming. Dream recall is deemed to be maximal in younger individuals with a sharp decline in older adults, coupled with an attenuation of the central characteristics of dream recall in the latter. However, in what manner the circadian-driven activation of dream frequency and dream characteristics varies with age remains still remains unknown. In this study, it was investigated whether the circadian modulation of dream recall modifies with age.

Methods: Dream recall was investigated in 17 young (age range: 20–31 year) and 15 older (age range: 57–74 year) healthy volunteers under a 40-hour multiple-nap paradigm (75/150 min sleep/wake schedule) under constant-routine conditions. Dream recall was assessed at the end of each nap trial with the Sleep Mentation Questionnaire, which addresses main characteristics of dream recall, such as number of dreams, dreams during the time falling asleep, emotionality, vividness, pleasantness, hostility and colourfulness.

Results: The number of dreams recalled varied significantly both across the naps and between the age groups, with older subjects exhibiting less dreams ($P<0.05$). Concomitantly, older participants had comparatively lower levels of the following characteristics of dream recall: dreams during the time falling asleep, emotionality, vividness, pleasantness and colourfulness ($P<0.05$). Furthermore, these dream characteristics, varied significantly across the circadian cycle ($P<0.05$), showing a circadian modulation which was closely associated with the circadian rhythm of REM sleep during the naps.

Conclusions: This study revealed an age-related decline in the number of dreams recalled, coupled with an age reduction in some of the core characteristics of dreaming. Furthermore, these central characteristics of dream recall fluctuated in accordance with the

circadian cycle, thus suggesting that the circadian modulation of dream mentation can possibly be modified by age.

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O114

Zolpidem and zopiclone effects on sleep structure and daytime driving performance in healthy elderly subjects

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Elderly people already represent a large part of drivers and the proportion will increase in the future in most occidental countries. Paradoxically, while insomnia is more frequent in elderly, most experimental studies assessing drugs effects are conducted on healthy young subjects. The purpose of this work is to compare the effects of zolpidem (Zp) and zopiclone (Zc) verus flunitrazepam (Fln) and placebo on sleep structure and on driving performance the following day, in healthy elderly subjects. 16 healthy elderly volunteers (age range 55–65 years, experienced drivers) were recruited. Each subject took, at 11.00 pm the day before each session, a tablet of either Zp 10 mg, Zc 7.5 mg, flunitrazepam (Fln) 1 mg or a placebo. Ambulatory polysomnographic (PSG) recordings were realized at home with an dream Medatec. The study was conducted according to a balanced, double blind, cross-over design. Mono-screen driving simulator was used. The task was monotonous driving during 1 h where no other vehicle or pedestrian was represented. Subjects had to ensure maximum lateral stability of the vehicle and respect driving at 110 km h^{-1}. The amount of weaving of the car was measured by the standard deviation of the lateral position (SDLP, m) it is an index of driving safety. Other parameter analyzed was the standard deviation of speed (SDS, km h^{-1}). PSG were visually scored under blind conditions by experienced raters according to standardized criteria. Self-rating of mood was assessed with a visual analog scale. Driving: Zp and Zc significantly increased SDLP ($P<0.00001$) and SDS ($P<0.01$). No effect was founded with Fln. PSG: all hypnotics increased rapid eye movement sleep ($P<0.01$), total sleep time ($P<0.04$) and decreased wake after sleep onset ($P<0.04$). The main result of this study is that Zp has residual effects in elderly subjects more than 10 h after intake. Our study is the first one showing residual effects of this hypnotic. It reveals that elderly subjects were differently sensitive to this drug than young subjects who participated in similar drug effects studies. Results will be interpreted in light of pharmacokinetics and PSG data.

O115

Effect of exogenous melatonin on urine output in older people

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The causes of age-related nocturia are not always urological but are hypothesized to also be due to age-related sleep disruption and/or dampening of hormonal rhythms. In two prior studies, melatonin decreased nocturnal urinary output and nocturia, although it is not clear whether this was achieved through a sleep or a circadian effect. In this study we examined the effect of melatonin on the circadian rhythm of urine output in healthy older people.

Methods: 12 healthy people (age 64.6 ± 6 [55–78], 6F) were enrolled in a 32-day inpatient study during which they were scheduled to live on a 20-h day (sleep = 6.67 h) for 30 cycles. Each subject was randomized to receive 0.3 mg melatonin on either the first 12 or final 12 cycles, and received placebo on the other cycles. Throughout the study, core body temperature (CBT) data were collected to assess circadian phase in each condition; fluid/electrolyte intake was controlled and the time and volume of each void was recorded. Urine output was averaged per 60-degree circadian bin according to CBT phase for each subject in both conditions. We compared the circadian rhythm of urine output in the 2 conditions, and then adjusted for circadian phase and sleep-wake (SW) state. Comparisons were done using a repeated measures mixed model analysis.

Results: A univariate analysis of the average rate of urine production across the circadian cycle showed it was similar in both conditions (placebo 1.89 ± 0.35 ml mn^{-1} versus melatonin 1.80 ml $mn^{-1} \pm 0.31$, $P = 0.18$). In a multivariate analysis, there was a significant effect of circadian phase ($P<0.0001$), whereby urine production was significantly lower in the 3 circadian bins corresponding to the biological night. There was no effect of SW state ($P = 0.35$). In the multivariate analysis, there was also a significant effect of condition ($P = 0.0295$).

Conclusion: We found a significant circadian variation in urine output under conditions of forced desynchrony, whereby urine output was lowest during the biological nighttime. There was an effect of melatonin on the circadian rhythm of urine output. We plan to conduct additional analyses to determine whether this effect was mediated via changes in sleep or via other mechanism (s).

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O116

The treatment of elderly patients with primary insomnia and daytime sleepiness with EVT 201 improves sleep initiation, sleep maintenance, and daytime alertness

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EVT 201 is a partial positive allosteric modulator of the GABAA system. A Phase II study of EVT 201 was conducted in elderly primary insomnia patients with daytime sleepiness. A randomized, multicentre, double-blind, placebo-controlled, parallel-group design was used to assess the hypnotic efficacy of EVT 201 1.5 mg and 2.5 mg during seven consecutive nights. Polysomnography (PSG) was performed on two consecutive nights for screening and on nights 1, 6 and 7 of treatment. At Screening, patients were required to have a mean Total Sleep Time (TST) of 240–410 min and a mean Multiple Sleep Latency Test (MSLT) latency of $\geq$ 4 min and $\leq$ 16 min. Daytime assessments on Day 8 included the MSLT, Rey Auditory Verbal Learning Test (RAVLT), Psychomotor Vigilance Task (PVT) and the Karolinska Sleepiness Scale (KSS). PSG Total Sleep Time (TST) was the primary endpoint. Participants were 149 elderly patients with DSM-IV primary insomnia (53 males, 96 females; mean age 71.3 years, range 65–86 years). Compared to placebo, EVT 201 1.5 mg and 2.5 mg increased TST (30.9, 56.4 min respectively, $P = 0.0001$, $P<0.0001$); reduced WASO (-15.2, -36.1 min respectively; $P = 0.01$, $P<0.0001$); reduced LPS (-15.9, -19.9 min respectively; $P = 0.009$, $P = 0.001$) and reduced WASO in hours 5–8 (-4.1, -16.3 min respectively; $P = 0.4$, $P = 0.001$). Both doses also improved subjective sleep quality and usual subjective efficacy measures. A significantly longer mean MSLT latency was observed on Day 8 with both doses, compared to placebo (2 min increase; $P = 0.03$, both doses). No serious or unexpected treatment emergent adverse events were noted. EVT 201 improved PSG measures of sleep onset and sleep maintenance, showing evidence of efficacy throughout the night in elderly patients at the same doses as in

adult patients. The improvement of sleep was accompanied by significantly improved physiological alertness during the day.

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O117

Daily light exposure profiles in older extreme morning and evening types

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Background: Extreme morning types have earlier sleep-wake timing than extreme evening types, and consequently differ in their exposure to the light-dark cycle. Younger extreme morning types have been shown to spend more time in bright light, especially in the morning, but less time in bright light in the evening, compared to evening types. This study aims to investigate if these patterns of daily light exposure are found in older extreme morning and evening types (measured by the Horne Östberg Morning-Eveningness Questionnaire (1976; HÖ MEQ)).

Method: Over a 2 week period (Oct-Feb), 24-h light exposure was measured actigraphically (Actiwatch-L) in 10 extreme morning types (3 men, 7 women, 64.5 ± 1.9 years, HÖ MEQ >70) and 10 extreme evening types (4 men, 6 women 70.6 ± 3.2 years, HÖ MEQ<47). All participants had self-reported good health. Mean time exposed to over 1000 lux per day was compared between the two groups by Student's *t*-test. Light data were log-transformed and averaged over each hour and analysed using group-by-time ANOVA.

Results: Extreme morning types (M) had significantly earlier sleep and wake times than extreme evening types (E) ($M = 22{:}49 \pm 00{:}51$, $E = 24{:}55 \pm 01{:}10$, $P<0.001$; $M = 06{:}33 \pm 01{:}13$, $E = 07{:}47 \pm 01{:}05$, $P<0.001$). There was no significant difference in the number of minutes of daily bright light (>1000 lux) exposure ($M = 00{:}53 \pm 4.8$ mins; $E = 01{:}05 \pm 5.5$ mins, $P = 0.119$). However, 24-h patterns of light exposure in relation to time show a significant group effect between morning and evening types ($F = 4.97$, $P = 0.039$). Extreme morning types received higher light intensity at 06:00 than extreme evening types ($P = 0.023$). Extreme evening types received higher light intensity at 16:00 ($P = 0.036$), 22:00 ($P = 0.005$), 23:00 ($P = 0.001$) and 24:00 ($P = 0.010$) compared to extreme morning types.

Conclusions: Our findings suggest that differences in patterns of daily light exposure found in younger extreme morning and evening types are also found in older extreme morning and evening types. However, these differences occur earlier in the day in older extreme morning and evening types than in younger extreme morning and evening times.

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O118

Activity dependent increase of extracellular lactate in the basal forebrain is compromised with age

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The basal forebrain (BF), through its reciprocal connections to the prefrontal cortex (PFC), is part of the attentional network, in which activity increases during sustained periods of active waking. Lactate, the main supplementary energy fuel in the brain, increases in the rat BF during active wakefulness and increased neuronal activation (Wigren et al. 2007), implicating that lactate in the BF is needed to maintain intense neuronal activity. In humans, the lactate response to cognitive stimulation in the PFC was absent in the aged subjects (Urrila et al. 2004). We hypothesized that lactate production is compromised also in the aged BF and that this contributes to the age-related problems in maintenance of active waking. We used in vivo microdialysis to measure extracellular lactate levels in the BF during sustained active waking (3 h, presentation of novel objects) and during experimental neuronal activation (3 h, infusion of 0.3 mM NMDA) in three age groups of male rats (young: 3 months; middle-aged, 12 months; old, 24 months). Fronto-parietal EEG was recorded to monitor vigilance states and waking EEG theta power (5–9 Hz), which is a marker of active waking. The lactate responses measured in the young during sustained active waking ($50 \pm 20\%$, $n = 9$) and during glutamatergic stimulation ($45 \pm 7\%$, $n = 5$), were suppressed in the old ($7 \pm 11\%$, $n = 9$; $8 \pm 14\%$, $n = 4$, respectively). Compared to young, active waking was reduced in the old as evidenced by the attenuated waking-theta during both treatments. These findings implicate that production of lactate in the BF is necessary to maintain efficient levels of active waking. In aging, the activity-dependent increase of lactate in the BF is compromised, leading to inability to sustain active waking.

O119

Sleep/wake cycle patterns and cognitive functions in hypertensive older adults

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Introduction: Sleep/Wake Cycle (SWC) patterns are modified with aging. These changes include frequent awakenings, reduced nighttime sleep and increased daytime sleepiness. Besides, cognitive functions decline with advancing aging. Few reports have examined the consequences of altered consolidation of SWC patterns on cognitive functions in older adults, in particular, the executive functions of the prefrontal cortex.

Objective: To evaluate the relationship between SWC patterns and executive functions of the prefrontal cortex in hypertensive older adults.

Methods: Subjects were 69 hypertensive older adults (19 men and 50 women) between 70 and 80 years of age. Motor activity was assessed for a whole week by mean of actigraphic recordings (Actiwatch-16/64) and the following SWC patterns were determined: sleep efficiency (SE), nighttime awakenings (NA), daytime naps (DN) and motor activity during nighttime sleep (MANS). Cognitive functions were evaluated through Stroop test and included the reaction time for congruent (RTC) and incongruent (RTI) correct responses and the percentage of congruent (PC) and incongruent (PI) correct responses.

Results: With regard to nighttime sleep, the groups of subjects with reduced SE or higher MANS showed similar results: slower RTC ($P<0.03$ and $=0.05$, respectively) and RTI ($P<0.02$ and <0.005, respectively) responses, and smaller PI ($P<0.01$ for both); moreover, those presenting $\geq$ 3 NA also showed reduced PC ($0<0.03$). In addition, the strongest associations resulted between NA and PC ($R = -0.33$, $P<0.01$) and MANS and PI ($R = -0.40$, $P<0.001$). Finally, during the daytime, the group pf subjects with $\geq$ 3DN showed reduced PI ($P<0.02$).

Conclusion: These results show a close relationship between SWP and Stroop test performance in this group of hypertensive older adults. Subject groups with more fragmented SWC patterns were those that presented lower performance of prefrontal cortex executive functions, suggesting that consolidated SWC patterns could be a contributing factor to counteract cognitive decline in the elderly.

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O120

Prevalence of fatigue, sleepiness and hypersomnia after ischemic stroke

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Background: Fatigue appears to be common after ischemic stroke. The simultaneous prevalence of other vigilance disturbances following stroke-including excessive daytime sleepiness (EDS) and hypersomnia-as well as their association with fatigue and other stroke-related factors have not yet been studied.

Objective: To assess the prevalence of fatigue, excessive daytime sleepiness, and hypersomnia after ischemic stroke, and to elucidate their relationship to demographic and clinical variables.

Methods: We assessed Fatigue Severity Scale (FSS) scores, Epworth Sleepiness Scale (ESS) scores, and mean bedtimes (as a measure of sleep need per 24 h) in 285 consecutive patients with a history of definite ischemic stroke.

Results: At 21 $\pm$ 18 (range 3–96) months after stroke, fatigue (FSS score $\geq$ 4.0) was found in 135 (47%), EDS (ESS $\geq$ 10) in 79 (28%), and hypersomnia in 77 (27%) patients. Fatigue was frequently associated with EDS (44%) and hypersomnia (36%) ($P<0.001$ and $P=0.003$, resp.). Multivariate analysis revealed that high disability at hospital discharge ($P<0.001$) and young age ($P=0.031$) are independent predictors of poststroke fatigue; old age ($P<0.001$) and female sex ($P=0.001$) were independent predictors of poststroke hypersomnia.

Conclusions: Poststroke fatigue affects almost one of two patients, and is often associated with EDS and hypersomnia. Severity and frequency of poststroke fatigue is higher at younger age, and is related to stroke outcome. Conversely, poststroke hypersomnia is more frequent in females and at older age.

O121

The effect of estrogen plus progestin treatment on sleep: a randomized, placebo-controlled, double-blind trial in premenopausal and late postmenopausal women

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In ageing sleep complaints increase in both sexes. Compared both to young women and to their male counterparts, premenopausal women report more sleep problems. The female predisposition in sleep problems is progressive across age, with even more significance in the elderly. Part of this could be explained by the reduction of female sex hormones since hormone therapy (HT) has reduced sleep complaints in women even after menopause. The consistent treatment response of HT in the subjective sleep quality is contrasted by less well-defined improvement of the objectively measured sleep. In this prospective randomized placebo-controlled and double-blind study, the objective was to investigate the effects of estrogen-progestin treatment (EPT) on sleep in pre- and postmenopausal women. Seventeen premenopausal (aged 45–51 years) and 18 postmenopausal (aged 58–70 years) women were studied in a sleep laboratory for two nights (an adaptation and a study night) before and after six months of treatment with EPT or placebo. During the treatment period, premenopausal women received cyclic EPT or placebo and the postmenopausal women continuous EPT or placebo. Polysomnography and questionnaires were used to evaluate sleep and well-being. At the end of the treatment period, premenopausal women receiving EPT had more awakenings from stage 1 sleep ($P=0.047$) and postmenopausal women with EPT had a greater total number of awakenings ($P=0.031$) than the corresponding placebo group. Further, sleepiness decreased less in premenopausal EPT group than in the placebo group ($P=0.031$). In postmenopausal women, EPT decreased and placebo slightly increased slow wave activity during the second non-rapid eye movement sleep episode ($P=0.046$). In conclusion, in premenopausal and late postmenopausal women EPT had only random and marginal effects on sleep. Although, the limited findings were mostly unfavorable for EPT, one cannot conclude that EPT deteriorates sleep. Further, neither middle-aged menstruating premenopausal women nor older postmenopausal women benefit from estrogen-progestin –treatment in terms of their sleep quality.

With Sleep in Mind

O122

Sleeping difficulties in relation to risk for depression. A 20-year longitudinal population study

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Introduction: Poor sleep may be a risk factor for depression. The aim of the present study was to examine if sleep disturbances in year 1983 may predict depression in year 2003.

Methods: In 1983, 1.687 subjects, aged 30–44 years, answered a sleep questionnaire (USI). In a follow-up in year 2003, 1.192 subjects, aged 50–64 years, answered the same sleep questionnaire. Subjects were asked about difficulties initiating sleep (DIS) and difficulties maintaining sleep (DMS), and not being rested by sleep (NRS). The questions were answered on a five-point scale (1 = no problems, 2 = minor problems, 3 = moderate problems, 4 = severe problems, 5 = very severe problems). At least severe problems (scores 4 and 5) were considered to be a complaint. Pre-sleep problems with anxiety and tension were rated in the same way, and depression was defined as the two highest scores on a 5-point scale.

Results: At baseline 4.4% reported DIS, 6.2% DMS and 6.2% NRS. In a logistic regression analysing risk for depression in year 2003, the risk was significantly increased with insomnia at baseline for men (OR 7.2 CI 3.1–16.8) but not in women. However, women with NRS had significantly higher risk for depression (OR 1.4 CI 1.1–1.7). In an analysis of pre-sleep symptoms, high tension and anxiety were significantly associated with depression in women and men, respectively. A sleep latency above 30 min significantly increased the risk for depression in both men and women, but a short sleep duration (<6 h.) was only significant in men. Persistent insomnia significantly increased risk for depression in both sexes.

Conclusion: Sleep complaints significantly increase the risk for depression in a long-term perspective.

O123

Decreased serotonin transporter function during early postnatal life induces long lasting impairments of REM sleep, stress response and emotional behavior

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The most widely used antidepressants are blockers of the serotonin reuptake (SSRI), and their use during development might lead to persistent anomalies (1). Some of these impairments, such as sleep disorders, might have been underestimated, notably because no study has investigated them on a very long term basis, even though SSRIs have been prescribed for more than 20 years. In mice, the data that we obtained recently confirm that transitory blockade of the serotonin reuptake during a "critical" postnatal period results in persistent (life long) alterations of notably sleep regulation and emotional behaviour (2). Indeed, mouse pups were treated daily from post-natal day 5 to 21 with the most selective SSRI, escitalopram. At adult age, a syndrome of depression was observed, i.e., sleep fragmentation, REM sleep increase, enhanced time of immobility in adverse situations (an index of helplessness), altered response to acute stress, and impaired 5-HT neurotransmission. In these adult animals, as expected from a depression model, helplessness was reversed by chronic -but not acute- treatment with the antidepressant fluoxetine. Conversely, we found that in mutant mice that display enhanced levels of serotonin in the brain due to transporter gene invalidation, and exhibit at adult age a syndrome of depression (but with increased level of anxiety), a lasting normalization of sleep and behaviour could be obtained after specific treatment during the "critical" period only (3). Such rescue treatment limited the serotonin impact on the brain, notably at 5-HT_{1A} receptors. Therefore, an excess of serotonin during development induces a life long syndrome of depression in the mouse. These results underline the need for studying long term effects of antidepressant exposure during development in humans. In addition, they open the way to new strategies for treating depression in the child or pregnant mother, or even for preventing anomalous development of such phenotypes due to genetic causes.

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O124

Subjective and objective sleep among depressed and non-depressed postnatal mothers– a population based questionnaire study supplemented by sleep diary and actigraphy

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Introduction: Women sleep less in the postnatal period, and mothers diagnosed with depression could alternatively be suffering from the effects of chronic sleep deprivation. Population based studies of depressive symptoms along with prospective sleep reports and objective sleep registrations have been lacking. Our aim was to study the prevalences of sleep problems and depressive symptoms in a normal population of postnatal women to identify risk factors, and to compare retrospective reports with objective and prospective sleep registrations.

Methods: All women ($n = 4191$) delivering at Stavanger University Hospital, Norway during one year were mailed a questionnaire 7 weeks after delivery, and 2831 (67%) participated. Pittsburgh Sleep Quality Index (PSQI) was used to measure sleep, and depressive symptoms were measured by the Edinburgh Postnatal Depression Scale (EPDS). A sub-study using sleep diaries and actigraphy recordings for 14 days was performed among 42 women, of whom 21 scored ≥ 10 on the EPDS.

Results: The prevalence of PSQI >5 was 57.4%, and the prevalence of EPDS ≥ 10 was 16.5%. The mothers slept on average 6.5 h nightly, with 73% sleep efficiency. Depression and sleep quality were strongly associated. There were significant differences according to depressive status in daytime dysfunction, but not in sleep, measured prospectively by the sleep diaries and the actigraphs. Independent of depression, being primipara, not fully breastfeeding, having younger infant, male infant or co-sleeping with the baby were associated with poorer sleep quality at the PSQI. In addition to sleep quality reported at PSQI, depression was associated with poor partner relationship, depression during pregnancy or previously, and stressful life events.

Conclusion: Although reporting poorer sleep at the PSQI, postnatal women with depression did not show worse sleep parameters than non-depressed women when measured objectively and prospectively. Women complaining of poor sleep or tiredness in the postnatal period should be evaluated for possible depression.

O125

Quetiapine improves sleep in acute mania: a case series

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At least 0.5 to 2% of the population suffer from bipolar affective disorder and mania is one of the most severe disorders in

psychiatry. Disturbances of the sleep-wake behavior are a key feature of this disorder. Disturbed sleep is not only an important part of the prodrome of ma-nia but sleep loss has also been demonstrated to trigger symptoms of hypomania and mania. A number of atypical antipsychotics, including quetiapine, have demonstrated therapeutic effi-cacy in bipolar mania. However, there is a lack of data on the effects of treatment on sleep architecture in manic patients and no information exists on the influence of quetiapine on polysomnographically registered sleep of these patients. To narrow this gap three manic patients were studied polysomnographically during 7 nights under baseline and treatment conditions. One night of adaptation to the sleep lab was followed by the baseline night. Immediate treatment effects were determined during the first two nights of titration with quetiapine while long term effects were registered after three weeks following one night of adaptation for two consecutive nights. Quetiapine was titrated up to 800 mg in two divided doses as clinically appropriate. At baseline the average Young Mania Rating Scale score of the manic patients was 24.7 (range 21–28), while it decreased to 12.3 (range 11–14) after three weeks of treatment. At baseline total sleep time was 322 min (range 166–424) and REM latency was 47.7 min (range 7–80 min). During the first two treatment nights total sleep time increased by nearly one hour to 377 min (range 215–520 min) and REM latency increased to 79 min (range 53–118). Af-ter three weeks of treatment total sleep time increased further to 408 min (range 251–511) and REM latency to 148 min (range 50–277). In this case series treatment of mania with quetiapine demonstrates a clinically significant im-provement of sleep already at the beginning of drug titration that is consolidated during fur-ther administration of this medication. The increase of total sleep time and prolongation of REM latency may be important for the therapeutic effect on the broader spectrum of sympto-matology.

O126

Sleep-wake disturbances in patients with cirrhosis: relations to neuropsychiatric performance and health-related quality of life

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Sleep-wake disturbances are common in patients with cirrhosis and have been traditionally attributed to hepatic encephalopathy, a neuropsychiatric syndrome that complicates hepatic failure. The aim of this study was to determine the exact relationship between sleep-wake disturbances and neuropsychiatric status/health-related quality of life (QoL) in patients with cirrhosis. The study population comprised 87 patients (51 men; mean [range] age 58 [34–80] yr), classified as neuropsychiatrically unimpaired ($n = 58$) or as having minimal (12) or overt hepatic encephalopathy (17). Nineteen healthy volunteers (12 men; 53 [32–85] yr) served as controls. Validated, self-rated questionnaires were used to assess sleep quality (Pittsburgh Sleep Quality Index [PSQI]); daytime sleepiness (Epworth Sleepiness Scale [ESS]); and diurnal preference (Horne-Östberg [HÖ] questionnaire). QoL was assessed using the 36-item Short Form Health Profile (SF-36v1) and the Chronic Liver Disease Questionnaire (CLDQ). Patients slept significantly less well than the healthy volunteers (PSQI: 8.4 ± 4.9 versus 4.6 ± 2.5, $P < 0.01$) and had more pronounced daytime sleepiness (abnormal ESS: 21% versus 0%; $\chi^2 = 3.8$, $P = 0.05$), but no significant shift in diurnal preference. No significant relationships were observed between sleep-wake indices and the presence/degree of hepatic encephalopathy. Health-related QoL was significantly impaired in the patients compared with the controls (SF-36v1 summary physical: 36 ± 15 versus 50 ± 10, $P < 0.001$; SF-36v1 summary mental: 46 ± 11 versus 50 ± 10, $P < 0.01$); night sleep disturbance was an independent predictor of poor health-related QoL ($P < 0.01$). In conclusion, sleep-wake abnormalities are common in patients with cirrhosis; they significantly affect health-related QoL, but are not related to, nor do they reflect the presence of hepatic encephalopathy.

O127

Prevalence of restless legs syndrome in psychiatric population

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Objective: The Restless Legs Syndrome (RLS) is a common condition, with reported prevalence between 1 to 15% in the general population. To the best of our knowledge, there is no data on the prevalence of RLS in psychiatric inpatient population.

Method: With the exception of drug/alcohol dependent and gerontopsychiatric patients, patients consecutively admitted to the Centre of Mental Health at the Klinikum Ingolstadt between December 2006 and March 2007 were interviewed by an experienced clinician to assess the presence of RLS. The clinician completed the Restless Legs Diagnostic Index after each interview. The severity of the symptoms was assessed by the International Restless Legs Severity Scale (IRLS). Anamnestic data concerning RLS were also collected.

Results: A total of 213 patients were interviewed (mean age 45.7 ± 14.7, 60% females, 40% males). 22 patients (10,3%) fulfilled the diagnostic criteria for RLS. Their mean age was 49.2 ± 15.0, 73% were women and 27% were men, mean IRLS score was 20 ± 8.9. In addition, 5.9% of RLS symptoms free patients reported to have had these symptoms in the history. There were slightly more RLS patients diagnosed with an affective disorder compared to the entire sample distribution and there were considerably less RLS patients in the group of psychotic disorders compared to the entire sample distribution. 4.4% of the total data sample had a positive family history for RLS. As assessed by simple regression analysis there were no particular differences in medication patters between the RLS patients and the entire sample.

Conclusion: We report here for the first time the prevalence of RLS in psychiatric inpatients. The prevalence rate is in the range of those reported for the general population. In addition, 5.9% of RLS symptoms free inpatients reported to have had these symptoms in the history. Patients with psychotic disorders are considerably less affected by RLS as expected from the entire sample distribution.

O128

Sleep and rest/activity cycle disturbances in schizophrenia patients in comparison to unemployed healthy controls

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Introduction: Sleep disturbances are a commonly reported in schizophrenia. In a small number of previous studies abnormalities in sleep onset, sleep maintenance and sleep structure have been reported in patients regardless of either their medication status or the phase of the clinical course.

Objectives: We studied the extent to which sleep abnormalities are a genuine problem in schizophrenia and whether abnormalities of the circadian timing system may contribute to the abnormal pattern of sleep often reported in this patient group.

Methods: Twenty medicated, mentally stable outpatients fulfilling DSM-IV criteria for schizophrenia and reporting poor sleep and 20 age- and gender matched unemployed subjects without self-

reported sleep complaints (mean age 39 years, range 25–58 years) wore an Actiwatch (CNT) with integrated light sensor for six weeks and collected urine samples for 48 h each week for establishing melatonin profiles. Self-reported measures included chronotype, sleep quality and mood profiles. Participants kept a diary of sleep times, naps, medication, and activities.

Results: The spectrum of disturbances in schizophrenia patients included sleep/wake reversal, arrhythmicity, delayed and non-24 h activity/rest cycles. Patients showed a lower amplitude in their rest/activity cycles than controls (Amp = 0.748 SD ± 0.180 versus 0.838 SD ± 0.073, respectively, $P = 0.046$), a later melatonin peak (06:46 h versus 04:58 h, respectively, $P = 0.026$), and a longer sleep onset-melatonin peak interval (302 ± 82 min versus 207 ± 78 min, respectively, $P = 0.001$). Schizophrenia patients exhibited significantly lower daytime activity, longer sleep latencies, less regular sleep periods, later sleep offsets, and less light when awake. Both groups had similar sleep efficiency.

Conclusion: Schizophrenia patients treated with second generation antipsychotics show greater sleep and circadian disturbances than unemployed subjects. The difference in the phase relationship between sleep/wake and the melatonin rhythm illustrates that a genuine sleep/circadian-related abnormality is apparent under an unemployed lifestyle in schizophrenia patients.

O129

Disturbances in sleep-wake rhythms correlate with cognitive impairment in schizophrenia

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Patients with schizophrenia suffer from negative symptoms, mainly lack of motivation and interest, flattened affect, and social withdrawal together with psychotic episodes characterised by positive symptoms, such as delusions and halluzinations. Moreover, neurocognitive dysfunction, which is partly related to these clinical symptoms, is a common feature in schizophrenia. In an ongoing ambulatory real life-study, we are investigating the relationship between the circadian rest-activity cycle characteristics, psychopathology and cognitive functioning in schizophrenic patients. Sleep-wake behaviour is recorded by wrist actimetry along with sleep diaries throughout a period of 20 ± 3.6 days in 10 treated schizophrenic patients so far (age range 28–56 y). Saliva samples are collected in 7-day intervals over 2 evenings to determine the onset of melatonin secretion. Clinical interviews document sociodemographic data and medication, and standardised questionnaires and interviews (BPRS, PANSS, PSQI) assess clinical status. Cognitive functioning such as attention, cognitive flexibility, executive functioning/reaction inhibition and verbal fluency, are assessed by the Trail Making Test A+B (TMT A+B), the Stroop interference task (SIT), and the Supermarket test (ST). The rest-activity cycle in six of the ten patients has showed abnormal patterns such as frequent awakenings during the main sleep episode, frequent napping during daytime, or hypersomnia, objectively measured by the relative amplitude (RA; median = 0.82, range 0.57–0.95) and the interdaily stability index (IS; median = 0.43, range 0.31–0.72). We found significant correlations between the cognitive performance and the degree of rest-activity cycle disturbances as reflected in RA (RA versus TMT A+B: $r = -0.65$, $P = 0.043$; SIT: $r = -0.94$, $P < 0.001$; ST: $r = 0.77$, $P = 0.009$) and IS (IS versus TMT A: $r = -0.83$, $P = 0.003$; TMT B: $r = -0.72$, $P = 0.019$; SIT: $r = -0.818$, $P = 0.004$). These findings indicate that poor cognitive functioning in schizophrenia can be related to disturbed sleep-wake behaviour. It remains to be established whether these findings are specific for schizophrenia.

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O130

The effects of background music on sleep quality and emotional measures in schizophrenia patients

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Introduction: Disturbed sleep is a common complaint among Schizophrenia patients. Since previous studies have demonstrated treatment resistance for sleep-medication for insomnia in these patients, the aim of the present study was to examine the effects of background music at bedtime as treatment for insomnia in Schizophrenic patients.

Methods: Twenty four Schizophrenic patients, who had no other major psychiatric, sleep, or neurological disorders, participated in the study (13 males and 11 females; mean age = 45.67, SD = 9.6). The study comprised a 7-day, running-in period, followed by a 7-day experimental period. The treatment was background music at bedtime. During each of these periods, subjects' sleep was continuously monitored with a wrist actigraph (Ambulatory Monitoring, Inc.) and subjects were asked to fill out a wide spectrum of questionnaires monitoring depression, anxiety, and life satisfaction.

Results: A paired-sample *t*-test was conducted, comparing objective sleep parameters manifested by patients with background music background at desired bedtime and without music exposure. A significant difference was found in sleep latency ($t(23) = 3.01$, $P < 0.006$), showing shorter sleep latency when music was played (21.04 ± 14.6 and 37.01 ± 32.4, respectively). Likewise, a significant difference was found in sleep efficiency ($t(23) = -3.35$, $P < 0.003$), showing higher sleep efficiency when background music was played (86.0 ± 15.5 and 82.44 ± 18.3, respectively). Similarly, a significant difference was found in total sleep minutes ($t(23) = 2.48$, $P < 0.02$), showing extension of total sleep time when music was played (1212.28 ± 469.8 and 987.44 ± 201.4, respectively). Moreover, background music improved total psychopathology score (PANSS) ($t(23) = 2.28$, $P < 0.03$), and decreased the level of depression (BDI) ($t(23) = 2.96$, $P < 0.007$). Furthermore, following music a significant correlation was found between the reduction in situational anxiety level and the improvement in sleep efficiency ($r = -0.468$, $P < 0.02$) and between the expansion in total sleep minutes and the reduction in depression scale ($r = -0.36$, $P < 0.043$).

Conclusion: The findings imply the beneficial effect of bedtime music as treatment for both insomnia and emotional measures in Schizophrenic patients.

O131

Actigraphic assessment of rest and activity in patients with psychotic disorders

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Objective: Excessive sedation and weight gain are common reasons for non-compliance to antipsychotic therapy of patients with schizophrenia. In present study we evaluated duration of rest,

daytime activity and sleepiness in patients treated with sedative antipsychotic drugs.

Method: 62 patients (20 F/42 M, mean age 28.6 ± 3.1) diagnosed with psychotic disorders treated with olanzapine ($n = 40$), risperidone ($n = 12$), quetiapine ($n = 4$), clozapine ($n = 1$) and perphenazine ($n = 5$) were examined during the last week before the discharge from the open psychiatric rehabilitation ward. The patients performed a vigilance task (Mackworth clock test) and filled out sleep diaries, Athens Insomnia Scale, Epworth sleepiness scale (ESS). Drug side effects were scored with UKU scale. Mental status was evaluated with the use of the PANSS and CDSS scales. An actigraphic recording (Actiwatch AW4, Cambridge Neurotechnology) was performed for seven days.

Results: During the night the mean time in bed, sleep duration and sleep latency were 601 ± 60, 506 ± 58 and 30.8 ± 20.2 min. During the day, only 19 patients presented activity at the comparable level of those of the healthy controls. Moreover, most of the patients showed increased napping behavior. Disturbed vigilance was found in 21 patients. Twelve patients showed increased scores in the ESS scale. Thirty-five patients attributed their prolonged sleep time and daytime sleepiness to the action of antipsychotics taken.

Conclusions: Patients treated with sedative antipsychotics show substantially increased rest periods and decreased daytime activity. Promoting a more active lifestyle should be considered as important primary prevention to reduce an increased metabolic disease and cardiovascular risk in these patients.

Spotlight on Circadian Clock Works On and Off Stage

O132

Effects of artificial dawn on waking up processes in the morning

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Background: Late chronotypes regularly suffer from sleep inertia after waking up. We tested whether an artificial dawn signal during the last 30 min of sleep (Wake up Light®, Philips DAP B.V. Drachten, The Netherlands) reduces sleep inertia complaints, and if so, whether these effects were accompanied by changes in the awakening cortisol response, in thermoregulatory processes, or in the circadian rhythm of melatonin.

Methods: Three studies were performed: (1) A home study ($n = 33$) with 3 conditions (0, 50 and 250 lux, light turned off at the alarm) lasting 2 weeks each; (2) A home study ($n = 25$) with 2 conditions (0 lux and self selected intensity) lasting 2 weeks each; and (3) A laboratory study ($n = 16$) with 2 conditions lasting 1 experimental night each whether with or without a dawn signal and lights on at waking up (300 lux).

Results: In study 1 and 2 significant reductions of the duration of sleep inertia complaints were found of 16 min between 250 lux and 0 lux ($P < 0.05$), of 9 min between 250 lux and 50 lux ($P < 0.05$), and of 26 min between the self selected intensity and 0 lux ($P < 0.05$). In study 3 a significant reduction in sleepiness, an increase in activation, but no effects on stress were found. The artificial dawn signal also had an acute effect on physiology; the decline in distal skin temperature was larger than in the control condition. The awakening cortisol response was not different between the 2 conditions, but this could be explained by the effect of light at waking up in the control condition. In a small additional study ($n = 7$) a significant increase in the awakening cortisol response was found between the condition with dawn and light at waking up compared to the condition without dawn and without light at waking up. No significant shift was observed in the onset of the melatonin rhythm after 2 weeks use of a high or medium intensity artificial dawn signal compared to the control study (study 1; DLMO 21:17 h $\pm$ 54 min, 21:25 h $\pm$ 51 min and 21:16 $\pm$ 64 min, respectively).

Conclusion: An artificial dawn waking up signal reduces symptoms of sleep inertia. This may be explained by acute effects of the light on thermoregulation and cortisol, but not by a shift of the circadian system.

O133

Blue light affects timing of sleep in rhesus monkeys but not sleep homeostasis

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Intrinsically photosensitive retinal ganglion cells (ipRGC) with peak blue sensitivity, and their projections appear to be the predominant pathway mediating the actions of light on circadian entrainment and alerting. Blue light pulses augment phase-shifting in humans, and evening blue light can decrease sleepiness and enhance performance. To test the responses of sleep and circadian rhythms to blue light in a standard 12-h day (LD 12:12), rhesus monkeys were given blue light using LEDs (peak wavelength 470 nm) for 4 days following 4 days in cool-white fluorescents. Both light exposures averaged 6.1×1013 quanta cm-2 s-1 at eye level. Animals were unrestrained and individually housed in their home cages. Sleep and brain temperature (Tbr) were recorded via biotelemetry, and sleep scored in 30-second epochs using standard polysomnography criteria. Delta EEG (0.375–4 Hz) power was derived from 2-second FFTs after removal of epochs with artifacts, and normalized to average total EEG power for comparison among animals. Performance was measured using the Psychomotor Test System. Distribution of sleep stages in L, D and 24-h were compared using repeated measures ANOVA, and timing of sleep stages, delta EEG and Tbr using the cosinor method. The fraction of time in sleep over 24-hours, and in L or D, did not differ between blue and white light. Shallow slow-wave sleep (stages 1 and 2, SWS12) and deep slow-wave sleep (stages 3 and 4, SWS34) also showed no significant differences. REM sleep was significantly elevated during D and over 24-h in blue light. No behavioral changes in vigilance and proficiency were seen in blue light, however a trend toward improved memory was seen. SWS12 during L showed an apparent phase advance in blue light, but the timing of nocturnal sleep, including SWS34, did not differ. The Tbr rhythm was significantly advanced during the first two days of blue light, and Tbr and sleep stages after two days of blue light continued to show apparent phase advances. Thus, 12 h of daytime blue light exposure resulted in phase realignment with little evidence for altered sleep architecture or sleep homeostasis.

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O134

Short wavelength light exposure in the elderly: acute and phase shifting effects

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Age-related changes in the eye result in a reduction in the transmission of short wavelength light and may impair non-image forming light responses in older individuals. Reduced short wavelength sensitivity with age has been shown for light-induced melatonin suppression. The current research assessed age-related changes in the response of subjective alertness and circadian phase advance to exposure to short wavelength light. Young ($n = 11$, 23.0 $\pm$ 2.9 years) and older ($n = 15$, 65.8 $\pm$ 5.0 years) healthy men were exposed to 2 h of intermittent monochromatic light on two separate occasions. Light exposure of short (456 nm) or medium (548 nm) wavelength ($\sim 6 \times 10^{13}$ photons cm^{-2}/sec) was individually timed to begin 8.5 h after their previously determined melatonin onset. Five older subjects participated in only the short wavelength light condition. Subjective alertness was assessed during and for 5 h after light exposure using a 9-point scale. The degree of phase advance was determined by comparing plasma melatonin onset and offset phase markers pre- and post-light exposure. The alertness response to short wavelength light was significantly diminished in the older group compared to the young group ($F_{1,24} = 23.6$, $P < 0.0001$), whereas the alertness response to medium wavelength light was not significantly different between the age groups. For the phase shifting response similar wavelength sensitivity was revealed for the two age groups: short wavelength > medium wavelength light, but with smaller phase advances in the older group (non-significant). The current and previous results for alertness and melatonin suppression reveal a reduced responsiveness to the acute effects of short wavelength light in older people. By contrast, the current findings indicate that the phase shifting response to short wavelength light is not significantly impaired with age.

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O135

Analysis of the PER3 promoter and haplotypes that associate with diurnal preference and delayed sleep phase disorder

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Diurnal preference, sleep architecture and waking EEG, variability in cognitive function, and DSPD (DSPS) have all been associated with polymorphisms in PER3. We sought to characterise PER3 haplotype associations in subjects with extreme diurnal preference and DSPD, and to define the promoter region and include potential promoter region polymorphisms in the haplotype analysis. PER3 promoter and coding region polymorphisms were genotyped ($n = 80$ for extreme morning and extreme evening groups, $n = 23$ for DSPD). The functional significance of polymorphisms and potential enhancer and repressor elements within the PER3 promoter was investigated with luciferase reporter constructs comprising different haplotype combinations and sequential deletions of the promoter. Three promoter region SNPs (G-320T, C-319A, G-294A) and five coding-region SNPs (T2115G, C2765T, 3206 4/5 VNTR, T3285C, A3648G) were identified in our samples. In addition, a novel 2-nucleotide-repeat VNTR polymorphism was found in the promoter (− 318 1/2 VNTR). In the promoter region, the -320T and -319A alleles occurred more frequently in DSPD compared to morning ($P = 0.042$ for each) or evening types ($P = 0.006$ and 0.033, respectively). Genotype frequency analysis for the nine polymorphisms predicted the existence of 16 haplotypes. Haplotypes containing the promoter allele combination TA2G were more prevalent in DSPD compared to morning ($P = 0.033$) or evening types ($P = 0.002$). Luciferase-driven expression was significantly reduced in the GC2A ($P < 0.05$) and the rare TA1G ($P < 0.001$) haplotypes compared to the TAG haplotype. Promoter deletion reporter constructs defined two regions between − 703 and − 605, and between − 283 and − 80 that significantly enhanced reporter gene expression. Within this region, we have identified a VNTR polymorphism and three SNPs, two of which associate with DSPD. Our findings show that the combined effect of polymorphisms in PER3 could affect gene expression and function, leading to phenotypic differences.

O136

Exogenous melatonin for delayed sleep phase syndrome: meta-analysis

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Objective: To conduct a systematic review of the efficacy and safety of exogenous melatonin in advancing sleep-wake rhythm in delayed sleep phase syndrome.

Data sources: Pub Med and sleep and chronobiological societies abstracts (1990–2005) Study selection: The efficacy review included randomised controlled trials. Quality assessment trials were assessed by using the Jaded Scale, the Downs and Black checklist and the criteria by Schulz et al.

Data extraction and synthesis: One reviewer extracted data and another reviewer verified the data extracted. The invariance method was used to weight the studies and the random effects model was used to analyse the data.

Main results: Five trials including 93 adults and three trials 207 children were included. Melatonin, administered before Dim Light Melatonin Onset, advanced mean endogenous melatonin onset with 1.23 h (95% c.i. 0.92 to 1.54 h.), sleep onset with 0.79 h. (95% c.i. 0.50 to 1.08 h.) and wake up time with 0.31 h. (95% c.i. 0.12 to 0.50 h.). Melatonin decreased sleep latency with 0.38 h (95% c.i. 0.21 to 0.55 h.). Total sleep time did not change.

Conclusions: Melatonin, administered before Dim Light Melatonin Onset, is effective in advancing sleep-wake rhythm and endogenous melatonin rhythm in Delayed Sleep Phase Syndrome.

O137

Circadian phase angle between sleep and melatonin in older individuals

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Accurate assessment of circadian phase has implications for treatment of circadian rhythm sleep disturbances. Because of practical limitations to precise phase measurement in clinical situations, there has been much interest in defining an algorithm by which easy-to-measure variables, such as habitual bedtime or waketime, may be used as proxies for circadian phase. We assessed phase angles among salivary melatonin onset (DLMO) and sleep timing in older persons, some of whom exhibited sleep maintenance insomnia (SMI). Twenty-four subjects >60 years (mean = 67 ± 8 y) who participated in at least 1 laboratory protocol contributed to analyses. Habitual sleep times were assessed using sleep diaries. DLMO was measured in the lab prior to any experimental manipulation. Waketime was significantly correlated with DLMO ($r = 0.72$), but bedtime was not ($r = 0.23$). The correlations were significant only in those subjects without SMI ($n = 13$). In contrast, DLMO was not associated with sleep times in subjects with SMI ($n = 11$). Regression equations were used to predict DLMO from waketime. The equations predicted DLMO within ± 1 h of actual DLMO in 77% of those without SMI, and in less than 50% of those with SMI. There were significant differences in phase angles between those with and without sleep maintenance insomnia. The DLMO-to-bedtime phase angle was − 1.43 ± 1.95 h v. − 3.06 ± 1.76 h ($P < 0.05$), and DLMO-to-waketime phase angle was − 9.82 ± 1.14 h v. 8.79 ± 1.21 h ($P < 0.05$) in those without SMI versus those with SMI, respectively. The results suggest that habitual wake time may be an accurate predictor of internal circadian phase in older persons without sleep maintenance problems. However, in the very individuals for whom chronobiological treatments for sleep disturbance may be useful, sleep timing may not be a reliable or accurate predictor of circadian phase.

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Molecular insights into human behavior

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Human beings exhibit wide variation in their timing of daily behavior. We and others have suggested previously that such differences might arise because of alterations in the period length of the endogenous human circadian oscillator. Using dermal fibroblast cells from skin biopsies of 28 subjects of early and late chronotype (11 ''larks'' and 17 ''owls''), we have studied the circadian period lengths of these two groups, as well as their ability to phase-shift and entrain to environmental and chemical signals. We find not only period length differences between the two groups, but also significant changes in the amplitude and phase-shifting properties of the circadian oscillator among individuals with identical ''normal'' period lengths. We therefore conclude that

human chronotype may be influenced not only by the period length of the circadian oscillator, but also by cellular components that affect its amplitude and phase. In many instances, these alterations may be investigated at the molecular level in primary dermal cells.

O139

Circadian modulation in subjective well-being under high and low sleep pressure conditions: effects of age and gender

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Introduction: Subjective well-being undergoes daily fluctuations. Forced desynchrony protocols with healthy young subjects have shown that subjective mood is influenced by a complex interaction between circadian phase and duration of time awake. To further investigate this interaction, we analysed the time course of subjective well-being under differential sleep pressure conditions in order to examine possible gender- and age effects.

Methods: Sixteen healthy young (8 women; 8 men, 20–35 years) and 16 older volunteers (8 women; 8 men; 55–75 years) carried out a 40-h sleep deprivation (high sleep pressure) and a 40-h nap protocol (low sleep pressure attained with a scheduled sleep-wake cycle of 75 min asleep and 150 min awake) in a balanced cross-over design under constant routine conditions. Subjective well-being was assessed at 20-min intervals during scheduled wakefulness using a composite of 100-mm bipolar visual analogue scales for mood, physical and psychic comfort.

Results : Variations in subjective well-being were significantly determined by the main factors ''age'', ''sleep pressure condition'' and ''time elapsed'' (p at least 0.012, repeated measures ANOVA). In both the high and low sleep pressure protocols, the elderly felt significantly less well than the young ($P = 0.01$). Overall, subjective well-being ratings were significantly lower during the high compared to the low sleep pressure condition ($P = 0.009$). Significant two-way interactions between sleep pressure condition and age ($P = 0.012$), and between sleep pressure and gender ($P = 0.003$), indicated that the elderly responded with a greater impairment in well-being under high sleep pressure than the young and women (but not men) more under high than low sleep pressure. All subjects displayed a significant circadian rhythm of subjective well-being, which was more prominent in women than in men, particularly during the high sleep pressure protocol.

Conclusions: Our results demonstrate significant age and gender-related modulation of circadian and sleep-wake-homoeostatic contributions to subjective well-being. These results point towards a possible age- and/or gender specific tolerance with respect to sleep deprivation and circadian phase. This could have important ramifications on the capacity for night work.

O140

Abstract withdrawn

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Sleep-wake cycle in ballet dancers

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Introduction: Ballet dancers are top athletes and artists with extreme demands on their body and intellectual functions. In this group a normal work schedule on a weekly basis is absent and moreover, half of the week working days last until late evenings.

Methods: We investigated the sleep-wake cycle over a period of three months prior to a premiere of a new performance by using actigraphy in 28 (17w, 11 m) ballet dancers (mean age 27 ± 5 years, BMI 19 ± 2) of the ''Staatsballett Berlin'', a big independent ballet institution of the three institutionalized opera houses in Berlin, Germany. Before starting the actigraphy recording (Actiwatch, Cambridge Neurotechnology Ltd, Cambridge, UK) which was accompanied by filling in activity diaries and sleep logs on a daily basis, a physical examination as well as a sleep medical examination and ambulatory polygraphy (Embletta PDS, Embla Systems, Broomfield, CO, USA) was performed.

Results: Out of the 28 ballet dancers who were included, 24 of them completed the study after three months. Altogether we found a regular sleep-wake cycle but no circaseptan rhythm in this population. In addition a delayed sleep phase was predominant. In the course of three month the sleep efficacy (SE) was reduced significantly (82 to 77 percent, $P<0.01$) without changes in the amount of movements and total sleep time (TST) during the night. These findings were independent of the gender of the ballet dancers. The parameters SE and TST are generally lower than in the general age matched German population. These results were accompanied by diminished mental health scores (SF12 questionnaire) and diminished concentration capabilities (d2 test).

Conclusion: The preparation time of a new performance in the course of three month caused additional stress in the investigated ballet dancers which was apparent in a diminished sleep quality. In order to guarantee a good status of health and the high degree of physical and mental capability a good management of rest and a activity is needed. As a consequence a dedicated room for rest has been installed at the opera for the ballet dancers.

Sleep as a Bodily Function

O142

Prediction of cardiovascular risk by overnight recordings of autonomic signals in patients with suspected sleep disorders

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Introduction: Sleep Disordered Breathing (SDB) is frequently but not uniformly associated with cardiovascular disease. Therefore, identification of patients at risk is of crucial importance. This study applied a new algorithm for overnight pulse rate and pulse wave analysis in order to detect associations with a well established cardiovascular (CV) risk matrix.

Methods: A sleep clinic cohort of 150 patients was investigated by overnight polygraphic recordings. Pulse rate and finger pulse wave form were recorded using a newly developed photoplethysmographic device. The composite autonomic variability index (ASIC) was calculated and correlated with the risk factor matrix determined from a detailed CV history, blood pressure assessment, and standard medical care information. 100 randomly selected patients were used as a training set of the algorithm. A second set of 50 patients constituted the validation population.

Results: In the training set, 84 patients were at low risk and 16 patients at high risk according to the CV risk matrix. Among low risk patients 69 (82.1%) of were correctly classified and 15 (17.9%) were misclassified. In the 16 patients with high CV risk, 12 (75%) were correctly assigned and 4 patients (25%) were not detected as high risk patients by ASIC. In the validation set, 32 (80%) and 8 (20%) low risk patients were correctly and incorrectly assigned, respectively. 7 out of 10 patients with high CV risk were correctly identified. Misclassification was mainly associated with concomitant beta-blockade.

Conclusion: This novel algorithm derived from modified overnight oximetry data may be helpful to detect patients with co-morbid CV- or at increased risk for incident CV- disease.

O143

Sleep-related impairment of cardiac vagal control in leptin-deficient obese mice

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The control of heart period (HP) differs widely among wake-sleep states and carries prognostic information in human patients. Leptin is a key modulator of the hypothalamic pathways that maintain energy homeostasis. We investigated whether the integrity of leptin signalling is required for the physiologic sleep-dependent control of HP. To this aim, we assessed cardiac autonomic control during different wake-sleep states in leptin-deficient obese mice. B6.V-Lep^{ob}/OlaHsd obese mice bearing a nonsense mutation in the leptin gene (ob/ob, $n = 4$) and lean wild-type littermates (WT, $n = 5$) were kept on a 12-h light-dark cycle, temperature of 25 °C, and free access to food and water. Animals were implanted with electrodes for discriminating wake-sleep states and a telemetry pressure transducer (TA11PA-C10, DSI) in the femoral artery. After a 10-day postoperative recovery, continuous recordings were performed for 3 days with the mice undisturbed and freely moving in their own cages. Episodes of wakefulness, non-rapid-eye-movement sleep, and rapid-eye-movement sleep of duration >60 s were identified. For each episode, beat-to-beat values of systolic arterial pressure and HP were computed from the arterial pressure signal. HP variability (HPV) and respiratory sinus arrhythmia (RSA) were quantified by the standard deviation of HP values and by the HP spectral power in the range 2.5–5.0 Hz, respectively. Cardiac baroreflex sensitivity (BRS) was estimated with the sequence technique. Data were analyzed with a 2-way analysis of variance with significance at $P < 0.05$. The wake-sleep state significantly affected HPV, RSA, BRS, and the mean value of HP. A significant main effect of the genetic group was observed for HPV, RSA, and BRS, with lower values occurring in ob/ob mice. The interaction effect between the wake-sleep state and the genetic group was significant on HPV, RSA, and BRS. These results demonstrate that congenital leptin deficiency in obese mice interferes with the physiologic sleep-dependent changes in the control of HP. Recent data indicate that RSA and BRS depend on vagal modulation in mice. Our results thus suggest that leptin signalling is required for the physiologic sleep-dependent changes of cardiac vagal control.

O144

PER3 polymorphism affects cardiac autonomic control in healthy people

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A variable number tandem repeat polymorphism in the coding region of the PERIOD3 gene has been shown to affect several markers of sleep homeostasis as well as the decline in performance when the wake episode is extended into the circadian night. The objective of the current investigation was to characterize variations in autonomic nervous system activity during sleep and wakefulness through analysis of heart rate variability (HRV) in subjects homozygous for the long (PER3-5/5) or short (PER3-4/4) variant of this polymorphism. The ECG and respiratory activity of 24 subjects was recorded continuously during a baseline sleep episode, a 40-h constant routine and a recovery sleep episode. Preliminary analyses of the ECG data revealed that the PER3-5/5 and PER3-4/4 subjects differ in various HRV indices. In NREM sleep during the baseline night, parasympathetic activity, reflected by the pNN50 and RMSSD, was significantly lower in PER3-5/5 subjects than in PER3-4/4 subjects ($P < 0.05$). This difference was confirmed by power spectral analysis of RR intervals which showed differences in the time course of HF between the two genotypes. A decrease in normalized HF/ (LF+HF) was observed during NREM in the PER3-5/5 subjects ($P < 0.05$), suggesting a loss of parasympathetic control on autonomic balance. Analyses of waking ECG during the constant routine confirmed these different levels of autonomic drive to the heart. The data show that this polymorphism in the circadian clock gene PER3 modulates the parasympathetic control on the autonomic balance during sleep and wake in humans.

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O145

Heart rate variability analyses of women with vasospastic syndrome and difficulties initiating sleep exhibit lower vagal nerve activity

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Women with primary vasospastic syndrome (VS), a functional vascular dysregulation, often suffer from difficulties initiating sleep (DIS). DIS belongs to DSM-IV criteria for primary insomnia, which has been characterised as a state of hyperarousal (higher sympathetic nervous activity). We aimed to compare women having both VS and DIS (WVD) with controls (CON) to test the hypothesis whether WVD exhibit a sympathetic predominance as measured by heart rate variability analysis. Nine CON and nine

WVD (luteal phase; 20–33 yr) completed a 40 h constant routine with 20 paced (0.2 Hz) or 20 unpaced (spontaneous) 3 min breathing episodes alternating at hourly intervals. Purified interbeat interval data (IBI) were analysed by histogram analysis of the Poincaré plot. We calculated the interdecile (90–10%) range of [(IBIt-IBIt-1)/sqrt2] ('Vagus') as an indicator of vagal nerve activity, the sympatho/vagal balance by the quotient of the interdecile range of IBIt and 'Vagus', and log-powerspectrum by FFT. Compared with CON, WVD revealed a narrower range in 'Vagus' ($P<0.05$, mean over all time points) in paced breathing data (similar trend in spontaneous breathing data, $P<0.1$). This finding could be confirmed by spectral analysis. In the spontaneous breathing data lower log power values occurred in low (LF, 0.04–0.15 Hz) and high frequency bands (HF, 0.15–0.4 Hz) in WVD ($P<0.05$); the paced breathing data revealed lower log power values selectively in HF ($P<0.05$), but not in LF, leading to a higher LF/HF-ratio ($P<0.05$). No significant interaction term between WVD/CON and time of day was found. To conclude, these findings indicate a general lower vagal activity and therefore a sympathetic predominance in WVD compared with CON. In both paced breathing- and spontaneous breathing data, ANOVA followed by trend analysis revealed a linear decrease of vagal activity and a linear increase of sympatho/vagal balance with elapsed time awake ($P<0.05$). This finding suggests that sleep seems to be crucial for regeneration of vagal nerve activity and hence for reduction of the sympatho/vagal balance.

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O146

Effects of ghrelin alone or combined with GHRH or CRH on sleep EEG and nocturnal growth hormone and cortisol secretion in young male subjects

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The neuropeptide ghrelin stimulates the somatotropic and the hypothalamic-pituitary-adrenal (HPA) systems, being crucially involved in sleep regulation. In young male subjects the key hormones of these systems exert opposite effects on sleep EEG and nocturnal hormone secretion. After growth hormone (GH)-releasing hormone (GHRH) slow-wave sleep (SWS) and GH increase and cortisol decreases, whilst after corticotropin-releasing hormone (CRH) wakefulness and cortisol increase and REM sleep and GH decrease. Ghrelin stimulates SWS, GH and cortisol in young men. Ghrelin's interactions with GHRH and CRH are not entirely clear. We aimed to elucidate these interactions in sleep regulation. Nocturnal GH and cortisol secretion (2200–0700) and sleep EEG (2300–0700)were investigated simultaneously in 10 healthy males (25.7 ± 3.0 years) four times, receiving placebo (PL)+PL (A), 50 μg ghrelin+PL (B), 50 μg ghrelin+50 μg GHRH (C), or 50 μg ghrelin+50 μg CRH (D) at 2200, 2300, 0000, and 0100 h, in a single-blind, randomized, cross-over study. Sessions were separated by one week. Non-REM sleep was increased significantly in all verum conditions (mean ± SEM: B: 355.3 ± 7.4; C: 365.4 ± 8.1; D: 371.4 ± 3.9 min) compared to PL (336.3 ± 6.8 min). SWS remained unchanged. REM sleep was decreased significantly (B: 84.3 ± 4.2; C: 74.2 ± 7.0; D: 80.4 ± 2.7 min) compared to PL (100.9 ± 8.3). CRH+ghrelin decreased the time spent awake (22.6 ± 3.5) versus PL (33.3 ± 9.1) more distinct than ghrelin alone (30.5 ± 5.4;D versus B $P<0.05$)and enhanced the sleep efficiency; furthermore, REM latency was decreased significantly (D: 66.0 ± 10.7)compared to the other treatment conditions (PL: 109.9 ± 21.4). CRH enhanced the ghrelin-induced cortisol secretion but had no relevant effect on GH secretion. In turn, GHRH enhanced the ghrelin-induced GH secretion but had no effect on cortisol secretion. In conclusion, ghrelin exhibited distinct sleep-EEG effects (particularly promotion of NonREM sleep) which were enhanced by trend by GHRH and significantly by CRH. Surprisingly CRH had sleep-improving (increase of NonREM sleep, decrease of wakefulness) and REM permissive (shortening of REM latency) effects when co-administered with ghrelin. These observations are in contrast to the effect of CRH alone in previous studies.

O147

Is hypocretin involved in stress-induced sleep alterations in mice?

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Hypocretin (hcrt), a hypothalamic neuropeptide, activates brain structures involved in sleep regulation such as Raphe Nuclei (RN), and conversely, RN serotonergic neurons inhibit the hypocretinergic system. Both hcrt and serotonin play an inhibitory role on rapid-eye-movement sleep (REMS). Interestingly, mutant mice deficient in serotonin transporter (5-HTT −/−) exhibit increased REMS compared to wild-type (WT) mice. The aim of our study was to specify interactions between serotonergic and hypocretinergic systems at baseline and their potential involvement in stress-induced sleep modifications. We used anatomo-functional approaches (double immunolabeling: cFos/Tph2 or cFos/preprohcrt) and radioactive assays of hcrt1 to assess the activity of serotonergic and hypocretinergic systems under basal conditions and after immobilization stress (90 min), in 5-HTT −/− mutants compared to WT mice (CD1 background). At baseline, we found no difference between the two strains in the number of activated neurons either serotonergic in RN, or hcrt in the Hypothalamus (HL). In contrast, hcrt1 levels in the RN were larger in mutants than in WT mice. After stress, the number of activated neurons (serotonergic in RN and hcrt in HL) were enhanced in both strains, while hcrt1 levels in RN were increased only in 5-HTT −/− mice. In parallel the REMS rebound normally present after stress in WT mice was not observed in 5-HTT −/− mice. We examined whether such lack of sleep homeostasis in mutant mice was related to their increased hcrt neurotransmission (hcrt1 level in RN after stress). Indeed, pharmacological blockade of hypocretinergic receptor 1 by SB-334867 (30 mg kg^{-1}, i.p.) immediately prior to the stress session restored the stress-induced REMS rebound in 5-HTT −/− mice. The same treatment under normal resting conditions did not affect vigilance states in either strain of mice. Altogether, these data show that integrity of the serotonergic system is necessary for homeostatic changes in REM sleep after a stress challenge, and that genetically driven loss of the 5-HTT function produces alterations of hypocretinergic neurotransmission, that might in turn underlie the disrupted sleep response to stress.

O148

Increased leptin and insulin-to-glucose ratio after cumulative partial sleep deprivation and subsequent recovery sleep in healthy young men

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Short sleep, due to increasing work demands, is common in modern 24 h societies. It has been associated with an increased risk to develop obesity by reducing serum levels of the satiety hormone leptin and reducing insulin sensitivity. We studied the effects of cumulative partial sleep deprivation simulating a working week with two nights of subsequent recovery sleep on several metabolic parameters. After 2 nights of 8 h in bed (baseline), 15 healthy young

men spent 4 h in bed for 5 days (sleep deprivation) and thereafter 2 nights of 8 h (recovery). 8 control participants spent 8 h in bed throughout the experiment. Serum leptin, insulin and glucose were measured at 8 AM after the second baseline night, the fifth sleep deprivation night and the second recovery night. Participants also rated their satiety feeling at these time points on a 1 to 5 scale. Results from each participant were normalised to his own baseline value to overcome individual differences. Leptin levels increased significantly after sleep deprivation and recovery sleep (to 163% and 123% of baseline levels, respectively). Satiety feelings showed a non-significant decrease after sleep deprivation and recovery sleep (83% and 92% of baseline levels). Insulin-to-glucose ratio increased significantly after sleep deprivation and remained elevated after recovery (157% and 118% of baseline levels respectively). This was due to a significant increase of insulin levels after sleep deprivation (157% of baseline) and a significant decrease of glucose levels after recovery (90% of baseline levels). In controls, all variables remained at baseline level throughout the experiment. Increased leptin and unaffected satiety feelings after sleep deprivation contradict previous work and suggest other roles for leptin than a satiety inducer. Moreover, it suggests that the mechanism by which short sleep predisposes to obesity is via reduced energy expenditure rather than increased caloric intake. Increased insulin and insulin-to-glucose ratio indicates that one week of modest sleep restriction already affects glucose metabolism and might add to the risk to develop obesity. Moreover, 2 nights of recovery sleep were not sufficient to fully restore any of the observed effects of 5 nights of partial sleep deprivation.

O149

Hypertension increases the rate of occurrence of arterial pressure surges during REM sleep in spontaneously hypertensive rats

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Surges of arterial pressure physiologically occur during rapid-eye-movement sleep (REMS) in human subjects and animal models. In hypertensive subjects, these pressure surges may represent a risk factor for acute cardiovascular events. We determined whether hypertension alters the rate of occurrence and the characteristics of the pressure surges during REM sleep in the Spontaneously Hypertensive Rat (SHR) model of genetic hypertension. We compared 7 SHR with 7 Wistar-Kyoto (WKY) normotensive controls and 7 SHR, in which hypertension was prevented by long-term enalapril treatment (ena-SHR). Rats were implanted with electrodes for electroencephalographic and electromyographic recordings, an arterial catheter for measuring beat-to-beat values of mean arterial pressure (MAP) and heart period (HP), and a nasal thermistor for measuring the ventilatory period (VP). One week after surgery, unrestrained rats were studied during spontaneous REMS episodes to identify MAP surges greater than 15 mmHg. The time series of MAP, HP, and VP during each MAP surge were averaged within rat using the peak of the MAP upswing as a zero time reference. Differences among and between groups were analyzed by one-way ANOVA and *t*-test (significance at $P<0.05$). During REMS, the rate of occurrence of the MAP surges was significantly higher in SHR than either in WKY or ena-SHR, whereas their magnitude was similar in the three groups. The MAP surges were accompanied by a decrease of HP, which was significantly less pronounced in SHR than either in WKY or ena-SHR. Although an increase of VP preceded the peak of the MAP surges, its magnitude was modest (<25% of the mean VP) and did not differ significantly among groups. These data demonstrate that central autonomic commands to the heart and blood vessels may cause surges of hypertension and tachycardia during REMS independently of sleep apnoea. In SHR, these central commands during REMS appear increased in frequency, but not in magnitude, with respect to either WKY or ena-SHR. Ena-SHR lack the hypertensive phenotype but are genetically identical to SHR. Data thus suggest that in SHR, the increased rate of occurrence of the MAP surges during REMS is an effect of arterial hypertension rather than an inherited irreversible trait.

O150

Evolution of blood parameters associated to cardiovascular risks during one working week: effects of partial chronic sleep restriction and recovery

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General trends of work hour organisation and increased social demands such as the 24 h network telecommunication contribute to reduce nocturnal sleep and to increase daytime sleepiness. Currently, about a third of adults report sleeping less than 6 h $night^{-1}$ and the overall prevalence of insufficient sleep in adults has been estimated at 20%. Numerous epidemiological data suggests that poor sleep is a predictor of increase in cardiovascular morbidity and events. Atherosclerosis, a major cause of cardiovascular disease, is a chronic inflammatory disease in which oxidative modification of low-density-lipoprotein (LDL) is thought to contribute to the recruitment and accumulation of foam cells hallmark of the disease. Catalytically active myeloperoxidase (MPO) is present within human atherosclerotic lesions and generates reactive oxidant species that oxidize low-density lipoprotein (LDL) into an atherogenic form myeloperoxidase modified LDL (Mox-LDL). Besides, elevations of the level of inflammatory markers C-reactive protein (CRP) have also been associated to risk of cardiovascular events. Using an experimental set-up that mimics a normal working week, we investigated inflammatory and oxidative stress parameters. Nine healthy young male volunteers were studied. Protocol consisted of three baseline nights, followed by five nights of sleep restricted to 5 h and three recovery nights. Blood samples were collected each morning at 7 am in fasting conditions except day 2 and 4 of restriction. Friedman Repeated Measures Analyses of Variance were performed. We report here that (i) CRP levels are unchanged throughout the study (ii) Mox-LDL peaks during the restriction and recovery periods ($P = 0.008$ versus basal value) (iii) MPO rises progressively during the restriction period to reach a maximum on the first recovery night ($P = 0.02$ versus basal value). In conclusion, our data suggest that chronic mild sleep restriction triggers oxidative stress as shown by the increase in Mox-LDL and MPO level considered as predictor of cardiovascular events.

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Synchronization between respiration and the heartbeat in sleep stages

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Introduction: A synchronization between respiration and the heart rhythm at rest is known as respiratory sinus arrhythmia. Heart rate increases during inspiration and lowers during expiration. Independent of this modulation of heart rate, intrathoracic pressure

changes during respiration cause periodic movements of the chest and this causes R peak amplitude changes in the ECG. This can be used to derive respiration from the ECG itself.

Methods: Cardiorespiratory polysomnography with a chest wall ECG and three channels for respiration (oronasal airflow, chest and abdominal movements) was obtained in 112 healthy subjects (SIESTA study). We derived an additional respiratory signal from the ECG using heart rate and the modulation of R wave amplitudes. The reliability of this trace was checked using cardiorespiratory polysomnography [1]. Then we calculate the synchronisation of the respiratory waveform and the heart beat by calculating the instantaneous phase shift using the Hilbert transformation.

Results: The reconstruction of breathing from the ECG was reliable in most subjects. Based on this we reconstructed the breathing patterns from the ECG without additional signals. In healthy subjects we found 3.8% of the time in non-REM with coupled respiration and heart beat and only 0.6% of the time spent in REM sleep. During wakefulness within the sleep recording we found 1.6% of the time with coupled respiration and heart beat. This amount of time decreases with increasing age and decreases with body mass index. There is no gender difference.

Conclusion: It is possible to derive respiration from a combination of R-R interval analysis and R peak amplitude variability. The varying synchronization between the heart beat and respiration changes with sleep stage and can give indications for the severity of sleep related breathing disorders because it relates to the cardiorespiratory regulation responsible for pathophysiology.

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Dynamic Modulation of the Upper Airway

S71

A novel approach for determining upper airway properties from a baseline sleep study

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Although physiologic methods for measuring critical pressure (Pcrit) are well established, their laborious nature limits their broader application to translational research. Of necessity, subject sample sizes have been severely constrained by the requirement that subjects sleep while breathing at subatmospheric nasal pressures. Exposure to specific paradigms for lowering the nasal pressure often disrupts sleep, thereby extending the exposure trial or precluding these measurements altogether. We have developed, a novel, light weighted, high fidelity airflow sensor. Preliminary data demonstrate that this sensor can discriminate nasal from oral breathing thereby allowing quantifying peak inspiratory airflow on a breath by breath basis in standard observational sleep studies. Statistical techniques were employed to utilize variations in peak inspiratory airflow for estimating structural and neuromuscular upper airway properties (passive and active Pcrit, respectively). Additional preliminary data show that estimations of Pcrit from standard observational sleep studies are comparable to Pcrit estimates obtained from interventional physiologic methods. Our approach will allow us to extend detailed physiology approaches to the study of upper airway physiology during sleep to entire populations of community and patient-based cohorts.

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Dynamic imaging of upper airway: awake and asleep

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The pharyngeal airway is a collapsible tube which during sleep behaves as a starling resistor. Patency of a collapsible tube is determined by the pressure gradient across the wall and its compliance; both of which are influenced by respiration. The dynamic modulation of upper airway calibre during respiration is fundamental to the pathophysiology of obstructive sleep apnoea (OSA) thus quantifying the changes in pharyngeal size and shape during eupneic, flow-limited and obstructive breathing will help elucidate the pathogenic mechanisms of upper airway collapse. Current understanding of the dynamic changes in pharyngeal patency is that cross-sectional area increases to maximum during early expiration and decreases to its minimum at end-expiration; the difference between maximum and minimum cross-sectional area being greater in those with OSA than without. Similarly, both anteroposterior and lateral airway dimensions are thought to increase during early expiration and decrease at end-expiration, with a greater change observed in the lateral dimension. However, inter- and intra-subject variability is often observed in this dynamic pattern and imaging modalities have largely restricted studies to awake or sedated subjects. Imaging data and simultaneous physiological recordings from these studies will be discussed. In addition, recent data from a new imaging modality anatomical optical coherence tomography (aOCT) recorded in parallel with measures of intramuscular genioglossus activity in subjects with and without OSA during wakefulness and sleep will be presented.

S73

Alterations in upper airway dilator muscle recruitment throughout the respiratory cycle and at sleep onset

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The activity of upper airway dilator muscles, such as the genioglossus (GG) and tensor palatini (TP), have been implicated in the pathogenesis of sleep related upper airway collapse because these muscles dilate the airway and have altered activity during sleep. The activity of the upper airway dilator muscles have primarily been investigated using multi-unit EMG recording techniques. Multi-unit recordings have proven informative for assessing changes in muscle activity throughout the respiratory cycle, in different sleep stages and during alterations in respiratory drive. However, a limitation of these recordings is that they tell us little about the details of motor control of the upper airway muscles. Single motor unit (SMU) recordings provide detailed information regarding the discharge properties of single motoneurones, thus it is possible to determine the firing rate, and to infer the level of neural drive the motoneurones are receiving. SMU recordings have been recently applied to the upper airway dilator muscles. These studies have determined that the multi-unit activity of the human GG is a complex interaction of different types of motor units, each of which fire through different portions of the respiratory cycle. Specifically, some units only fire during inspiration or expiration, whereas other units fire continuously throughout the respiratory cycle and may or may not modulate their firing rate with respiratory cycle. These different units likely reflect differing inputs to the hypoglossal motor nucleus and thus allow hypotheses with regard to human hypoglossal control to be generated. We have recently shown that the different types of motor units in the human genioglossus behave differently at sleep onset, with the reduction in multi-unit activity being largely driven by cessation of SMUs that fire during inspiration only. In addition, we have begun investigating the SMUs changes accompanying increases in respiratory drive with increased CO2 and resistive loading. These data will be reviewed in this presentation.

S74

Upper airway biomechanical coupling, tissue hysteresis and surface properties

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Examining the modulation of upper airway flow dynamics within and between single breaths has important physiologic implications for investigating the control of upper airway function during sleep. Within breath changes in upper airway properties can provide an indication of the dynamic modulation of the mechanical and neuromuscular components of upper airway collapsibility. We have shown that the development of pharyngeal occlusion within a breath influences the dynamic modulation of upper airway flow during transtracheal insufflation in sleeping apneic patients. Furthermore, we have shown that the upper airway is more stable in the early compared to late phase of inspiration, and that once the upper airway has occluded during sleep, it is much harder to reopen. It appears that late inspiration and early expiration represent the mechanical characteristics of the upper airway, which predispose to collapse, whereas there is neuromuscular component added during late expiration and early inspiration, providing stability. The ability to identify and assess dynamic upper airway properties will provide greater flexibility in delineating the effects of acute interventions such as surfactant instillation, changes in lung volume, mandibular position, and electrical or pharmacologic stimulation on upper airway neuromuscular activity.

The Cognitive Element of Cognitive/Behaviour Therapy for Insomnia

S75

The mediating role of dysfunctional beliefs and attitudes about sleep in the management of insomnia

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This presentation will discuss the mediating role of dysfunctional beliefs and attitudes about sleep in chronic insomnia and highlight the importance of targeting such beliefs in the management of insomnia. A conceptual model of insomnia will be described in which sleep-related beliefs are presumed to heighten arousal and contribute to the development and maintenance of insomnia. We will then describe a self-report measure, the Dysfunctional Beliefs and Attitudes about Sleep (DBAS), which has been used widely in insomnia research in the last fifteen years; its clinical usefulness for identifying dysfunctional sleep beliefs and for tracking changes with treatment will be highlighted. Sleep-related cognitions related to four domains will be discussed: sleep expectations (e.g., the absolute need of 8 h of sleep every night), causal attributions of insomnia (e.g., insomnia is primarily the result of a biochemical imbalance), perceived consequences of insomnia (e.g., insomnia is to be blamed for all daytime impairments), and sleep-promoting practices (e.g., staying in bed longer will necessarily produce more sleep). We will review research findings from clinical studies showing that (1) individuals with insomnia tend to endorse erroneous sleep-related beliefs more strongly than good sleepers; (2) cognitive-behaviour therapy alleviates such beliefs; and (3) more adaptive sleep-related beliefs at posttreatment are associated with better maintenance of sleep improvements over time.

S76

Information processing bias in insomnia; research evidence and implications for therapy

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Background: Several theoretical perspectives implicate cognitive processes in the aetiology and maintenance of insomnia. The Psychobiological Inhibition Model suggests that insomnia represents a violation of the 'automaticity' of normal good sleep, mediated by the development of a sleep-inhibiting Attention-Intention-Effort pathway (Espie et al. 2002; 2006). This paper summarises results from numerous experimental studies of such information-processing bias, including previously unpublished data.

Methods: A series of studies employing Stroop, Dot Probe, Inducing Change Blindness and Modified Posner Paradigms. These are computerized tasks which index selective attention bias. Data are reported on insomnia relative to good sleepers and Delayed Sleep Phase Syndrome controls, and also treatment outcome data following a randomized trial of CBT.

Results: Findings show that people with insomnia identify sleep-related words and picture stimuli more quickly, that processing such information slows down responding to task instructions, that they are slower to disengage from such stimuli, and that CBT is associated with reduced selective attention bias.

Conclusion: Information processing bias may help to account for the characteristic sleep preoccupation of the psychophysiological insomnia phenotype. Potentially behavioural as well as cognitive components of CBT could reduce this aetiological/maintaining factor.

S77

The CBTI treatment of worry associated with insomnia

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Worry and mind-racing are reported as among the primary problems by those who have insomnia. Although there have been a number of suggested treatments, there has been little in the way of a thorough analysis of why worry and mind-racing are particularly problematic in insomnia. In this presentation, the literature about the effect of sleep loss and circadian rhythms on problem solving and judgment will be reviewed. Treatments that have been recommended to reduce worrying and mind-racing, e.g., instructions to set a worry-time before going to sleep, to use "thought-stopping", "articulatory suppression", and stress-reduction procedures such as mindfulness meditation will be evaluated.

S78

The cognitive discrepancy between "healthy" sleep and that perceived by the insomnia sufferer

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Most people suffering insomnia experience a discrepancy between their belief about normal sleep and the perception of their own sleep. It appears that most people believe that only 7–8 h of "solid" sleep is normal and healthy. On the other hand, chronic insomniacs typically report fragmented sleep totaling only 3–5 h per night. This cognitive discrepancy would produce agitation or worry to the extent that it is seen to be dangerous or a threat to their health and well-being. In turn, this worry will likely contribute to chronic hyper-arousal and to the maintenance of the insomnia. Public campaigns stressing the dangers (increased risk of accidents, impaired memory, cardio-vascular disease, obesity, diabetes, mortality) of too little sleep and, by implication, insomnia would increase this perceived threat and exacerbate the insomnia. It would be unfortunate if these beneficially intended public campaigns (and arguably beneficial effect for those with excessive daytime sleepiness) had an opposite, detrimental effect on the most prevalent sleep disorder of insomnia. In any case the dissonance between "healthy" and perceived sleep can be reduced in two ways and thus potentially be therapeutic in the treatment of chronic insomnia. Beliefs about the nature of normal sleep can be changed with education about 90 min sleep cycles, periodic light sleep and normal, benign awakenings especially prominent in older age groups. The second way to reduce the belief/perception discrepancy is to present objective feedback of sleep that is usually longer and better quality than that perceived. There is now some evidence that this feedback of actual sleep is therapeutic for insomnia. Although lab-based PSG is generally not indicated for cases of insomnia, technological developments in portable, home based PSG and automatic analysis could make this an affordable new avenue of treatment for chronic insomnia.

Latest News on the Functioning of Hypocretin/Orexin Neurons and their Role in Vigilance States Regulation, from Physiology to Pathology

S79

Metabolic sensing by hypocretin neurons

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We are studying the electrical activity of single hypocretin-containing neurons by performing whole-cell patch-clamp recordings from actutely isolated mouse brain slices where hypocretin neurons are directly and unambiguously identified by transgenic expression of Green Fluorescent Protein. Our patch-clamp recordings indicate that the firing rate of orexin neurons is profoundly suppressed by small physiological elevations in ambient glucose levels, even in the range 1 to 2.5 mM. This mechanims is of great interest because it potentially provides a direct link between body energy levels and different states of consciousness. Glucose-induced silencing of hypocretin neurons involves activation of post-synaptic leak-like K channels. These channels appear to be activated by glucose through a novel pathway not involving glucose metabolism. The sugar-selectivity of this pathway appears to be different from any known glucose-binding proteins. Over 90% of hypocretin neurons respond to glucose with hyperpolarization and electrical inhibition. However, in some hypocretin neurons these responses are transient, whereby the membrane potential and firing rate of the neuron returns to pre-stimulation baseline despite continuing presence of elevated extracellular glucose. This may provide a potential explanation for how the hypocretin system can track fluctuation in body energy state while preventing narcoleptic instability of consciousness.

S80

Molecular characteristics of the hypocretin/orexin neurons, a trancriptomic study for a better understanding of their mode of regulation

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Most cases of the human narcolepsy with cataplexy are due to hypocretin deficiency although the cause of the hypocretin cell death remains unknown. Narcolepsy with cataplexy is one of the diseases the most tightly associated with a specific HLA allele, and most diseases with a tight HLA association are autoimmune in nature (for review Chabas et al. 2003). The main predisposing allele is the DQB1*0602, found in 85–95% of patients with narcolepsy-cataplexy. Furthermore, being homozygous for the HLA DQB1*0602 genotype doubles or quadruples the risk for narcolepsy. In heterozygote subjects, the relative risk for narcolepsy increases when DQB1*0602 is associated with DQB1*0301 and decreases when associated with DQB1*0501 and DQB1*0601 alleles. Epidemiological data with a young and bimodal age at onset and frequent triggering factors support also the autoimmune hypothesis. Acting on a specific genetic background, an autoimmune process targeting hypocretin neurons, in response to yet unknown environmental factors, is nowadays the most probable hypothesis for narcolepsy-cataplexy. Our research project aimed at identifying the candidate protein (s) targeted by the auto-immune attack using a post-genomic approach the serial analysis of gene expression (SAGE) combined to the very recent high-throughput sequencing technology Solexa (illumina Inc), in order to drastically increase the depth of sequencing and detect the entire transcriptome. As hypocretin neurons are degenerated and melanin-concentrating hormone (MCH) neurons located within the same region were intact (Peyron et al. 2000), the candidate protein targeted has to be expressed by hypocretin and not by MCH neurons. Thus, we studied the transcriptome of hypocretin and MCH neurons in mice and compared them to each other. Only molecules expressed specifically by hypocretin neurons are considered as candidates. The identification of trancriptomes uncovered the entire panel of protein expressed by hypocretin neurons including the different type of receptors. The object of this talk will be to present these results.

S81

Optogenetic probing of hypocretin neuronal network

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Hypocretin (Hcrt, also known as Orexin or Ox)-producing neurons in the lateral hypothalamus (LH) are important for arousal stability, since loss of Hcrt function has been linked to narcolepsy. However, it is unknown if electrical activity arising from Hcrt neurons is sufficient to drive awakening from sleep states, or is simply correlated. We directly probed the impact of Hcrt neuron activity on vigilance state transitions with in vivo optogenetic. We found that direct, selective photostimulation of Hcrt neurons increased the probability of transition to wakefulness from either Slow Wave Sleep (SWS) or Rapid-Eye Movement (REM) sleep depending on the frequency of stimulation.This study establishes a causal relationship between frequency-dependent activity of a genetically defined neural cell type, and a specific mammalian behavior central to clinical conditions and neurobehavioral physiology.

S82

Assessment of hypocretin functioning in various neurological disorders

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Animal models as well as human studies have clearly shown that a complete loss of hypocretin signalling will lead to narcolepsy with cataplexy. Some of the sleep symptoms of several neurodegenerative disorders resemble the symptoms of narcolepsy. Note that cataplexy is always absent in these disorders. However, there are interesting case reports describing cataplexy in the Prader-Willi Syndrome. The presence of cataplexy is very significant as in narcolepsy without cataplexy, the association with undetectable hypocretin levels is much lower than in narcolepsy with cataplexy. Considering the recent findings of a partial loss of hypocretin neurons, but of normal lumbar CSF hypocretin levels in patients with neurodegenerative and neurotraumatic disorders, the question arises whether partial hypocretin neuronal loss results in true hypocretin dysfunction and narcolepsy-like sleep-wake disturbances. Lesion studies in rodents show that a loss of 60–70% of hypocretin functioning causes REM-sleep disturbances in rodents, but if this is the case in humans remains to be established. Animal studies suggest that only a large decrease in hypocretin neurons is sufficient to impair CSF hypocretin levels. It appears probable that CSF hypocretin levels

do not necessarily reflect the integrity of hypocretin neurons. On the other hand, we found a significant correlation between hypocretin cell number and ventricular CSF content in a group of controls and PD patients. However, to reliably assess the hypocretin system it is advisable to directly study hypocretin brain concentrations and the actual hypocretin neurons. In this talk, recent post-mortem data about hypocretin functioning in various neurological disorders will be discussed (i.e. Parkinson's Disease, Huntington's Disease and the Prader-Willi Syndrome). Furthermore, data will be presented about the role of the hypocretin system in sleep disturbances in normal ageing and in advanced ageing, i.e. Alzheimer's Disease. The final part of the presentation will cover the intriguing possibility that the hypocretin system is disturbed in HLA DQB1*0602 positive healthy subjects.

Normal and Abnormal Motor Control in REM Sleep: Basic and Clinical Perspectives

S83

REM sleep behavior disorder

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REM sleep behavior disorder (RBD) is a parasomnia affecting mostly elderly men and characterized by recurrent episodes of abnormally vigorous body, head or limb movements during REM sleep and stereotyped dreams of self-defense in response to an aggression. Clonazepam is effective in most patients. Although much has been learned, there are many questions to be answered. 1) Why are RBD behaviors in humans always bilateral? There are no descriptions of patients with abnormal RBD movements affecting only one side of the body. In cases of unilateral lesions producing RBD in humans the behaviors are bilateral despite that there are centers regulating muscle tone in REM sleep for each side of the body. In contrast, other movement disorders (tremor, dystonia, rigidity) may be unilateral. Are RBD behaviors a ''package'' of motor patterns that can only be liberated as a whole, no matter where the lesion is? 2) Are RBD behaviors in humans generated in the cortex, the brainstem or the amygdala? Some simple RBD limb movements could be generated in the brainstem but the cortex appears necessary to generate talking or singing. Is there any other area in the brain that can generate complex vocalizations? 3) The abnormal motor behaviors during REM sleep are interpreted as if the patients were ''enacting their dreams''. By analogy, do we accept that a rat with a brainstem lesion and RBD behaviors is enacting a dream? An alternative interpretation is that the the abnormal movements are generated in the first place and the patient dreams about their movements. If so, what generates the abnormal movements? 4) Why RBD affects mainly men and why does it respond so exquisitively to clonacepam and not other benzodiacepines? Is there any basis for these findings in animal models of RBD? These and other questions need to be explored to improve the knowledge about this parasomnia.

S84

Cataplexy and RBD in narcolepsy

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Classically, narcolepsy has been regarded as a disorder of disrupted sleep-wake regulation, in which REM-sleep abnormalities play a prominent role. The most objective indicator for this is the occurrence of multiple sleep-onset REM periods during the Multiple Sleep Latency Test. Furthermore, several key symptoms have been regarded as signs of REM-sleep dysregulation, including hypnagogic hallucinations, sleep paralysis and especially cataplexy. Cataplexy is often portrayed as a dissociated occurrence of REM-sleep atonia. This hypothesis is widely adopted, although it has seldom been put directly to the test. Interestingly, there are several reports which suggest an increase of REM sleep behaviour disorder in narcolepsy. Prevalence estimates range from 12 up to 35%, although for an important part this may be related to the use of antidepressant medication for cataplexy, which are known for their ability to induce RBD. Nevertheless, the challenge will be to integrate the various symptoms of narcolepsy into a pathophysiological model. Intuitively, cataplexy and RBD are the exact opposite of each other. Theories purely based on the concept of 'dissociation' are not (yet) substantiated by neurobiological mechanisms. Furthermore, RBD in Parkinson's disease is never associated with cataplexy, suggesting different underlying mechanisms. The recent knowledge on the crucial role of hypocretin defects in narcolepsy may lead the way to a further understanding. However, while the mechanistic concept of the hypocretin-stabilized 'sleep switch' elegantly explains excessive daytime sleepiness in narcolepsy, the model for REM sleep dysregulation and cataplexy is not as convincing. Altogether, it is important to keep an open mind towards alternative explanations for cataplexy. Relating cataplexy to the animal behaviour called 'tonic immobility' may yield new approaches in this respect.

S85

REM sleep generating mechanisms

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In the middle of the last century, Michel Jouvet discovered paradoxical sleep (PS), a sleep phase paradoxically characterized by cortical activation and rapid eye movements and a muscle atonia. Soon after, he showed that it was still present in ''pontine cats'' in which all structures rostral to the brainstem have been removed. Later on, it was demonstrated in cats that the pontine peri-LCα (corresponding to the sublaterodorsal nucleus, SLD, in rats) is responsible for PS onset. It was then proposed that the onset and maintenance of PS is due to a reciprocal inhibitory interaction between neurons presumably cholinergic specifically active during PS localized in this region and monoaminergic neurons. In the last decade, we have tested this hypothesis with our model of head-restrained rats and functional neuroanatomical studies. Our results indicate that the SLD contains putative glutamatergic neurons responsible for the onset and maintenance of PS. These neurons induce muscle atonia and sensory inhibition via direct excitatory projections to the glycinergic/GABAergic neurons localized in the medullary ventral reticular nuclei and EEG activation via direct intralaminar thalamic projections. During W and SWS, the SLD neurons are tonically inhibited by GABAergic PS-off neurons localized in the ventrolateral periaqueductal gray (vlPAG) and the dorsal part of the deep mesencephalic reticular nucleus immediately ventral to it (dDpMe). At the onset and during PS, these PS-off neurons are tonically inhibited by co-localized GABAergic PS-on neurons and additional PS-on GABAergic neurons located in the dorsal and lateral paragigantocellular reticular nuclei. These GABAergic PS-on neurons are also responsible for the inhibition of locus coeruleus noradrenergic and dorsal raphe serotonergic neurons during PS. In normal condition, the onset of PS is not possible directly from W because the wake-active hypothalamic hypocretinergic neurons and brainstem monoaminergic neurons tonically excite the vlPAG/dDpMe PS-off GABAergic neurons. The decrease or cessation of activity of these wake-active neurons during SWS or narcolepsy weaken the activity of vlPAG/dDpMe PS-off GABAergic neurons inducing a desinhibition of the co-localized GABAergic PS-on neurons and by this way PS.

S86

Brainstem circuitry of REM sleep, RBD, cataplexy, and Parkinsonism

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REM sleep, a paradoxical state of cortical/hippocampal arousal (dreaming) and sleeping body (muscle atonia). We have previously proposed switch model for REM sleep control. The core of the switch is consisted of GABAergic and glutamatergic neurons in the pontine tegmentum. Here, we conditionally knocked-out GABA

and glutamate transmissions by Plox-Cre recombinase technique to test the roles of GABA and glutamate in REM sleep. In consistent with our model, removal of GABA transmission in REM-off and REM-on neurons produced significant increase and decrease in REM sleep respectively. Removal of glutamate transmission in the REM-on region produced REM without atonia (REM sleep behavior disorder, RBD). Parkinsonism (akinesia, rigidity and tremor) shared by many neural degenerative diseases is thought to be caused by substantia nigra (SN) dopamine neurons; however lesions in the neural degenerative diseases and late stage of Parkinson's disease likely reaches the brainstem motor circuit. For motor control, the SN is thought via the descending pontine relay that may includes the mesencephalic locomotor region (MLR) and midbrain extrapyramidal area (MEA), both regions contain high level of orexin 2 receptor. Based on our data (tracing, neurotoxin lesions and genetic deletion), we hypothesize two major pathways: (1) SN GABAergic neurons → MEA (glutamate) → dorsal MLR (glutamate) → spinal locomotion circuit; (2) SN dopamine neurons via D2 receptors → ventral MLR (glutamate) and ventromedial medular (glutamate) → spinal postural circuit. Loss of SN dopamine neurons would result in a dis-inhibition of pathway (2), producing rigidity. Loss of dopamine also activates pathway (1), producing akinesia. Finally, loss of orexin signaling to the MLR reduces the vMLR activity, which in conjunction of emotion triggering activation of pathway (2) would result in cataplexy. This model predicts that loss of SN dopamine neurons prevents cataplexy, and cataplexy and RBD can occur in same subjects.

Dreaming

P01

Auditory and verbal contents of dreams in congenital deaf

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Dream content studies have shown that characters, their interactions, emotions, misfortune and good fortune events are relatively similar among individuals and relatively independent of the cultural background. Despite the significant sensorial attenuation that occurs during sleep, previous studies have shown that auditory stimuli activate cortical structures in a way similar to wakefulness. Congenital deafness constitutes therefore an interesting model to study both these issues regarding auditory memories and events in dreams.

Objectives: Dream content analysis in congenital deaf with specific analysis of auditory and verbal activity

Material and Methods: Cases: 8 congenital deaf, (age between 25 and 50 years) half males and 8 normal hearing volunteers; dreams were collected by dream diaries (15 days) followed by nocturnal REM awakenings in the laboratory under full PSG. Dream content was analysed by the Hall and Van Castle coding system. Cases were compared to published normative Hall and Van Castle data, through DREAMSTAT Excel spreadsheet. Statistics analysis was based on frequencies and comparisons of percentages through the "h" statistic (Cohen).

Results: Deaf dream reports have auditory contents (e.g "I heard the noise of the sea") 3/316 in comparison with 5/458 activities and frequent verbal activities (e.g. I was talking with my mother") 29/316 in comparison with 41/458 activities. Deaf dreams had significantly less male characters 23/257, familiar characters 19/257, friends characters 10/257, negative events 6/6 and emotions 6/11 in comparison with 33/399, 56/399, 35/399,15/15, 14/40 respectively in normal hearing. Although more aggressive and sexual interactions: 88% in contrast with 0% when the dreamer is the aggressor and 5% in comparison with 1% in sexual events.

Conclusions: Despite the absence of auditory stimulation, dream auditory hallucinosis seems to persist in congenital deaf dreams. Verbal communication is frequent, although it is not possible to discriminate between oral and sign language in our study. Changes in other dream contents require a systematic evaluation on psychopathology probably common in these subjects.

P02

Abstract withdrawn.

P03

Dream imaging – how to read the sleeping brain

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Since the discovery of the close association between REM sleep and dreaming, much effort was devoted to search for parallels between physiological aspects of REM sleep and contents of associated dreams, with modest results. For example, speculations about high extrastriate activation and prefrontal deactivation in REM sleep resulting in vivid dream images and a loss of attention and volition in dreams are far from associating discrete dream contents with certain neurophysiological events. The main obstacle in decoding dream content from brain activity is, unlike 'brain reading' in the awake state, the inability of subjects to volitionally perform predecided mental actions which could be reliably associated with brain activity. We identified neural correlates of concrete dream contents by combining brain imaging with polysomnography and the technique of lucid dreaming, i.e. the learnable ability to become aware of the own dreaming state. Subjects were instructed to signal their lucid dreaming state with a pre-decided pattern of eye movements, the only motor actions possible in REM sleep related atonia. Once lucid, they should alternately clench their left and right fist in their dream and signal the changeover with eye movements again. Using the eye signals as temporal markers, the neural activity measured by functional magnet resonance imaging (fMRI) and near-infrared spectroscopy (NIRS) could be related to the dreamed fist clenchings, while parallel polysomnography showed the subject being in REM sleep. Considering recent endeavours in decoding mental states from brain activity in the waking state, we view this technique as a most promising tool for expanding such 'brain reading' research on the dreaming brain.

P04

Evaluation and time course representation of the emotional tone of dreams using machine learning and automatic text analyses

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Most of the studies on dreams have used time consuming coding systems that depend on a rater's judgment. It is of interest to develop an efficient mean of scoring dreams that can be used with large data banks and reproduced across laboratories. We report on our exploration of dream's emotional content using automatic analysis tools. A sample of 776 dreams, reported by 274 individuals of varied age and sex, was used for word-correlation analysis. A subset of 477 was rated by a judge using two 0–3 scales describing negatively and positively orientation of the dream. LIWC dictionary was used to identify affective words while CMU Link Grammar Parser was used to identify adverbs. Hence, the LIWC reported affect, was modified for better representation. We also attempted to develop a novel dynamic representation of changes in affect with respect to dream progression. Of various machine learning models used, the Multinomial Logistic Regression Model provided the most accurate results with least mean squared error. The agreement between machine rating and the human judge score on a scale of 0–3 was 59% (MSE = 0.37); significantly better than chance probability of 25% and baseline accuracy of 30–33%. This indicates that estimates were at most one level away from human judge score. As for the progression of emotions along the dream reports, our model appears successful at using the estimates to provide a time course graphical representation. These results offer a promising perspective for the automatic analysis of dream emotions, which is recognized as a primary dimension of dream construction. Larger database should facilitate analysis and data mining, and emotion specific parameters may add resolution and improve accuracy. To the extent that dream narrative corresponds to the time course of dream experience, graphical representation should provide a new tool to explore models of dream formation.

P05

REM dream reports in congenital deaf and normal hearing and association with EEG components

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Congenital deafness provides a good model for dream research due to the specific sensorial deprivation.

Objectives: Evaluate whether REM dream reports in congenital deaf and normal hearing subjects were associated with different frequency EEG components.

Methods: Five congenital deaf and 5 normal controls were recorded for 2 consecutive nights by Full-PSG. Awakenings via a vibrator were done in REM periods, after 5 min. EEG mapping of the 5 min prior to the awakenings and therefore corresponding to dream reports was performed, for the frequency bands delta, theta, alpha, sigma, beta and gamma using FFT. The 5 min were subdivided in 30 seconds epochs.Statistical analysis used multivariate analysis using repeated measurements.

Results: The number of collected awakenings per night was higher in normals (2.91 $\pm$ 1.45) then in deaf (2.41 $\pm$ 1.3) $P = 0{,}0001$; the number of awakenings per subject was also higher in normals (4.5 $\pm$ 2.7) versus (3.35 $\pm$ 2.1); the percent recall was 85 and 88 respectively.Mapping of the all the awakenings: the Delta, Theta, Alpha show both statistically significant differences between diagnosis and across time but not so clear for topography. All of them were lower in deaf subjects. Delta was lower in deaf subjects, but in the periods prior to awake it is higher in deaf in Fp2, Fz, Fp1. Alpha, Theta and Sigma in normals are higher in O2, O1, Pz and T6; in deaf are higher in O2, O1 and T5. Beta and gama in normals is higher in Cz, F4, O2, O1, Fp1, Pz and T6 in deaf it is higher in C3, T3 and T5. Comparison dream report/no report: delta activity only showed differences between diagnostic groups and the temporal evolution; theta provided a similar profile. The presence of a dream report was associated with different temporal evolution of alpha in normals and deaf. Sigma and beta were significantly different between the two groups. Gamma activity was lower in epochs associated with dream reports.

Conclusion: Congenital deaf presented different activation patterns when compared with normal subjects, furthermore there were different lateralization issues with the deaf activating mainly the left side and normal hearing controls the right side. The sigma and beta band were significantly associated with dream recall.

P06

Cognition during sleep: a therapeutic intervention in nightmares

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Controlled Studies on the treatment of nightmares by means of psychotherapeutic methods are rare. The aim of the present study was to determine the effects of gestalt therapy and lucid dreaming on nightmares. Thirty-two subjects with recurrent nightmares completed the study. All of them participated in a gestalt group therapy program (GT) over 10 weeks, 16 were additionally instructed in lucid dreaming (LD). Subjects were randomly assigned to one of the two groups (GT versus GT+LD). The subjects completed sleep logs over 10 weeks. Actigraphic data were obtained at the beginning and at the end of the study for a period of two weeks each. Examinations with respect to sleep quality, nightmare frequency, anxiety, depression and quality of life were carried out at the beginning of the study, after 5 weeks, after 10 weeks and at a follow-up after 3 months. In both groups anxiety and depression were reduced and quality of life was improved after 10 weeks of therapy. Subjective sleep quality (PSQI), which at baseline had been deteriorated compared to normative data, was found improved as well for both groups at the follow-up ($P < 0.05$, Wilcoxon Test), but only the LD-group already showed significant improvement at the end of therapy ($P < 0.05$). Actigraphic data showed a consolidation of the sleep-wake rhythm and a more pronounced differentiation between diurnal and nocturnal activity in both groups. Concerning nightmare frequency a significant reduction was found in both groups after the 10-week study period as well as at the follow-up ($P < 0.01$), but for subjects having succeeded in learning lucid dreaming (12 out of 16) the reduction was sooner, higher and longer lasting. Cognition during sleep, i.e. lucid dreaming, is a learnable skill that can be used in coping with nightmares and is also able to improve sleep quality.

P07

Disappearance of gender differences in dreams at late adulthood?

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Normative studies have typically shown gender differences in dreams in the young adults. For example, women report more familiar characters, less aggressive interactions and less physical aggressions than men. It has been proposed that dream characteristics remain relatively constant with age, more specifically once adulthood is reached (Domhoff, 2003). However, it has been observed that in women whose social roles have evolved more closely to those of men, their dream characteristics become more comparable to those of men. In the context of a normative study of dreams of Canadians, we have analyzed the dreams of 42 men and 42 women, from the general population, aged from 40 to 64 years old. We used the Hall and Van de Castle scales (1966). More specifically, the scales of characters, interactions, and emotions were applied. Dreams were scored by two judges and inter-rater reliability, based on the percentage of perfect agreement, ranged from 0.60 to 0.90 for the various scales. Statistical analyses were conducted using DreamSAT. Contrary to expectations, comparisons using Cohen h showed no gender differences on any of the major dream content scales. These results suggest that gender differences in dreams may disappear with age or that their absence may reflect the evolution of sex roles in modern society. Comparisons with contemporary young adults should bring more light into this phenomenon.

P08

Morning dreaming recall in Temporal Lobe Epilepsy (TLE) patients

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TLE is a clinical model for dream functional anatomy studies. 1st, because of phenomenological factors. 2nd, stimulation studies showed that temporal cortex can be responsible for the visual imagetic in nightmares and for the visual aura. 3rd, PET studies described a relative activation of limbic and paralimbic structures during REM. Our aim was to prospectively evaluate the morning dream recall dream rate (MDRR) and characterise dream content (DC) in TLE according to epileptogenic zone. During 2 years, all the patients for Video-EEG were asked for written morning dream recall (MDR). Dream recalls per morning, dream word count and Hall and Van Castle analysis (HVC) were obtained. Seizure distribution recorded. The population included 30 patients (16 males) with a mean age of 36.8 years old (20–59). The multimodal TLE diagnosis was prospective. 22 patients had mesial TLE (MTLE) and 8 non-MTLE (NMTLE). Laterality of ictal onset zone (IOZ) was: 12 right, 16 left and 2 bilateral. 19 TLE patients (63,3%) had at least one MDR and 9 (30%) had dreams with more than 40 words (30%). 16 patients with MTLE (72.7%) versus

3 patients with NMTLE (37.5%), had at least one MDR. The number of patients with MDR was not different in right/left groups. MDRR was 29.5% for entire population, 36.8% for MTLE versus 11.6% for NMTLE ($P = 0.0023$), 17.8% for right versus 35.3% for left ($P = 0.018$). In HVC, patients with TLE had a higher family characters percentage and reported less aggression, friendliness, sexuality, fortune and success. Comparing MTLE with NMTLE, aggression/friendliness and negative emotions were lower in MTLE but did not reach significance. Right MTLE patients had a significant higher proportion of animal characters. Seizures increased until day 3. MDR had a maximum in day 2. The percentage of patients with MDR is similar to that described in ambulatory dream diary studies. MDRR was higher for MTLE patients and for patients with a left IOZ. The number of MDR after the 2nd morning decreased in association with seizure increase (possibly due to REM deprivation). In TLE patients, the higher family characters percentage could be interpreted by their social isolation. The low MDRR for fortune and success could also mirror their absence of future perspectives.

Narcolepsy-Hypersomnias

P09

Co-morbidity in narcolepsy

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Background: Currently the evidence for diseases associated with narcolepsy and their siblings is unconvincing. Narcolepsy has been linked to psychiatric disease but the association of autoimmune disease remains speculative. The aim of this project is to evaluate the prevalence of co-morbid disease in narcolepsy patients and their siblings.

Method: A questionnaire-based, case-control study was undertaken from June to October 2007. Questionnaires were mailed to all narcoleptics currently registered with the Department of Sleep Medicine, Royal Infirmary of Edinburgh. They were asked to provide sibling addresses. A separate questionnaire was mailed to the siblings. Health professionals and students were approached to fill out the control questionnaire.

Results: Sleep apnoea ($P<0.003$), hypertension ($P<0.008$), diabetes ($P<0.04$), depression ($P<0.01$), myocardial infarction ($P<0.01$), rheumatoid arthritis (RA) ($P<0.05$), and headaches ($P<0.004$) were all significantly more prevalent in narcoleptics compared to controls. Diabetes ($P<0.04$) and depression ($P<0.01$) were significantly higher in siblings than controls.

Conclusions: In this study sample, autoimmune diseases were not significantly more frequently associated with narcolepsy. Only RA was significantly more likely to be present in narcoleptic patients compared to their siblings or controls. Siblings of narcoleptics were significantly more likely to suffer from depression and diabetes compared to population controls.

P10

The SleepMed Insomnia Index (SMI) and Epworth Sleepiness Scale (ESS) as outcome measures of sleep disturbance in treated narcolepsy

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Objective: Narcolepsy is characterized by excessive daytime sleepiness (EDS), disturbed nocturnal sleep, and manifestations related to REM sleep such as cataplexy, sleep paralysis, and hypnagogic hallucinations. The ESS is a validated measure of daytime sleepiness while the SMI is a validated measure of an insomnia component. This is a retrospective study to examine the use of the SMI combined with the ESS in evaluating treatment outcomes in two groups of patients: those who were treated with either wakefulness enhancing medications alone or treated with wakefulness enhancing medications plus sodium oxybate.

Design/Methods: A total of 42 patients with narcolepsy were studied retrospectively to retrieve scores of the SMI and ESS scales at baseline and when stable on therapy. There were 2 groups of 21 patients studied: one group wakefulness enhancing medication (Group A) and the second group on wakefulness enhancing medication and sodium oxybate (Group B). ESS scores of >10 as a measure of EDS and SMI scores of >20 as a measure of insomnia/sleep disruption are reported. Means, standard deviations, and *t*-tests are reported.

Results: Group A had 16 females (76%) and 5 males (24%) with a mean age of 34 and Group B had 12 females (57%) and 9 males (43%) with a mean age of 40. Group A pre SMI scores were 25/40 (9) and post SMI scores were 17/40 (8)with *t*-tests significant $P<0.002$. Pre ESS scores were 19/24 (4) and post ESS scores were 15/24 (5) with $P=0.004$. Group A frequency of pre SMI scores of $>20=11$ (52%); post SMI scores $>20=6$ (29%); pre ESS scores $>10=20$ (95%); and post ESS scores $>10=18$ (86%). Group B pre SMI scores were 19/40 (8) and post SMI scores were 11/40 (7) with *t*-tests significant $P<0.0003$. Pre ESS scores were 16/24 (5) and post ESS scores were 11/24 (5) with $P=0.001$. Group B frequency of pre SMI scores of $>20=11$ (52%); post SMI scores $>20=3$ (14%); pre ESS scores $>10=18$ (86%); and post ESS scores $>10=11$ (52%).

Conclusions/Relevance: SMI and ESS scores showed improvement with therapy. A significant proportion of narcolepsy patients had an insomnia component. Patients treated with sodium oxybate showed a greater improvement in ESS/SMI scores.

P11

24-hour ambulatory monitoring of sleep-wakefulness patterns in narcolepsy

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Introduction: Narcolepsy is characterized by excessive daytime sleepiness (EDS), cataplexy and other dissociated manifestations of rapid eye movement sleep (hypnagogic hallucinations and sleep paralysis). EDS is common and associated with a broad range of medical, sleep and psychiatric disorders. The diagnosis of narcolepsy should be confirmed by a whole night polysomnographyic recording followed by a Multiple Sleep Latency Test (ICSD-2). However, MSLT is designed to provide information about the sleep tendency when the patients lie down. We try to detect SOREMPs by 24-hour ambulatory monitoring and diagnose more precisely.

Method: 24-hour polygraphic recordings were performed with ambulatory monitoring system. Patients were instructed to maintain wakefulness in their rooms, reading books, listening to the radio during the day. Sleep stages were visually scored for 20-second epochs according to Rechtschahffen and Kales criteria.

Results: Case 1: A 19-year-old girl with EDS, cataplexy, hypnagogic hallucinations and sleep paralysis. Nocturnal sleep finding: SOL, 19.0 min; RL, 1.6 min; WASO, 25.3 min; stage1, 48.3 min; stage2, 297.7 min; stage3+4, 45.0 min; stage REM, 116.3 min. Diurnal sleep: 5 sleep episodes (3 SOREMPs) Case 2: A 29-year-old man with EDS, cataplexy, hypnagogic hallucinations and sleep paralysis. Nocturnal sleep finding: SOL, 3.0 min; RL, 1.3 min; WASO, 101.0 min; stage1, 142.7 min; stage2, 211.3 min; stage3+4, 35.0 min; stage REM, 89.7 min. Diurnal sleep: 4 sleep episodes (3 SOREMPs).

Conclusion: 24-hour ambulatory monitoring appears to be a useful procedure for diagnosis of narcolepsy. It provides information about the number, duration and types of daytime sleep episodes, as well as documenting nocturnal sleep disturbance.

P12

Prevalence of narcolepsy in Norway

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Objectives: Narcolepsy is a life long disabling disorder that may be alleviated by relevant treatment. Patients frequently report 10–15 years from the first symptoms to the time they get the diagnosis and treatment can be started. In order to offer a sufficient diagnostic and

therapeutic service to this patient group, a reliable estimation of the prevalence of the disorder is important. A study of the prevalence of narcolepsy in Norway was therefore undertaken.

Materials and methods: The Ullanlinna Narcolepsy scale (UNS) was sent to 14548 randomly selected Norwegians between 20 and 60. Responders with ≥ 14 points on the UNS, cataplexy symptoms, daytime sleep episodes >3 times weekly, and a nightly sleep latency <40 min were interviewed by telephone. Those with possible narcolepsy had sleep recordings (PSG and MSLT) and were HLA-typed.

Results: 8992 answered the questionnaire (response rate 61.8%), 267 had ≥ 14 points on the UNS, 156 were interviewed and 15 had sleep recordings. In two HLADQB1*0602 positive patients sleep recordings were compatible with narcolepsy.

Conclusions: The results indicate a prevalence of 0.022% and approximately 1000 patients with narcolepsy in Norway. About half the Norwegian narcolepsy population may therefore still be undiagnosed.

P13

Hypocretin deficiency syndrome or narcolepsy Type 1

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Research on narcolepsy has been difficult to interpret because different subgroups of narcolepsy have been included in the same study. Out of 100 narcolepsy patients we selected 20 patients with low hypocretin (below 110 pg ml^{-1}) and compared with 20 patients with normal and high hypocretin (above 450 pg ml^{-1}). The 2 groups were compared for quality of life including job situation, hospitalization and dependency. Group A consists of 5 male and 15 female aged 13–80 years with a mean hypocretin level of 78 pg mL^{-1} (range 5–115 pg mL^{-1}) and Group B consisting of 4 males and 16 females aged 16–78 years with a mean hypocretin level of 525 pg mL^{-1} (range 477–577 pg mL^{-1}).

Results: In group A only 4 narcoleptics had been able to work full or part time, 7 patients have lengthy stays in institutions and 11 patients suffered with severe psychosocial problems, life quality was very low. In group B14 patients were in full or part time work, 4 patients were retired and 2 were on rehabilitation. No one had been institutionalized and none reported psychosocial distress other than mild depression related to limitation of job opportunities. We treated 13 of the patients in group A with Xyrem for their cataplexy all with extremely good effect. We concluded that the most striking result comparing narcoleptics with and without hypocretin is the dramatic difference in life quality; patients with low or no hypocretin are severely affected with a need for multidisciplinary treatment and a much closer follow up. We propose that narcoleptics with low hypocretin should be classified specifically for diagnostic and therapeutic purposes and suggest Hypocretin Deficiency Syndrome or Narcolepsy Type I as an appropriate classification.

P14

A case of periodic hypersomnia with extremely long repetition rate: a Kleine-Levin variant?

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Kleine-Levin syndrome is characterized by periodic hypersomnia with a repetition rate of few months to year, confused mental state during the hypersomnolence period and hyperphagy. Here we present the case of a 29 years old woman. She was admitted to the hospital because of progressive decline of the consciousness. No abnormal physical neurological signs were found. Lab tests, toxicology, MR and liquor examination showed no pathological abnormalities. EEG showed no fast background activity (which can exclude the possible endozepine stupor). Polysomnographic examination showed the alternation of non-REM and REM periods without pathological respiratory or movement signs. After 3 weeks, the hypersomnolence disappeared gradually and spontaneously. Seven years earlier she was observed with the same symptoms (altered state of consciousness-hypersomnia, negative (no epileptic activity and no signs of structural origin alteration) EEG, lab tests, MR and liquor examinations, and spontaneous recovery). Between these two episodes of hypersomnolence, no any sign of a milder form of periodic hypersomnia was recognized. Polysomnographic recording showed normal sleep structure without pathological respiratory or movement events. Due to the absence of structural, metabolic and toxicological abnormalities and relatively normal ultradian regulation of sleep, we concluded that this form of periodic hypersomnia represents a Kleine-Levin variant with extremely long asymptomatic periods.

P15

Comparison of polysomnographic data of young patients with excessive daytime sleepiness

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In this study polysomnographic data of 97 young patients (18–25 years) with the complaint of excessive daytime sleepiness were compared. Patients with excessive daytime sleepiness were selected by the Epworth Sleepiness Scale. Diseases standing behind the symptom were diagnosed by polysomnographic (PSG) study and multiple sleep latency test (MSLT) according to the international protocols. Results showed that the distribution of the patients was the following: 48 narcoleptic [22 male (45.8%) and 26 female (54.2%).], 47 UARS [21 male (44.6%) and 26 female (55.3%)], 1 patient with circadian rhythm disorder (male, 19 years) and 1 patient with idiopathic hypersomnia (male, 20 years) participated this study. From the PSG parameters sleep stage shift (SSS), PSG sleep latency (PSG SL), PSG microarousal, PSG slow wave sleep percent (PSG SWS%), from the MSLT parameters the MSLT sleep latency (MSLT SL) were compared. By the narcoleptic patients: mean SSS was 32 (STD: 8), mean PSG SL was 10.3 min (STD: 3.6), mean PSG microarousal was 14.6/h (STD: 2.8), mean PSG SWS % was 16.8 (STD: 3.6), mean MSLT SL was 5.2 min (STD: 1.5). By the UARS patients: mean SSS was 127 (STD: 52), mean PSG SL was 17.2 min (STD: 4.2), mean PSG microarousal was 47.1/h (STD: 6.5), mean PSG SWS % was 10.2 (STD: 2.2), mean MSLT SL was 6.3 min (STD: 2.8). By the patient with idiopathic hypersomnia: SSS was 28, PSG SL was 16.5 min, PSG microarousal was 10.8/h, PSG SWS % was 26, MSLT SL was 5 min. By the patient with circadian sleep disorder: SSS was 35, PSG SL was 21 min, PSG microarousal was 9.3/h, PSG SWS % was 19, MSLT SL was 11 min. Polysomnography and the multiple sleep latency test are essential diagnostic methods in the diagnosis of diseases with excessive daytime sleepiness.

P16

A multicentric study of health-related quality of life in Portuguese patients with narcolepsy

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Prevalence of narcolepsy in Portugal is 47/100 000 inhabitants, similar to other European Countries (Ohayon et al. 2002).

Objectives: 1) To evaluate the health-related quality of life (HRQoL) in Portuguese narcoleptics; 2) To evaluate factors associated with deterioration in HRQoL; 3) To compare the date obtained in this study with data from national surveys and equivalent studies in literature (SiL).

Results: 70 questionnaires were send to patients from sleep centres in Coimbra and Lisboa; 51 were received, response rate 80%. Equal gender distribution, average age 43.4; divorced 8% (4 times higher when compared with Census (2001), but lower than SiL; Traffic accidents is referred by 50% of the respondents. 90% of the narcoleptics had cataplexy (values higher than SiL). Characteristics of cataplexy, sleep paralysis, and hypnagogic hallucinations were similar to SiL. Epworth Sleepiness Scale (ESS) = 17.7, considerably high, and 60.7% had some degree of depression. HRQoL domains were significantly lower than national surveys, except Physical Function (PF) and Bodily Pain (BP) (P between 0.000 and 0.006) and similar to SiL. SF-36 presented lowest score in Vitality (39.93). Deterioration was significantly lower in Physical Role ($P = 0.006$), Vitality ($P = 0.011$), and Mental Health ($P = 0.008$) in women and in PF ($P = 0.003$) and BP ($P = 0.045$) in elder subjects. Narcoleptics with cataplexy had worse health profile of PF ($P = 0.020$) and General Health (GH) ($P = 0.032$), and those with longer disease duration were worse in PF ($P = 0.048$), BP ($P = 0.015$) and GH ($P = 0.044$). Those with higher literacy had better PF ($P = 0.046$). The higher levels of depression related significantly with deterioration of all SF-36 dimensions ($P < 0.002$). Depression was higher when longer time elapsed after diagnosis. No relation with marital status, professional activity and situation, symptoms of narcolepsy (except cataplexy), accidents, and treatment was found.

Conclusions: HRQoL is significantly deteriorated in narcoleptics, affecting all dimensions (except PF and BP) when compared with general Portuguese population.

P17

REM sleep without atonia in narcolepsy

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Introduction: While there are a number of observations/quantifications indicating a greater proportion of REM sleep without atonia (RWA) in narcolepsy, the intra-night distribution of this parameter has not been evaluated.

Patients and methods: We evaluated in retrospect 95 polysomnography recordings of patients admitted in our Sleep Disorder Centre between 1997 and 2007 (77 patients with narcolepsy - cataplexy and 18 patients with isolated narcolepsy). Signs of RWA (REM sleep without atonia in more then 20% of the total REM sleep duration ascertained by polysomnography) were found in 34 patients suffering from narcolepsy with cataplexy and in 3 patients with isolated narcolepsy (16 men and 21 women; mean age 44.9 ± 18.9 years). Seven of them had clinically manifest RBD. Hypnagogic hallucinations were present in 24 cases and sleep paralysis in 16 patients. Polysomnographic recordings were scored with particular regard to REM sleep without atonia across all the nocturnal REM periods.

Results: This study confirms a high prevalence of RWA in narcolepsy (38.9%). Of interest is our finding that RWA occurs in both men and women equally (16 men and 21 women) in contrast to idiopathic RBD cases. What came as an absolutely new finding in our study was a significant RWA increase during successive nocturnal REM periods ($P < 0.0001$, F 16.85, df 36). Asimilar RWA increase was found also in the group of 7 patients with clinically manifested RBD ($P < 0.0001$). No correlation was found between the percentage of RWA and the severity or duration of the disease.

Conclusion: The study demonstrates for the first time an increasing amount of RWA during the night suggesting enhanced nocturnal REM sleep motor disturbance.

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P18

Comorbidity in a patient cohort with narcolepsy

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Introduction: Narcolepsy frequently goes along with other significant sleep disorder comorbidities, e.g. REM sleep behavior disorder (RBD), restless legs syndrome (RLS), periodic limb movements in sleep (PLMS), and obstructive sleep apnea syndrome. Furthermore, an association of narcolepsy with an increased body mass index (BMI) has been reported.

Methods: In this retrospective study, 64 patients with PSG confirmed narcolepsy according to ICSD 2 criteria were included. Information regarding sleep disorder comorbidities was gathered from patient histories, medical and polysomnography reports. Frequencies of the sleep disorders are presented in comparison to published data from the general population.

Results: Sixty-four patients (37 men, 27 women) with a mean age of 42.0 ± 15.4 years were analyzed. Fifty-six patients (87.5%) had narcolepsy with cataplexy. The following additional sleep disorders were frequent among patients with narcolepsy according to published data: RLS 23.4% (general population: 5–10%), PLMS 54.8% (general population: 5–44%), RBD 6.6% (general population: 0.5), REM sleep without atonia 70.5%, sleep talking 16.4% (general population: 5%), bruxism 13.1% (general population: 6–12%), confusional arousals 16.7% (general population: 3.6–4.8%), obstructive sleep apnea syndrome 29.5% (general population: 2–4%). Eighteen patients (28.1%; 10 men, 8 women) had a BMI above the 90th percentile (general population: 10%).

Conclusion: This study confirms that narcolepsy is associated with multiple other sleep disorders, and replicated that the BMI percentiles of patients with narcolepsy are more often above 90. In patients with narcolepsy all these comorbid sleep disorders should be carefully assessed and treated if indicated.

P19

Sodium oxybate improves coexisting REM behavior disorder in narcolepsy with cataplexy

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Coexisting REM behavior disorder (RBD) has been reported to occur in about a third of patients with narcolepsy. Sodium oxybate has recently been licensed in the United Kingdom for the treatment of narcolepsy with cataplexy. We interviewed seven patients with narcolepsy with cataplexy (and partners if available) who had started treatment with sodium oxybate in the last six months. We also reviewed the pretreatment polsomnograph for evidence loss of normal rapid eye movement sleep atonia, characteristic of RBD. Of the seven patients interviewed four patients had symptoms of REM behaviour disorder. Symptoms included acting out of dreams, striking bed partner and abnormal movement in sleep. Pretreatment nocturnal polysomnography showed loss of normal REM sleep atonia in the 2 studies that were available for review. All four patients reported improvement or disappearance of REM behaviour disorder symptoms since commencing sodium oxybate.

P20

Narcolepsy and emotions: preliminary data of an EEG and FMRI study

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Intense emotions provoking laughter can cause cataplexy, the pathognomonic symptom of narcolepsy. Cataplexy is characterized

by REM-sleep muscles atonia occurring during waking with consciousness remaining fully preserved. Studies in animals have shown the involvement of basal forebrain cholinergic activity in regulating cataplexy; however little is know about human narcolepsy and emotional susceptibility. We present data from an ongoing EEG and fMRI study aimed at detailing both the time-course and the brain areas involved in emotional encoding. Participants were 12 narcoleptic patients and 14 healthy controls matched for age, gender and body mass index (BMI). A 32 channels EEG was recorded and the visual evoked potential (VEP) elicited by positive, neutral and negative pictures (International Affective Picture System) and by ad hoc selected funny pictures, was analyzed. All stimuli were randomly and briefly presented in a rapid serial torrent at a speed of 3 Hz. The block-design fMRI paradigm consisted of 27 randomly presented video clips from funny, scary and neutral movies. Participants were instructed to simply watch the movies and to listen to the embedded soundtrack. Preliminary results show that the P1, a positive VEP deflection occurring 100 msec after stimulus onset, and a posterior positivity (PP) occurring at 300 msec after stimulus onset, were selectively both attenuated by presenting funny pictures in patients but not in controls. On the other hand, and in partial accordance with a recent report (Schwartz, Ponz, Poryazova, et al. Brain 2008 131 (2):514–522), fMRI data show in patients, but not in controls, an increase of the BOLD response in specific limbic structures such as the hippocampus during humorous, but not during scary or neutral movies. It is concluded that the emotional susceptibility to humorous pictures or movies in narcolepsy is associated to a failure in early processes of emotional encoding and to specific limbic brain activation.

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P21

Narcolepsy and depressive patients: interim results of a comparative analysis

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Introduction: Narcolepsy is a chronic sleep disorder, characterized by excessive daytime sleepiness and additional symptoms, such as cataplexy, hypnagogic hallucinations, sleep paralysis and disturbed nocturnal sleep. High rates of depression have been described in narcolepsy patients. However, typical symptoms of narcolepsy could be confused with depression.

Aim: To compare depressive symptoms between narcolepsy patients and out-patients clinically diagnosed with a depressive episode (F32.0–1/33.0–1) without an identified primary sleep disorder.

Method: 78 narcoleptics (N), 27 outpatients with mild to moderate depression (D) and 57 controls (C) were seen for psychological testing. They completed Beck Depression Inventory (BDI), Zung self-rating depression scale (ZSD), Profile of Mood States (POMS), Numeric Subjective Depression Scale (NDS) and Epworth Sleepiness Scale (ESS). The majority of patients were under pharmacological treatment.

Results: 1. Depressive symptoms in N were higher than C but less than D in BDI, ZDS and NDS. In POMS total mood disturbance score (TMDS) means of N (67.7 SD = 32.1) were significantly lower than D (91.7 SD = 37.1 $P<0.01$), but higher than C (34.6 SD = 23.2, $P<0.01$). N and D were more impaired in all the subscales in comparison with C. 2. When selecting only patients with BDI scores $\geq$ 10 for an item analysis we obtained groups of N ($n = 31$) and D ($n = 21$) with a comparable degree of depression. They had similar means in BDI (N: 19.1, D: 18.8), ZDS (N: 47.3, D: 46.6) and NDS scores (N: 4.7, D: 5.1). Based on items in the BDI, N were less "dissatisfied and bored" ($P = 0.006$), had less "sadness" ($P = 0.04$) and less "loss of appetite" ($P = 0.04$) than D. In ZDS N had higher scores in "getting tired" ($P = 0.001$) and were more impaired in "decision making" ($P = 0.04$) in comparison with D.

Conclusion: We conclude that (1) Narcoleptics are on average more depressed than controls and less depressed than patients with depression. (2) In the item by item analysis we found differences in essential features of depression between Narcolepsy and Depression but further analysis must be performed.

P22

Metabolic syndrome in narcolepsy-cataplexy

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Background: Several studies indicated that body weight and other metabolic parameters are altered in narcoleptic patients.

Aim: To explore metabolic alterations in hypocretin deficient Narcolepsy-Cataplexy (NC) subjects.

Design: We studied increased body mass index (BMI), metabolic syndrome parameters (Adult Treatment Panel III-ATP III criteria), and daily calorie intake in NC patients versus Idiopathic Hypersomnia (IH) patients. We enrolled 28 patients: 14 male patients with NC (HLA DQB1*0602, clear cut cataplexy, 2 or more sleep-onset rapid-eye-movement periods in multiple sleep latency test-MSLT and hypocretin deficiency, i.e. less than 110 pg ml^{-1}); and 14 male patients with IH without long sleep time. The diagnosis have been made following the International Classification of Sleep Disorders 2nd edition. The two groups were comparable for age.

Methods: In all patients BMI, waist circumference, arterial blood pressure, and glucose, triglicerids, and HDL cholesterol in plasma samples have been measured. The daily calorie intake was obtained as daily average of a three day food diary.

Results: Respect to patients with IH, the ones with NC are dramatically overweight and satisfy at least 3 of the 5 ATP III diagnostic criteria, fulfilling the diagnosis of metabolic syndrome for male subjects (waist circumference >102 cm, arterial blood pressure >130/85 mmHg, plasma glucose >110 mg dl^{-1}; triglicerids >150 mg dl^{-1}, HDL cholesterol <40 mg dl^{-1}) with a significant difference between the two groups (BMI, $P = 0.012$; metabolic syndrome, $P<0.05$). Daily calorie intake is also significantly lower in NC patients ($P = 0.027$).

Discussion: The striking prevalence not only of a higher BMI, but also of a definite metabolic syndrome in NC patients, confirm the hypothesis of a metabolic dysregulation intrinsic to NC. The lower daily calorie intake indicates that the weight increase is depending on other mechanisms than feeding behaviour. At the moment, these results stress the utility of clinical metabolic assessments for NC patients and of a strict follow up for the important cardiovascular risk linked to metabolic syndrome.

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REM sleep behaviour disorders in narcolepsy/cataplexy patients: a quantitative method of analysis of submentalis muscle EMG activity during REM sleep

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Introduction: REM sleep behaviour disorder (RBD) is a common diagnosis in Narcolepsy/Cataplexy, but a quantitative method for

studying REM muscle activity is rarely adopted. We intended to evaluate quantitatively the amplitude of the submentalis muscle EMG activity during sleep in patients with Narcolepsy/Cataplexy with or without RBD.

Methods: We recruited 34 consecutive patients with Narcolepsy/Cataplexy and 35 age-matched normal controls. Clinical and video polysomnographic diagnosis of RBD was present in 50% of patients (17 subjects). The average amplitude of the rectified submentalis muscle EMG signal was used for the assessment of muscle atonia and the new REM Sleep Atonia Index was computed; moreover, also chin muscle activations were detected and their duration and interval analyzed.

Results: The REM sleep Atonia Index was significantly lower in both patient groups (narcoleptics with RBD showing the lowest values), with respect to controls and did not correlate with age as it happened in controls. The total number of chin EMG activations was significantly higher in both patient groups, with respect to controls; no significant differences were found between the two groups of patients, even if narcoleptics with RBD tended to have a higher number than those without. Moreover, the altered REM sleep atonia index in both patients was mostly due to an increase in short-lasting EMG activity (approximately from 0 to 5 s).

Conclusion: This study showed that a certain degree of polysomnographically evident RBD was present in many patients with Narcolepsy/Cataplexy and that this feature might be specific to Narcolepsy/Cataplexy, reflecting a peculiar form of REM sleep related motor dyscontrol (i.e. status dissociatus) paving the way to enacting dream behaviours.

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Disturbed eating behaviour in patients with narcolepsy

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Orexins are fundamentally involved in the regulation of food intake and sleep. Narcolepsy, a disorder characterized by a central orexin deficiency, is a particular interesting clinical model to investigate the interaction between both systems. Recent studies report an increased body weight and an elevated prevalence of eating disorders in narcolepsy.

Methods: 61 patients with polysomnographically verified narcolepsy (F/M 38/23: 48.1 ± 17 years; BMI 28.6 ± 4.9 $kg\,m^{-2}$) were included in the study. Eating behaviour was assessed with the German version of the 'Three Factor Eating Questionnaire' (TFEQ 'Fragebogen zum Essverhalten'). In addition, anthropometric measurements including body weight and height were performed in all participants. The TFEQ is a self-rating instrument with 56 items that assesses three distinct dimensions of eating behaviour: Disinhibition, susceptibility to hunger and cognitive control. Control subjects were selected from a large-scale random population study unrelated to the present investigation. A total of 236 subjects were individually matched for gender and age ('GA' control group) and further 173 subjects were matched for gender, age and BMI ('GAB' control group). Controls subjects had completed the TFEQ as part of their initial assessment. Matching criteria were gender and age difference of ± 1 year for the GA control group, and gender, age difference ± 5 years and BMI difference ± 1 $kg\,m^{-2}$ in the GAB control group.

Results: Ratings of disinhibition (7.1 ± 3), susceptibility to hunger (6 ± 3.5) and cognitive control (9.5 ± 5.4) were significantly elevated in the narcoleptic patients compared with both GA and GAB-matched controls (disinhibition GA: 4.1 ± 3; GAB: 5.3 ± 3, hunger GA: 3.3 ± 2.4; GAB: 3.6 ± 2.4, control GA: 8 ± 4.9; GAB 7.8 ± 4.9).

Conclusion: These preliminary results suggest a disturbed eating behaviour in narcoleptic patients possibly as a consequence of orexin-deficiency associated neuroendocrine changes in the control of appetite and food intake. These factors may lead to a previously reported elevated prevalence of metabolic abnormalities in patients with narcolepsy.

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Narcolepsy and nicotine

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Introduction: Nicotine is a stimulant, available in multiple formulations, that could theoretically increase alertness. However, the typical health risks are magnified in narcolepsy since falling asleep while smoking creates a risk of burns and fires. No study has examined the extent or consequences of nicotine usage by narcolepsy patients.

Methods: As a first phase unpublished data was obtained from the community-based study of narcolepsy (Silber et al. 2002). The second phase consisted of a 25 item questionnaire distributed at the 2007 Narcolepsy Network national meeting to obtain more information.

Results: In the Olmsted County database 62.5% of narcolepsy patients were past or present smokers. Seventeen questionnaires were completed. 47% of respondents were past or present nicotine users (all smokers at one point). All respondents identified nicotine as an effective in decreasing sleepiness. 37% fell asleep while smoking. 25% smoked in bed. Burns were reported by 75% involving clothing, furniture or carpet. One respondent started a fire. One respondent substituted nicotine patches for cigarettes years ago to continue a "powerful" means to decrease cataplexy. All tried to quit smoking but described difficulty because sleepiness worsened without nicotine.

Conclusion: This is the first description of nicotine use by narcolepsy patients. Burns are a potentially serious complication for patients smoking nicotine. Although burns appear to be common in our preliminary survey, the lack of a denominator precludes conclusions about their frequency. Narcolepsy patients who smoke may have more trouble quitting because of increased sleepiness. The role of nicotine, particularly in transdermal forms, to self-medicate sleepiness and cataplexy merits more study. A survey study of a clinic patient population is underway.

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A case report of narcolepsy

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Background: Narcolepsy is a chronic disease, of unknown aetiology, characterized by cardinal clinical symptoms such as irresistible sleep and cataplexy attacks. It has some specificities at a polygraph level and is associated with certain imunogenetic markers. This disease may determine important consequences in a person's global functioning and psychosocial adjustment, significantly affecting quality of life. In this report the authors describe the case of a 18 years old male, admitted to the Psychiatric Clinic of the Coimbra University Hospital, with the probable diagnosis of Kleine Levine Syndrome. After careful clinical and organic evaluation, the definite diagnosis was Narcolepsy.

Objective: To describe a clinical case of Narcolepsy. Based on this case report the authors undertake a theoretical review of the pathology, mainly concerning its clinical picture, diagnostic evaluation, differential diagnosis and therapeutic approaches.

Material and Methods: Clinical file review, bibliographic review.

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REM sleep under high and low sleep pressure in narcolepsy patients and healthy controls

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The interaction between a circadian and homeostatic sleep-wake dependant process determines the occurrence of sleep and wakefulness as well as the sleep structure. In the present study duration of REM sleep, REM latency and number of interventions to prevent REM sleep are used to explore REM regulation in narcolepsy patients and healthy controls under varying sleep pressure (SP).

Methods: Ten HLA DQB1*0602 positive and hypocretin deficient patients (7/7) with narcolepsy-cataplexy (NC) and ten age, gender and body mass index matched controls (C) underwent a four session crossover sleep-study protocol. There were two sessions with a night of sleep deprivation to increase the SP and 2 sessions with a 4 h night time sleep episode (23:00–3:00 h) to reduce SP, followed by daytime sleep (DS, 7:00–15:00). In two sessions (one with high and one with low sleep pressure) the subjects were repeatedly awakened during the first four hours of the DS episode to prevent REM. DS was undisturbed in the other 2 sessions. Group comparisons were based on *t*-tests.

Results: The number of interventions (NOI) to prevent REM was higher in NC compared to C in both conditions (high SP, 26.5 ± 12.8, resp. 10 ± 4.4, $P = 0.003$; low SP, 26.2 ± 10.1, resp. 12.9 ± 5.5, $P = 0.003$). Different SP did not change significantly the NOI in NC, whereas in C a trend towards higher NOI under low SP was observed. The amount of REM in C (within the first four hours of undisturbed DS) was significantly higher under the condition of low SP compared to high SP ($P < 0.001$). In NC no significant differences were observed. Low SP shortened significantly REM latency in controls ($P = 0.013$). Nine NC and four C showed sleep onset REM (SOREM) under low SP. Under high SP again nine NC showed SOREM (the patients entering sleep in NREM being different for the two conditions) but only one C (same patient had also SOREM under low SP).

Conclusion: We suggest that markers of REM sleep behave differently in NC and C, obeying the interaction between the circadian and the homeostatic regulating processes in C but not in NC.

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Factors with daytime sleepiness in narcolepsy and obstructive sleep apnea syndrome

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Objectives: To evaluate and compare clinical-polysomnographic-genetic characteristics of Korean patients with narcolepsy or sleep apnea syndrome.

Methods: One hundred subjects were diagnosed as narcolepsy with cataplexy or without cataplexy, OSAS or dual diagnosis of narcolepsy and OSAS through the revised ICSD-2 diagnostic criteria made by clinical evaluation, nocturnal polytsomnography (NPSG) followed by multiple sleep latency test (MSLT) and cerebrospinal fluid (CSF) hypocretin-1 level.

Results: 1) On clinical interviews and questionnaires: ESS scores of the patients of OSAS or narcolepsy with cataplexy or without cataplexy were not different each other. The patients with dual diagnosis had higher ESS scores than those of OSAS, narcolepsy with cataplexy or without cataplexy. 2) On NPSG: The patients with OSAS showed more stage 2 sleep, and less stage 3 and 4 sleep. 3) On MSLT: The patients with OSAS had longer mean sleep latency (SL), and less sleep-onset REM periods (SOREMPs) on MSLT than those of narcolepsy with cataplexy or without cataplexy or dual diagnosis. 4) On HLA typing and CSF-hypocretin measurement: The patients with OSAS represented lower frequency of HLA DQB1*0602 positive than narcolepsy and normal level of CSF-hypocretin 1.

Conclusions: Although the patients with OSAS showed poorer quality of night sleep than narcoleptics, they had longer sleep latency and less SOREMPs on MSLT. The patients with OSAS represented lower frequency of HLA DQB1*0602 positive than those of narcolepsy and normal level of CSF-hypocretin 1. OSAS and narcolepsy seem to have clearly defined pathogenesis causing pathologic daytime sleepiness.

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The diagnostic value of CSF hypocretin-1 for narcolepsy in a Danish population of patients with narcolepsy, other sleep disorders, neurological disorders and healthy controls

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Background: Lack of the sleep/wake-regulating neuropeptide hypocretin-1 (hcrt-1) in the brain and the cerebrospinal fluid (CSF hcrt-1) is central in the pathophysiology of the severe sleep disorder, narcolepsy. Narcolepsy is mainly characterized by sleep attacks and cataplexy (atonia triggered by emotions) but can be difficult to diagnose. Low CSF hcrt-1 has therefore recently been proposed as a specific diagnostic tool for narcolepsy. No systematic Danish narcolepsy data exist, so it is unknown whether low CSF hcrt-1 is characteristic of Danish narcolepsy patients.

Aim and methods: Systematically investigation of CSF hcrt-1 in Danish narcolepsy patients and controls. We included 61 with narcolepsy ($\pm$ cataplexy), 18 other hypersomnias, 62 neurological controls and 27 healthy controls. All participants were lumbar punctured, CSF kept at $-80\,^{\circ}C$ until duplex-analysis by radio-immuno-assay (Phoenix Inc). Analysis was blinded to diagnose.

Results: The normal area of CSF hcrt-1 was defined as mean $\pm$ 2SD in normal controls ($430\,pg\,ml^{-1} \pm 94\,pg\,ml^{-1}$). Cut-off value defining low levels was $129\,pg\,ml^{-1}$ (30% of normal mean value). Significantly low CSF hcrt-1 was exclusively found in the narcolepsy group ($P < 0.0001$): 91% (41/45) of patients with cataplexy and 19% (3/16) without cataplexy (range $10–85\,pg\,ml^{-1}$).

Conclusion: The positive predictive value of CSF hcrt-1 in the diagnosis of narcolepsy in our Danish population is 100% and the negative predictive value is 86.6%. Our results confirm that low CSF hcrt-1 is specific for narcolepsy, but also confirm that normal levels do not exclude narcolepsy. The analysis will be introduced as an additional specific diagnostic tool for the disorder in Denmark.

Neurology

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Prevalence of sleepiness among adults with and without epilepsy in Georgia: preliminary findings

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Introduction: Excessive daytime sleepiness is common, occurring in 0.5–5.0% of the population and often accompanies epilepsy (1). Although few studies have been devoted to investigate sleep-related problems in Georgian general population, daytime sleepiness (DS) in this population is not identified; as epilepsy is detected in 0.57% of Georgian population, this study was aimed to investigate prevalence of DS in both healthy subjects and epilepsy outpatients.

Participants and methods: The non-paid volunteer 91 healthy subjects (18 males, 73 females) and 84 epilepsy outpatients (28 males, 56 females) with mean age 33.33 years (SD = 12.908), range 18–69 years, were asked to complete the Epworth Sleepiness Scale. The outpatients with diagnosis of epilepsy were divided into two groups: T, taking antiepileptic drugs (AEDs), 60 subjects (19 males, 41 females), and NT, 24 subjects (9 males and 15 females) currently not being on medication. Data analyses were performed by SPSS 13.0 for Windows.

Results: Eight individuals (8.8%) among healthy subjects and fourteen outpatients (16.7% out of total subjects with epilepsy) had DS. Percentage of T group individuals with DS prevailed healthy subjects having this problem (18.3% versus 8.7%; $P = 0.084$). The overall prevalence of DS in epilepsy patients was higher in males than in females (28.6% versus 10.7%; $P < 0.05$). Although there were no significant differences in DS between the NT (12.5%) and T (18.3%) outpatients, DS was more prevalent among males than females in the NT group ($P = 0.017$).

Conclusion: The findings of present study are in correspond with the reports indicating that DS frequently coexist with epilepsy, particularly during the treatment with AEDs. Unlike the healthy individuals the gender differences in DS were noted in epilepsy outpatients, in untreated individuals, in particular. Further research is needed to estimate prevalence of sleep and DS problems among Georgian general population as well as in patients with epilepsy.

Reference: 1. Malow, BA., Bowes RJ., Lin X. Predictors of sleepiness in epilepsy patients. Sleep, 1997, 20 (12):1105–1110.

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Agrypnia excitata: a thalamic-limbic disorder?

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Introduction: Agrypnia Excitata (AE) is characterized by loss of slow-wave sleep, oneirism and marked motor activation. AE was described in fatal familial insomnia (FFI), Morvan's fibrillary chorea (MC) and delirium tremens (DT). We describe the recurrence of AE in three cases.

Methods: All patients performed video-polisomnography. The first case was a sporadic Creutzfeldt-Jakob (sCJD) disease. 1H-MRS and neuropathologic examination showed thalamic involvement. Molecular studies revealed a VV2 sCJD subtype. The second case was a 71-year old male patient with a MC. He presented with severe weight loss, depression, burning legs pain, insomnia, excessive sweating and gait disturbance. Thoracic CT scan showed the presence of thymoma and laboratory investigations antibodies against acetilcholine receptor. Electromyography documented neuromyotonia and the absence of sympathetic skin responses (SSR). The third case was a 69-year-old male patient with a one-year clinical history of daytime somnolence, complex motor behaviour in sleep and mild dementia. 1H-MRS failed to show spongiform degeneration.

Results: Video-PSG documented in the first patient polygraphic data consistent with those of FI with alternating epochs of Wake/Wake-REM (55% of total recording time) and N1/N1-REM (45%) and subcontinuous motor activity (parcellar and segmental myoclonic jerks or more complex repetitive behaviours). Actigraphy showed an almost continuous motor activity. In the second patient PSG documented the presence of wake-stage for most (81.3%) of the time, intermixed with brief period of theta activity and rapid eye movements, and continuous motor activity. The patient was treated with plasmapheresis and immunoglobuline leading to significant improvement of insomnia, neuromyotonia and sleep pattern. In the third case the PSG showed the presence, for most of the recording (64.1% of total recording time), of sleep pattern consistent with that of FI. PSG also documented subcontinuous motor activity (myoclonic parcellar and segmental jerks) in all stages.

Conclusion: Agrypnia excitata may characterize different neurological diseases and offers some interesting issues for discussion on involvement of thalamic-limbic-cortical circuits in neurophysiology of sleep.

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Rhythmicity of epileptic seizures over a 24 h day, detected by intracranial EEG-electrodes

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Background: Up to now evidence that the occurrence of seizures is influenced by time of day or circadian rhythm is limited. In humans, all studies give data only on wake or sleep or are limited to sleep stages. In a previous study we differentiated more exactly the occurrence of seizures within the 24 h day using superficial EEG recording. The current study aims to describe the rhythmicity of epileptic seizures over the 24 h day using intracranial EEG recording.

Patients and methods: In 25 patients intracranial EEG-data was obtained after placing intracranial grid electrodes. Seizures were documented during longterm video and intracranial EEG registration (at least 40 h). A seizure was defined as a clinical and electroencephalographic epileptic event over at least 5 seconds. We noted the details of the epileptic seizures, the moment of the 24 h day and whether the patient was awake or asleep during the seizure.

Results: In total 316 seizures were assessed, of which most seizures occurred during the periods of 2–8 h (26%) and 14–20 h (32%). Of all seizures, 37% was of frontal origin, 38% of temporal, 12% of unknown and 13% of other origin. Complex partial seizures were seen mainly in the period from 14–20 h (35%) and generalized seizures from 2 to 8 h (37%). In wake patients seizures occurred mainly from 14 to 20 h (47%) and in patients asleep or just out of sleep most seizures were documented during the night (2–8 h, 42%).

Conclusion: To our knowledge this is the first study with intracranial EEG recordings that differentiates the occurrence of epileptic seizures within the 24 h day. Most seizures were seen in the periods 2–8 h and 14–20 h. Differentiated for wake and sleep, nearly half of the seizures in wake patients occurred from 14 to 20 h. In patients asleep or just awake seizures mainly occurred from 2 to 8 h. Most complex partial seizures were recorded from 14 to 20 h and generalized seizures at night (2–8 h). For the other epileptic seizures rhythmicity was not evident.

Acknowledgement: The patients were discussed in the Dutch Epilepsy Surgery Group by neurologists from the Epilepsy Centres in Heeze, Oosterhout, Heemstede and Zwolle. Recordings were performed in the University Medical Centre Utrecht (Drs. Leijten and van Reijen).

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Sleep actigraphy in brain injured patients with chronic low functioning upper limb hemiparesis

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Introduction: Few studies have used actigraphy to examine sleep behaviour in brain injured patients with chronic hemiparesis. This is possibly due to suggestions that actigraphy recordings in those with motor difficulties are likely to produce inaccurate sleep/wake detection (Sadeh and Acebo, 2002). However, actigraphy provides a favourable alternative to PSG when observing long term sleep behaviour. Therefore, we aimed to further validate the use of actigraphy in low functioning hemiparetic patients by comparing subjective sleep diaries (SD) with actigraphy recordings to examine: 1) concordance between SD and actigraphy, and 2) the relationship between motor deficits and activity.

Method: Twelve patients with chronic upper limb hemiparesis (>12 months) completed SDs and wore an actiwatch (Cambridge Neurotechnology Ltd.) on the non-affected wrist for two weeks. Residual motor ability was assessed through a series of neurobehavioural motor tests.

Results: Comparison of SD and actigraphy revealed significant dissociations between final wake time, sleep efficiency, number and duration of night awakenings. Good concordance between SD and actigraphy was found for retiring time, get up time, time in bed, total sleep time and sleep onset latency. Mean activity counts, during the day or night, were not associated with residual motor ability.

Discussion and Conclusion: Actigraphy of the non-affected wrist, in conjunction with SDs, are a valid apparatus for assessing long term sleep behaviour in patients with hemiparesis. The results are in line with previous studies in healthy persons without motor difficulties whereby SDs and actigraphy correlate well, apart from parameters which rely on subjective night time awakenings (Lockley et al. 1999). The latter can only be determined by PSG studies.

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Paroxysmal nocturnal behaviours in extrapyramidal diseases: not only RBD

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Paroxysmal sleep disruptive nocturnal behaviours (PSDNB) are frequently reported in subjects affected by extrapyramidal diseases, REM sleep behaviour disorder episodes (RBD) being reportedly the most frequent ones. Less is known about the occurrence and features of NREM arousal-related paroxysmal episodes (NREM-PA) in these disorders. We studied 95 subjects [71 PD, 10 LBD, 13 MSA, 4 PSP, 2 Parkinsonian syndrome; 61 M; mean age 67.3 ± 8.4 (range 41–86)]on dopaminergic treatment, with and without anamnestic report of PSDNB, coming to the Sleep Laboratory from the Motor Disorders Unit of our Institute in a one year period. A full night video-PSG caught PSDNB in 52 patients, with a pattern of RBD (45 cases), NREM-PA (9 cases), alone or in overlapping. The NREM-PA consisted of episodes either mimicking RBD or showing a complex symptomatology including wandering, disperceptive phenomena or aggressive and sex behaviours. The 52 patients with PSDNB were compared to a subgroup of patients with PSG and clinical history negative for any PSDNB, with respect to demographics (age; sex), clinical features (type, age at onset, duration of the disease; MMSE score, BECK depression inventory questionnaire score, Epworth Sleepiness Scale score) and sleep comorbidities (Sleep disordered breathing, Periodic Limb Movements). The patients with PSDNB were characterized by higher frequency of cognitive decline (MMSE score below 24, 25.5% versus none, $P<0.05$), overrepresentation of men (67.3% versus 33.3%, $P<0.05$), higher prevalence of sleep disordered breathing (25.0% versus 6.7%). The prevalence of NREM-PA in patients with SDB was three times as high as in patients without SDB (30.7% versus 12.8%). In four of the nine patients (44.4%) with NREM-PA, the episodes occurred upon arousals at the end of apneic events. RBDs represent the most commonly encountered nocturnal motor-behavioural paroxysmal episodes in extrapyramidal diaseases. However the occurrence of NREM arousal related motor behavioural paroxysmal episodes, alone or in overlapping with RBD, is not negligible and should be taken into account. The profile of patients at risk of PSDNB seems to be one of male subjects with cognitive decline and co-morbid sleep pathologies, namely SBD which seems to trigger, in a proportion of cases, NREM-PA.

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Sleep characteristics in the non-convulsive status epilepticus: report of four cases

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Purpose: To determine the sleep characteristics in the non-convulsive status epilepticus (NCSE).

Background: NCSE is defined by prolonged loss of awareness and epileptiform activity on electroencephalogram. There are several types of NCSE depending of the clinical and electroencephalographic manifestations: generalized (typical or atypical absence status, status epilepticus during sleep) and partial (complex partial and simple partial status epilepticus). Little information is available on the interrelation of sleep characteristics and NCSE.

Methods: To distinguish from continuous spikes and waves during slow sleep (CSWS) and to clarify the sleep characteristics of the NCSE; all four patients were recorded during full night prior to treatment. Recordings were done using an Embla Recording Systems with somnologica software (Medcare, Reykjavik, Iceland) which was included continuous video-EEG monitoring and polysomnography.

Results: Prior to treatment in NCSE, total sleep times were decreased, sleep latencies were decreased, the percentages of stage 1 and 2 were increased, the percentages of stage 3, 4 and REM were decreased, the percentages of wake after sleep onset (WASO) were increased and sleep efficiencies were decreased. All of these sleep characteristics were returned to normal values at the end of first week of treatment.

Conclusions: NCSE is not uncommon and comprises at least one-third of all cases of SE. Making the diagnosis of NCSE is diffucult and NCSE must be distinguish from CSWS using by continuous video-EEG monitoring and full night polysomnography. This monitoring is going to give valuable information about sleep characteristics of NCSE also. This study demonstrated that sleep structure was markedly abnormal in the NCSE during ictal period. We have no enough information about sleep characteristics of NCE yet. But, larger studies which are going to do same protocol, are

going to give more information about sleep characteristics of NCSE.

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Neuropsychological profile of mild cognitive impairment in patients with REM sleep behavior disorder

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Introduction: REM Sleep Behavior Disorder (RBD) may precede the onset of Mild Cognitive Impairment (MCI) and Dementia with Lewy Bodies (DLB), but not Alzheimer's disease. Neuropsychological profile in DLB is characterized by visuoperceptive and executive dysfunction. DLB is preceded by MCI. It is unknown which is the MCI pattern of those patients previously diagnosed with idiopathic RBD, and if such a cognitive pattern is similar to that is observed in DLB.

Patients and methods: We identified 15 patients with idiopathic RBD that later developed MCI with a mean age of 72.4 years. An extensive neuropsychological battery that included five main cognitive areas (memory, language, praxis, visuoperceptive functions and executive functions) was administered. Results were compared with normative data.

Results: Eleven patients (73.3%) presented visuoperceptive dysfunction. In five of them this was the only cognitive domain affected. In the other six patients other domains were impaired: 2 patients failed in memory, 1 in executive functions, 1 in both memory and language, 1 in praxis, and 1 in both executive functions and praxis. In the remaining 4 patients neuropsychological profile was the following: 1 patient with executive dysfunction, 1 patient with memory impairment, 1 patient with amnestic, executive and language deficit and 1 patient with executive and memory failure. Memory impairment was characterized by free short term memory recall deficit that benefited from semantic clues.

Conclusion: In most MCI patients with associated RBD, visuoperceptive function is altered. Also, other cognitive domains are impaired, particularly memory and executive functions. This cognitive profile is similar to what is seen in DLB and different from Alzheimer's disease.

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Sleep disorders in an epilepsy monitoring unit

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Aim: Although inpatient video-EEG monitoring is mainly used for epilepsy evaluation, it is also sometimes used to assess sleep disorders. The purpose of this study was to focus on two groups of patients referred by neurologists to the video-EEG monitoring unit. The first group of patients were referred for 'sleep studies' to confirm or exclude a sleep disorder. The second group of patients were referred because of uncertainty regarding a diagnosis of epilepsy.

Methods: We reviewed the diagnoses of all adult patients, who underwent inpatient video-EEG monitoring at Southern General Hospital, Glasgow over an 11 year period.

Results: In total, 1120 inpatient video-EEG monitoring sessions were done. 701 (63%) sessions were diagnostic studies. 386 (34%) sessions were presurgical evaluations. There were 33 (3%) sleep studies (Group 1). 8 patients had normal studies, 7 had inconclusive studies, 6 had narcolepsy, 3 had REM sleep behaviour disorder (RSBD), 3 had idiopathic hypersomnolence, 2 had confusional arousals, 2 had periodic limb movement disorders (PLMD), 1 had sleep-related rhythmic movement disorder and 1 had hypersomnolence post stroke. Of the diagnostic studies, 12/701 (2%) had sleep disorders (Group 2). 2 patients had narcolepsy, 2 had propriospinal myoclonus at sleep-wake transition, 3 had confusional arousals, 2 had night terrors, one had excessive daytime sleepiness secondary to poor nocturnal sleep, one patient had PLMD and one had probable RSBD. 4/12 (33%) of patients in group 2 were on anti-epileptic medication at the time of referral.

Conclusions: A small percentage of patients were referred by neurologists for 'sleep studies' in our video-EEG monitoring unit. 2/3rds of these patients were diagnosed to have a sleep disorder. In the other group of patients where the referring physician was unsure of the diagnoses, various sleep disorders were diagnosed in a small percentage of patients.

P38

Sleep correlates of motor recovery in chronic stroke: a pilot study using sleep diaries and actigraphy

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Introduction: Sleep facilitates neuroplasticity (Tononi & Cirelli, 2006), an important process for post-stroke recovery, particularly when re-learning motor skills. Associations between poor sleep and poorer recovery during the acute phase have been reported (Good et al. 1996; Gottselig et al. 2002). In addition, increased subjective sleep needs have been associated with poorer outcome during the chronic phase (Hermann, et al. 2008). However motor recovery, which is of particular relevance for sleep dependent neuroplasticity, has not been addressed. We aimed to investigate sleep behaviour in the context of motor recovery within a homogenous stroke patient sample during the chronic phase.

Method: Twelve patients with chronic upper limb hemiparesis (>12 months) completed sleep diaries (SD) and wore an actiwatch (Cambridge Neurotechnology Ltd.) for two weeks. The SD included twice daily Karolinska Sleepiness Scale (KSS) and Daily Fatigue Scale (D-FIS) measures. Residual motor ability was assessed through a series of neurobehavioural motor tests.

Results: Increasing daytime nap length (SD and actigraphy) significantly correlated, or by near significant trend with better motor ability on all neurobehavioural tests. Age was not associated with napping behaviour or residual motor ability. Chronicity, psychological adjustment, health, or nocturnal sleep did not correlate with napping behaviour (SD and actigraphy) or motor ability. Furthermore, increased subjective fatigue was associated with increased napping behaviour.

Discussion and Conclusion: Patients who habitually napped had better residual movement ability at least one year after stroke. It may be that the benefits of napping facilitate performance as well as consolidating motor learning. This has been shown in healthy persons (Backhaus & Junghanns, 2006; Nishida & Walker, 2007) which may translate into motor skill re-learning during stroke recovery. Although the data is suggestive, previous rehabilitation and medical care will contribute to residual motor ability in addition to the reported napping behaviour, therefore further clarification is required.

P39

The implication of nigrostriatal dopaminergic degeneration in the pathogenesis of REM sleep behavior disorder

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Involvement of dopaminergic system has been hypothesized in the pathogenesis of REM sleep behavior disorder (RBD) because of its

frequent association with Parkinson's disease (PD). We tried to find out abnormality of dopamine transporter (DAT) density in patients with RBD. Also, we investigated the relationship of DAT density with polysomnographic RBD scores among RBD patients. Fourteen patients with RBD (11 men, 3 women; mean age 66.6 ± 4.5 yr), 14 patients with Parkinson's disease (11 men, 3 women, 67.0 ± 4.1 yr) and 12 normal controls (8 men, 4 women, 63.3 ± 5.7 yr) were included in the study. The diagnosis of RBD was confirmed on polysomnography. All the participants performed single-photon emission computed tomography (SPECT) imaging 3 h after injection of [123I]FP-CIT. During REM sleep, each 30-second epoch was rated as "tonic" when there was at least 50% of tonically maintained chin electromyographic (EMG) activity in the epoch. Phasic EMG density was represented as the percentage of EMG bursts (leg and chin, separately) in each 3-second REM mini-epoch. The RBD patients showed a trend of lower binding in the striatum than normal controls (3.24 ± 1.02 versus 3.97 ± 0.76, $P = 0.07$), but the significance was revealed only in the putamen (2.82 ± 0.92 versus 3.61 ± 0.64, $P = 0.02$). In 11 individual cases of 14 RBD patients, the DAT finding still remained within normal range. In comparison between RBD and PD patients, DAT bindings of the whole striatum and all subregions in RBD patients were significantly higher than those in PD groups. Meanwhile, caudate to putamen uptake ratio (C/P ratio) in RBD patients was negatively correlated with the severity of RBD by means of phasic leg-EMG activity ($r = -0.59$, $P = 0.027$). Nigrostriatal dopaminergic degeneration could be a part of the pathogenesis of RBD, but not essential for the development of RBD. The reverse correlation between the severity of RBD and rostrocaudal gradient might suggest that another pathogenic process not related with nigrostriatal dopaminergic transmission could be implicated in RBD.

P40

REM sleep behaviour disorder (RBD) and its associations in young patients: a case series from the United Kingdom

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Study objectives: REM sleep Behaviour Disorder (RBD) is a neurological disorder mainly known through its relationship with the synucleinopathies in middle aged patients. In contrast there is much less data concerning its development, evolution, and association with other disorders in younger patients.

Design: Patients Review of the units' data base for patients with RBD diagnosed over the last 7 years. Ninety one patients were separated into two groups according to their age (< 50 and ≥ 50) at time of diagnosis. Clinical and polysomnographical data were reviewed.

Results: Sixty two were male; mean age was 52 y (SD ± 19). 39 were < 50. In both groups the majority of the patients had the idiopathic form of RBD (51.2% group < 50, 63.4% group ≥ 50). The secondary form was associated in 38.4% with narcolepsy in the group < 50 and in 28.8% with a synucleinopathy in the group ≥ 50. Associations were noted between RBD and non-REM parasomnias, antidepressants, atenolol and Palatal myoclonus with ataxia syndrome.

Conclusions: In a population of patients with RBD more than a third of patients were < 50 y at time of diagnosis. Narcolepsy is the major cause of secondary RBD whilst Parasomnia overlap syndrome of idiopathic RBD in patients < 50 years.

P41

Clinical and epidemiologic features of patients with sleep complaints evaluated at two academic neurology services in Rio de Janeiro, Brazil

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Background: Sleep disorders have a high incidence and prevalence in general population, and are associated with poor quality of life, clinical diseases, and accidents. Although most physicians are not familiar with sleep disorders.

Objective: Our objectives were to describe the prevalence of sleep disorders in two specialized university centers, and identify the association between demographic data and health conditions.

Methods: We studied 100 sequential patients of the Sleep Disorders Clinic of the Antônio Pedro University Hospital between July 1999 and October 2002 and 459 patients seen at the Estácio de Sá University Sleep Institute between August 2001 and October 2002. Demographic data collected included age, gender, color, marital status, years of formal study, alcohol use, drug use, and social position. Sleep and psychiatric disorders were classified using the international classification of sleep disorders DSM-IV respectively. Comorbid conditions were also collected. Adhering to formal guidelines concerning formal indications, 294 polysomnography exams were performed. We analyzed the association between sleep disorder diagnoses and the other variables, using the chi-square distribution test.

Results: This study represents the first descriptive epidemiologic and clinical analysis of a large cohort of Rio de Janeiro patients that were referred or presented spontaneously to two university services specialized in sleep disorders. We found that 1) sleep breathing disorders and insomnia were the most prevalent in our patients (64.9% and 24.9%); 2) the prevalence of sleep disorders is similar to that found in the literature; 3) insomnia is related to alcohol use in 21.9% and symptoms of depression im 25.8% ($P < 0.01$) and; 4) drugs use, academic degree and skin color did not represent significant differences in relation to the variable diagnosis ($P > 0.05$); 5) Alcohol use, sex, marital status, age and social class represent significant impact when related with the variable diagnosis ($P < 0.01$); 6) Obstructive sleep apnea was diagnosed in 73.8% of individuals with hypertension ($P < 0.01$).

Conclusions: These findings give a solid base to future considerations and comparison with future studies about sleep disorders epidemiology in Rio de Janeiro.

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Psychogenic hypersomnia or pseudo-narcolepsy: a parallel with psychogenic pseudo-epileptic seizures?

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Background: Hypersomnia and unvoluntary daytime naps are a frequent complaint in a regular sleepcentre. Obstructive sleep apnea and periodic limb movements in sleep can easily be excluded by ambulant polysomnography. The diagnosis of narcolepsy can be made by the multiple sleep latency test (MSLT). When these investigations are reported normal, despite high scores on the Epworth Sleepiness Scale, this may indicate a psychogenic disorder and require further video/polysomnography.

Results: We report two cases with hypersomnia, frequent daytime naps, and kataplexia-like symptoms suggesting narcolepsy. On registration both patients appeared to be fully awake during their self-reported naps, and showed no signs or symptoms of narcolepsy on the MSLT. One patient even showed feigned kataplexy attacks. A video/polysomnography fragment of a pseudo-nap can be

shown. The underlying psychopathological mechanism of pseudo-narcolepsy and the parallel with psychogenic non-epileptic seizures will be discussed. Also a comparison with pseudo-hypersomnia associated with bilateral paramedian thalamic lesions and psychiatric hypersomnia will be made.

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Neuropsychological assessment of 50 patients with idiopathic REM sleep behavior disorder

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RBD is strongly associated with neurodegenerative diseases, such as Parkinson's disease (PD) and dementia with Lewy bodies (DLB). Symptoms of RBD often precede the development of these neurodegenerative disorders by several years. Studies have demonstrated waking EEG slowing and decreased cerebral blood flow in patients with idiopathic RBD, suggesting that this parasomnia might be associated with cognitive impairment. The aim of this study was to assess cognitive functioning in a large cohort of patients with idiopathic RBD. Fifty patients meeting polysomnographic criteria for idiopathic RBD (39 men; mean age, 67.12 ± 8.38; mean education, 12.50 ± 3.96) and 32 healthy subjects (22 men; mean age, 67.22 ± 6.73; mean education, 13.56 ± 3.82) underwent an extensive neuropsychological evaluation. None of the subjects had dementia according to DSM-IV criteria and no patients had an MMSE of < 27. Student *t*-tests were used to assess between-group differences. Compared to controls, patients with idiopathic RBD showed a poorer global cognitive functioning as assessed by the Dementia Rating Scale ($P = 0.001$). Moreover, RBD patients had lower performances compared to controls on tests measuring executive functions, attention and speed processing [Trail making test part B ($P = 0.001$), letter ($P = 0.003$) and semantic ($P = 0.05$) verbal fluency, Similarities ($P = 0.01$), Coding ($P = 0.04$), and Digit span ($P = 0.02$)]. RBD patients showed also poorer performance compared to controls on verbal memory [Rey auditory verbal learning test ($P = 0.004$) and Logical stories part A from the WMS-III ($P = 0.05$)] and a visuospatial task [Block design from WAIS-III ($P = 0.05$)]. This study shows that patients with idiopathic RBD often have cognitive impairment similar in nature to that found in early stages of PD and DLB. Long-term follow-up of patients with idiopathic RBD is needed to verify if the presence of subtle cognitive impairment is a risk factor for the development of neurodegenerative disease in RBD.

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Idiopathic REM sleep behavior disorder is not always associated with decrease in cardiac 123I-MIBG radioactivity

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Objective: To evaluate the consistency of decrease in cardiac iodine-123 metaiodobenzylguanidine (123I-MIBG) radioactivity in idiopathic REM sleep behavior disorder (RBD) and its relation to the pattern of progression of RBD symptoms.

Background: Decreased cardiac uptake in 123I-MIBG scintigraphy has been considered one of the possible markers of Lewy body diseases (Parkinson's disease (PD) and dementia with Lewy bodies (DLB)), representing sympathetic cardiac denervation. This finding has been also reported in idiopathic RBD, which partly supports the assumption that RBD could be as one of the possible early markers of PD and DLB. However, this does not explain the fact that nearly all patients with multiple system atrophy have been reported to be accompanied with RBD or REM sleep without atonia (RWA) on polysomnography (PSG).

Methods: Cardiac sympathetic denervation was examined using cardiac 123I-MIBG scintigraphy in consecutive 13 patients (10 men and 3 women, 67 ± 5.4 years of age) with various durations (from one to 20 years) of idiopathic RBD. Diagnosis of RBD was based on clinical characteristics (dream-enacted behaviors and sleep talk) and confirmed by PSG with video recording, demonstrating at least jerky limb movements and/or sleep talk associated with RWA.

Results: The early heart-to-mediastinum uptake ratio (H/M ratio) of cardiac MIBG uptake was overall decreased (1.51 ± 0.24), ranging from 1.2 to 2.0. In one patient H/M ratio is within normal limits. There was no correlation between H/M ratio and the duration of RBD, nor the present severity of RBD.

Conclusion: Myocardial accumulation of 123I-MIBG has been decreased in most, but not all, of idiopathic RBD patients.

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Normal levels of CSF hypocretin-1 and daytime sleepiness during attacks of relapsing-remitting multiple sclerosis and monosymptomatic optic neuritis

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Background: There is emerging evidence that multiple sclerosis (MS), the hypothalamic sleep-wake regulating neuropeptide hypocretin-1 (hcrt-1) and the sleep disorder narcolepsy may be connected. Thus, the major pathophysiological component of narcolepsy is lack of hcrt-1. Dysfunction of the hypocretin-system has been reported in MS case reports with attacks of hypothalamic lesions, undetectable CSF hcrt-1 and hypersomnia, but not found during remission in small samples. Finally, daytime sleepiness, the major symptom of narcolepsy, is reported in several MS populations, and there are case reports of co-existent narcolepsy and MS. However, it is unknown if hcrt-1 and daytime sleepiness generally change during MS attacks.

Aim and methods: The aim was to analyze whether daytime sleepiness (using Epworth sleepiness scale (ESS)) and CSF hcrt-1 levels differ between MS attack and remission phase. Forty-eight consecutively referred patients with relapsing-remitting MS (RRMS) or monosymptomatic optic neuritis (MON) were included. The age range was 21–57 years, range of disease duration was 0.1–228 months and range of expanded disability status score (EDSS) was 0–5.5 with a mean EDSS of 3.15 ± 1.75.

Results: Twenty-seven patients were in attack and 21 in remission. ESS was normal both during attacks (5.4 ± 3.0) and remission (5.8 ± 2.6), and mean CSF hcrt-1 was normal ($456 \pm 41\ \mathrm{pg\,ml^{-1}}$). No statistically significant differences in ESS or CSF hcrt-1 were found between attack and remission ($P = 0.70$, $P = 0.64$). MRI scans revealed no hypothalamic lesions.

Conclusion: The results show that the hypocretin-system is intact and sleepiness is not typical in RRMS and MON without hypothalamic lesions on MRI.

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A man who rocks himself awake

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Rhythmic movements in association with sleep or sleep onset are not uncommon in children. We report a case of a 32 year old man whose childhood onset sleep related movement disorder persists, causing diagnostic difficulty and proving resistant to therapy. Rocking movements at night were first reported by his mother in infancy. Movements continue to occur intermittently throughout the night and may be vigorous enough for him to fall out of bed. They may waken him, or can be aborted by someone awakening him. The frequency decreases during summer months and if he sleeps during the day, so he now works night shifts. He is also reported to shout out and grind his teeth. He can awake having bitten his arms and tongue. He often finds it difficult falling asleep, and occasionally experiences sleep walking and vivid dreams. There is a family history of night terrors. At the age of 27, witness accounts of jerking led to a diagnosis of juvenile myoclonic epilepsy. Treatment with sodium valproate was ineffective. Neurological review suggested a diagnosis of frontal lobe epilepsy or sleep disorder. A trial of clonazepam and various anticonvulsants, antidepressants, anxiolytics, hypnotics and other sleep modifying drugs were ineffective. Lamotrigine reduced the frequency of rocking but increased vivid dreaming and sleep walking. Investigations included normal MRI and EEG. In 2007 he was admitted to an Epilepsy Assessment Unit for overnight video-EEG monitoring. Typical side to side body rocking was seen exclusively in REM sleep and a diagnosis of REM sleep related movement disorder was made. Although relieved to be told he does not have epilepsy, his sleep disorder remains resistant to treatment. Sustained relationships are difficult and he now lives apart from his partner and child. Review of the literature reveals very few similar cases of early onset rhythmic movement disorder persisting to adulthood and there is little information on effective treatment.

P47

Epilepsy is a major risk factor for disturbed sleep

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Background: Sleep and epilepsy have many interactions, for example epilepsy syndromes with seizures only during sleep, higher frequency of seizures after sleepdeprivation, etc. Intuitively, patients with active epilepsy often have disturbed sleep, but systematic studies in this respect are scarce and regard limited numbers of patients.

Setting: Teaching hospital and tertiairy epilepsy clinic.

Patients and Methods: 486 Patients with active epilepsy were compared to individually matched controls. Sleep was assessed using validated questionnaires on sleep quality, sleepiness (ESS) and Quality of Life (QoL, SF-36).

Results: Over the last 6 months sleep was disturbed for 39% of the patients with epilepsy and in 18% of the controls ($P<0.001$). The patients were more sleepy during daytime. Patients with abnormal sleep had lower QoL than patients with similar epilepsy but no sleepdisturbances ($P<0.001$).

Conclusion: Epilepsy patients have a prevalence of disturbed sleep twice that of controls. This might be due to anti epileptic drugs, but this factor is probably of low importance. The underlying encephalopathy may be more important for the co-existence of epilepsy and sleepdisorder. Furthermore, epilepsy patients have primary sleepdisturbances just like patients with no epilepsy.

Parasomnias-Other Sleep Disorders

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Prevalence of possible parasomnias in the general population

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Introduction: Parasomnias are undesirable physical events or experiences that occur during entry into sleep, within sleep, or during arousals from sleep. The prevalence of many of the parasomnias is unclear, since there are few population-based epidemiological studies.

Methods: Population based cross sectional study. 1000 randomly selected adults (51% female), 18 years and above, participated in a telephone interview in Norway, employing the next birthday technique. Mean age was 47.0 years (SD = 17.6, range = 18–96 years). The respondents were asked about lifetime prevalence and current prevalence, the latter defined as having experienced the parasomnia at least once during the last three months.

Results: Lifetime prevalence of sleep walking was 22.4% and current prevalence 1.7%. Confusional arousal: 18.5% lifetime and 6.9% current prevalence. Sleep terror: 10.4% lifetime and 2.7% current prevalence. Nightmare: 66.2% lifetime and 19.4% current prevalence. Sleep related eating disorder: 4.5% lifetime and 2.2% current prevalence. Sleep related groaning: 31.3% lifetime and 13.5% current prevalence. Dream enactment: 15.0% lifetime and 5.0% current prevalence. Injured yourself during sleep: 4.3% lifetime and 0.9% current prevalence. Injured somebody else during sleep: 3.8% lifetime and 0.4% current prevalence. Sexual acts during sleep: 7.1% lifetime and 2.7% current prevalence. Sleep talking: 66.8% lifetime and 17.7% current prevalence.

Conclusion: This is one of few population based studies investigating the prevalence of different parasomnias. The data suggest that several parasomnias are highly prevalent in the general population. Caution in the interpretation of the data is suggested due to methodological issues, i.e. single questions, telephone interview etc.

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Maternal beliefs and expectations about infant sleep: relationships with inset of postnatal depression

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Background: Literature suggests that mothers are ill prepared for sleep problems in the infant. Mothers of infants are at increased risk of post natal depression, even within the first few weeks, if their baby is difficult to settle. This research aimed to examine antenatal expectations of infant sleep patterns (and explore the extent to which these expectations match what is experienced after the child is born). The study assessed whether any differences found between expected and actual experiences are associated with postnatal depression in the first few weeks of life.

Methods: First time mothers in Adelaide, South Australia are asked to complete questionnaires (Edinburgh Post Natal Depression Scale, Sleep Expectations Scale, Generalised Self Efficacy questionnaire) and describe infant sleep patterns one month before birth (Stage 1) and 6 and 12 weeks after birth. Pre and post expectations and infant sleep pattern measures will be compared and their contribution to the emergence of depression examined.

Results: Ten mothers [mean age 25.9 (SD = 3.6)y] have to date completed stage 1. Preliminary analyses of stage 1 data suggest that mothers expect: their sleep to be disrupted that their baby will go back to sleep fairly quickly without needing help to be happier than they have ever been that they will have significant support from their partners. Stage 2 and 3 data have not been collected at time of going to press.

Conclusions: Preliminary data suggests that mother's expectations of their child's sleep and their well being may be untenable and unprepared for difficulties in the first few months of life.

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Sleep-related eating disorder: polysomnographic features in eleven patients

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SRED is characterized by recurrent episodes of involuntary eating and drinking ocurring during the main sleep period. It is a heterogeneous syndrome combining both eating and sleeping disorders. The recent revision of the ICSD (2005) has stablished new diagnostic criteria for SRED and has classified it as a parasomnia. Three males and eight females with age ranged from 30 to 57 years, underwent clinical test and videopolysomnographic (vPSG) recordings carried out according to standard methods. All patients referred a chronic course of the disorder-often since the adolescence-triggered by a stressful life event. The majority of our patients had a psychiatric profile (mainly depressive-ansioux disorder). Three of them were members of the same family. vPSG studies captured a variable number of awakenings from both, NREM (more frequently) and REM sleep which were followed by food intake. All eating episodes occurred during EEG-defined wakefulness and patients appeared to be awake and conscious. All patients were able to remember these episodes the next morning. Only in one case we observed partial awareness during a first nocturnal episode and normal consciousness during a second one. EEG activity recorded was characterized by delta activity and normal alfa activity, respectively. The patient recalled a single episode the next morning. All the patients presented a fragmented sleep, with increased number of arousals and time spent awake. Additionaly, we observed increased NREM light sleep and decreased NREM deep sleep and sleep efficiency index. Respiratory disturbance index was increased in five patients and periodic movement index of lower limbs was pathological in three patients. To conclude, we can say: SRED is a heterogeneous syndrome with variable consciousnes during nocturnal episodes and variable association with other sleep disorders. We observed a female predominance, comorbidity between SRED and mood disorders and a strong familial aggregation in our patients. vPSG recording allows confirmation of the clinical diagnosis and offers essential information to better characterize this disorder.

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Arousals and nocturnal groaning

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Introduction: Nocturnal groaning is a rare sleep disorder currently classified as a parasomnia. It is characterized by monotonous vocalization during prolonged expiration, occurring in clusters and prevailing during REM sleep. Daytime consequences are unknown and it is considered to be more social than health problem.

Objective: To evaluate sleep macrostructure and microstructure, frequency and duration of groaning episodes, their sleep stage distribution and their connection with arousals.

Patients and methods: During a 6-year period we evaluated 8 patients with nocturnal groaning (5 male, 3 female, age range 11–32 years, mean age 23 ± 7,1). Patients underwent standard neurologic examination and nocturnal videopolysomnography for 2 consecutive nights. The second night polysomnography data were used to evaluate sleep parameteres. Groaning episodes (bradypneic episodes) were counted separately not as clusters.

Results: Sleep macrostructure did not reveal any significant changes. Number of groaning episodes during the night varied from 40 to 182 (total number 725). Duration of bradypnea was from 2 to 46 sec (mean duration 12.5 sec). Episodes prevailed in REM sleep (76.5%). In NREM 2 sleep 21.5% of episodes was present and only sporadic episodes in delta sleep were noted (1,9%). 63% of groaning episodes were associated with arousals or awakenings. Arousal index (AI) was increased in 5 patients (mean AI 20.4). Bruxism was present in 4 cases, in 1 patient appearing in a close association with groaning episodes. Ronchopathy was noted in 4 cases.

Conclusion: Almost two thirds of groaning episodes were connected with arousals or awakenings. We can hypothetise that nocturnal groaning might be a source of sleep disruption in some cases.

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Clinical, neurophysiologic and treatment aspects in patients with nocturnal eating syndrome

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Background: NES has a prevalence of 1.5% in the general population (Rand et al. 1997), 12.3% in psychiatric outpatient population (Lundgren et al. 2006), 5.8% in insomniac referrals (Manni et al. 1997), and 9% to 28% among extremely obese patients seeking bariatric surgery (Rand et al. 1997). The association with increased weight and periodic limb movements has been recognized (Manni et al. 1997). The eating episodes arise most frequently after complete awakening from stage 2 NREM (Vetrugno et al. 2006).

Objectives: 1. To describe clinical and neurophysiologic characteristics of night eating episodes; 2.To compute the correlation between clinical and neurophysiologic parameters.

Methods: Study of outpatients prospectively enrolled in a sleep center using Videopolysomnographic (VPSG) recordings and sleep questionnaires (Stanford, Pittsburg, Epworth (ESS).

Results: 23 patients were evaluated in 2007/8; 57.9% were women, mean age 45.9 years (17 years to 70 years). 25% had psychiatric complaints (depression, panic disorder, anxiety) and were medicated with psychoactive substances. Main complaints were: difficulty falling asleep (42%), awakenings (47% in the first half of the night and 42% in the second half), and fatigue (57.9%). Mean Body Mass Index was 28.2 Kg m^{-12} (20 Kg m^{-12} to 42.6 Kg m^{-12}). Mean ESS was 12 (0 to 21). VAS-comparison to current sleep = 3.7 ± 1.5, VAS-morning vigilance = 4.9 ± 2.8. Sleep latency = 25.6 ± 20 min. Sleep efficiency = 84.5 ± 5.7. N1 = 13.8 ± 8.3%; N2 = 53.9 ± 11.2%; N3 = 18.2 ± 6.6%. Mean REM latency = 114.8 min; REM = 14.3 ± 6.0%. PLMS-I = 10.1 ± 6.7. No sleep apnea or O2 desaturations. 90% had eating episodes during the VPSG. Most arise from stage N1 or N2. In one 1 subject they arise from N3 and REM. All patients were conscious of the episodes. Treatment included antidopaminergics for PLMS. 80% improved from sleep complaints, eating episodes and some reduced weight.

Conclusions: All our patients had complete recall of the episodes of night eating in laboratory as well as at home. The episodes arose mainly from NREM, with full consciousness. Nearly all patients had PLMS, the PLMS-I was high and PLM treatment improved both, the movement and eating disorders, raising questions upon common pathogenic pathways. SRED, PLMS.

Restless Legs Syndrome

P53

Role of melatonin on the worsening of RLS symptoms at night

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Introduction: A recent study conducted in our laboratory showed that melatonin secretion started approximately two hours before the worsening of restless legs syndrome (RLS) symptoms at night and could perhaps explain their circadian variation. The aim of this study was to verify the hypothesis of direct involvement of melatonin in this phenomenon. The effects on RLS symptoms of melatonin administration and conversely those of its suppression by exposure to bright light were studied.

Methods: Eight RLS subjects (2 men, 6 women, mean age = 53.3 ± 9.1 years) were studied in three conditions. First, the control condition allowed to measure the PLMS index and the severity of the sensory and motor symptoms during the Suggested Immobilization Test (SIT). The second and third conditions were the administration of melatonin (3 mg at 7:00 pm) and the exposure to bright light (3000 lux from 7:00 pm to midnight), respectively. These two experimental nights were separated by one week and the order of those conditions was inverted for half the subjects. The SIT was administered twice for each condition: before the habitual appearance of symptoms (from 7:30 pm till 8:30 pm) and after (from 11:00 pm till 00:00 am).

Results: The administration of exogenous melatonin and exposure to bright light did not significantly influence sleep architecture, PLMW, PLMS or the sensory symptoms experienced during the SIT. However, a difference on motor symptoms during the first SIT was observed between the two experimental conditions (exogenous melatonin increased the number of leg movements whereas bright light decreased it; $P = 0.002$). No effect was found for the second SIT.

Conclusion: Although exogenous melatonin may have a detrimental impact on motor symptoms; increased melatonin secretion at night is unlikely the cause of the circadian variation of RLS symptoms.

P54

Is the sleep pressure score the connection between periodic leg movements in sleep (PLMS) and daytime fatigue?

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Role of periodic leg movements in sleep (PLMS) is unclear. They are associated with complaints of non-restorative sleep and may have impact on daily well-being. This notion has been challenged by numerous authors. In two studies we have investigated the use of a numeric algorithm for polysomnographic assessment of sleep disruption (and resultant sleep pressure) by leg movement disturbances (SPSL) in order to shed new light on this old controversy. The SPSL is comparable to a previously described sleep pressure score (SPS) in apneu syndromes. This SPS is the reciprocal relationship between the total arousal index (ARtotI), respiratory arousal index (RAI), and spontaneous arousal index (SAI). This algorithm appeared to be a useful measure for the study of the relationship between nocturnal sleep and wake during daytime in adults and young children (Tauman, 2004). In analogy to the SPS in apneu syndromes we defined the SPSL as in the equation : SPSL = (LMAI/ARtotI)× (1-SAI/ARtotI). In a previous study of mild PLMD patients (mean PLMI 16.3) we found that there was only a correlation ($r = +0.51$) between the SPSL and the duration of deep sleep and no significant correlation at all for other sleep parameters or with aspects of subjective sleep quality or tiredness during daytime. To be sure of the value of this instrument we performed a similar investigation in a second group of patients with severe PLMD. (mean PLMI 51.3, range 14.8–119.1). In contrast to mild PLMD patients, we even did not find any correlation with sleep parameters and no correlation between the SPSL and subjective sleep quality or daytime tiredness. These results once again underline that PLMS are probably of no importance in terms of relation to quality of sleep and wake.

P55

Leg movements, RLS and growing pains in children

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The diagnosis of RLS in children is difficult. The adult criteria for the diagnosis pertain also for children, but cases are seldom that clear and additional criteria as growing pains, periodic limb movements (PLMs) and RLS in the family have to make the diagnosis likely. Unfortunately, the existing literature is scanty on most aspects of RLS in children even in basic data. Our nationwide survey aims at better insight in the presenting symptoms, comorbidity, findings from polygraphy and success of therapy. Children with sleepdisorders are seen in the major sleepcenters in The Netherlands. All participated in the survey. The entry criteria were: RLS according to the adult criteria, PLMI >5, or both and clinically suspect (insomnia, tired, positive family history, etc.) Thirteen children (8 boys) were found. The age at onset was 1–15 years (median 6); age at inclusion was 3–20 years (median 10). Well regulated epilepsy, slight retardation, ADHD, Asperger syndrome, migraine and spina bifida with minor deficit were reported as co-morbidity. Anti-epileptic drugs, methylphenidate and zolpidem were used by some children. RLS occurred in the family in four cases, always at Mother's side. Bad sleep quality (DIMS) and tiredness during the day, were present in all 13 patients. Growing pains in the legs (N = 4), frequent nightmares and other parasomnias (N = 3) were reported as major presenting symptoms as well. The classical criteria for RLS were found in one patient only. PSG and actigraphy revealed frequent arousals and awakenings, prolonged SOLAT and WASO, normal deep and REM sleep in all. Naps during the day were seen in four cases. Relevant apneas did not occur. Leg movements during sleep were seen at a wide range with a median of 89/night. The PLMI ranged from 6–25 (median: 10). Treatment (iron in 1 patient, dopamine agonists in 5, gabapentine in 3, and clonazepam in 4 cases) were successful in 9 out of the 11 patients who received therapy. In the other two patients and in those who had no therapy the outcome was moderate. The survey gave some relevant data, but its size is too small to give additional information for the existing literature on this subject. We hope to enlarge the study to other countries or large sleepcenters to make the survey more comprehensive.

P56

Restless legs syndrome is common among female patients with fibromyalgia

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Background: The prevalence of restless legs syndrome (RLS) among the general population is 2–15% and with fibromyalgia

syndrome (FMS) 2%. Both RLS and FMS are more common among women. The aim of our study was to evaluate the prevalence of RLS in a group of female patients diagnosed with FMS and to compare the occurrence of symptoms of daytime sleepiness and experienced sleep disorders between fibromyalgia patients, with or without RLS.

Method: Three hundred and thirty two patients, all women between 20 and 60 years diagnosed with FMS at Skonviks Rehab between 2002 and 2006, answered a questionnaire mailed to their home address. The questionnaire consisted of the international RLS study group (IRLSSG) criteria as well as questions concerning symptoms of insomnia and daytime sleepiness measured according to the Epworth Sleepiness Scale.

Results: Nearly 64% of the women were also suffering from RLS. More of the patients suffering from both RLS and FMS were affected by problems of initiating and maintaining sleep than those suffering from FMS only. More of the patients suffering from both RLS and FMS did not feel refreshed on awakening compared with those suffering from FMS without RLS. The patients with concomitant RLS and FMS were more hypersomnolent than those suffering from FMS only.

Conclusion: This study shows that all of 64% of a group of female patients diagnosed with fibromyalgia also suffer concurrently from RLS. More patients who suffer from both FMS and RLS experience sleep disturbances and have more pronounced daytime sleepiness than patients who suffer from FMS only.

P57

RLS in women: gender differences in northestern Sicily

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Introduction: According to most literature reports, the prevalence of RLS in women is higher than men (2:1), especially during specific periods of life such as pregnancy or menopause. We decided to evaluate the differential impact of RLS on women in a sample of patients referred to our sleep center.

Materials and Methods: We consecutively analyzed all features of all patients we diagnosed for RLS from January 2007.

Results: 47% out of 42 RLS patients were women. Mean age was 51 in women and 53 in men. The mean age for RLS symptoms onset 43 in women and 44 in men. In 5 women symptoms started with the first pregnancy (mean parity index 2.3),in 3 with menopause. 9 women and 18 men had a idiopathic RLS. In 30% of women RLS was secondary to iron deficient anemia (mean ferritine 12.9 μg dl^{-1}). Mean IRLS-RS score was comparable in women (27) and men (25). 9 women and only 2 men reported familial RLS. OSAS was present in 61% of men and 20% of women. 23% men and 38% women had mood disorders (nocturnal eating disorders in 25%). 43% of women had thyroid disease. 6 women and 8 men hypertension. Different Dopa-agonists (Cabergoline mean dose 1 mg die^{-1}, Pramipexole 0.25 mg die^{-1} and Ropinirole 0.50 mg die^{-1}) were prescribed to all patients with IRLS-RS improving (mean IRLS-RS 5.5, $P<0.01$) after 1 month.

Discussion: RLS prevalence in our sample contradicting most recent literature reports showed no gender differences as far as prevalence and mean age of onset are concerned. However idiopathic RLS was more represented in men whereas a positive familial history more frequent in women. Predisposing factors (parity, thyroid and iron deficit) seemed to play a crucial role. Sleep co-morbidities (sleep apnea, depression and EDS) were differently distributed by gender. Dopa agonists proved clinically effective as shown by the statistically significant reduction of the IRLS severity rating scale.

P58

Impaired sensory-motor integration in restless legs syndrome is restored by dopamine agonists

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Background: Restless legs syndrome (RLS) is a disorder characterized by unpleasant leg sensations coupled with an irresistible inner urge to move from a resting position. Several evidences suggest a nigrostriatal dopaminergic system dysfunction in RLS patients. These findings are supported by a good pharmacological response to dopaminergic treatment. In addition, recent studies hypothesize that abnormalities within the sensory-motor cortex may play a pivotal role in the pathophysiology of RLS.

Objective: In the present work we aimed at assessing whether patients with idiopathic RLS showed alterations of short-latency afferent inhibition (SAI) and long-latency afferent inhibition (LAI). Both SAI and LAI measure the modulation of cortical excitability by sensory inputs. LAI is probably dependent on cortico-cortical connections involving the motor cortex and both primary and secondary somatosensory cortical areas, whereas SAI is likely to reflect a direct inhibitory modulation of the primary motor cortex.

Materials and Methods: Ten patients with idiopathic RLS and ten age and sex-matched control subjects were recruited. SAI and LAI were studied using the conditioning-test protocol described by Tokimura and co-workers (2000). Moreover, we studied SAI and LAI in 8 of 10 patients with idiopathic RLS after a single dose and after 4 weeks of treatment with dopaminergic agonists.

Results: In untreated idiopathic RLS patients, the amount of SAI was lower than in healthy subjects, whereas LAI did not significantly differ between the two groups. After dopaminergic treatment, SAI was restored.

Conclusion: Our data demonstrated that sensori-motor integration modulated by SAI is impaired in idiopathic RLS patients but may be reverted to normal values by dopaminergic medication. The present findings confirm a pivotal role of the dopaminergic system in the pathophysiology of RLS.

P59

Correlation of overall improvement and daytime-symptom improvement in phase IV trials of pramipexole for restless legs syndrome

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Purpose: Although restless legs syndrome (RLS) occurs or worsens at night, the related sleep disruption causes daytime detriment. Using data from two large-scale, Phase IV pramipexole trials, we analyzed the statistical relationship between reduction of overall RLS severity and reduction of daytime symptoms of RLS.

Methods: Each trial was a 12-week randomized double-blind test of pramipexole (at ≤ 0.75 mg day^{-1}) versus placebo, for which all patients were required to have a baseline score >15 on the International RLS severity scale (IRLS). In addition, one trial also required an IRLS item-10 score ≥ 2. Primary outcome measures included IRLS score, secondary measures included Questions 4, 5, and 6 of the RLS-6, which ask the patient to rate daytime facets of RLS—severity while resting, severity while engaged in activities, and daytime tiredness on a scale of 0 to 10. For assessing correlation between changes in RLS-6 and IRLS findings, a Spearman correlation coefficient ≥ 0.5 was interpreted as a strong positive relationship.

Results: In all, 759 patients received double-blind study drug: 381 for pramipexole and 378 for placebo. At baseline, the groups' mean IRLS scores were highly similar, at 25.8 versus 25.9 in one trial and 24.6 versus 24.3 in the other. After 12 weeks, each trial's pramipexole group showed a greater improvement, with a mean treatment effect adjusted for baseline, of 6.1 points in one trial ($P<0.0001$) and 3.8 in the other ($P=0.0001$). For daytime severity while resting, a median baseline score of 4.0 across both trials improved to 1.0 for pramipexole versus 2.0 for placebo ($P=0.0162$ and $P=0.0017$, Wilcoxon-Mann-Whitney rank test). Correlation coefficients with change in IRLS scores were 0.5402 and 0.6284. For daytime tiredness, a median baseline score of 5.0 in one trial improved to 2.0 for pramipexole versus 3.0 for placebo ($P=0.0007$), and a median of 4.0 in the other trial improved to 1.0 versus 2.0 ($P=0.0024$). Correlation coefficients with change in IRLS scores were 0.5673 and 0.5290.

Conclusions: In both of two large-scale Phase IV trials, pramipexole's overall improvement of RLS showed a strong correlation with improvement of daytime tiredness and of daytime RLS symptoms while resting.

P60

Association between relief of restless legs syndrome and relief of depressive symptoms in a phase IV pramipexole trial

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Purpose: Restless legs syndrome (RLS) symptoms can have psychological consequences, including a heightened risk of depressive symptoms. This clinical trial was designed to determine whether pramipexole might benefit both RLS and concurrent mood disturbance.

Methods: In a 12-week, Phase IV trial of double-blind pramipexole versus placebo, all patients had a baseline score >15 on the International RLS severity scale (IRLS), including a subscore ≥ 2 (''moderate'') on IRLS Item 10: ''How severe is your mood disturbance from your RLS symptoms?'' The pramipexole dosages were 0.125 to 0.75 mg day^{-1}. At baseline and endpoint, patients' depressive symptoms were assessed using the Beck Depression Inventory 2nd edition (BDI-II). To analyze the correlation between BDI-II and IRLS findings, a Spearman coefficient was calculated at baseline and for change from baseline.

Results: In all, 203 patients were randomized to receive pramipexole and 200 to receive placebo. At baseline, the groups' mean IRLS scores were similar, at 25.9 ($n=202$) and 25.8 ($n=196$), in the range signifying severe RLS, and the groups' mean BDI-II scores were similar, at 14.3 ($n=200$) and 13.6 ($n=194$), in the range signifying mild depression. 48.7% of patients had a score ≥ 14. After 12 weeks, the mean IRLS score was reduced -14.5 to 11.4 in the pramipexole group versus -8.3 to 17.4 for placebo; the mean difference, adjusted for baseline, was 6.1 ($P<0.0001$). On IRLS item 10, 75.9% of the pramipexole group gave themselves a rating of 0 (''none'') or 1 (''mild'') for mood disturbance, compared with 57.3% for placebo ($P<0.0001$). Mean BDI-II scores were in the normal range, at 6.5 for pramipexole versus 7.8 for placebo, representing, after adjustment for baseline, a change of -7.3 versus -5.8 ($P=0.0199$). At baseline the correlation of BDI-II and IRLS scores was small (rho = 0.274), the Spearman correlation coefficient for change from baseline between BDI-II and IRLS scores was still limited at 0.334.

Conclusions: For relief of RLS and depressive symptoms, pramipexole was superior to placebo. Despite substantial responsiveness to placebo, as often reported in trials of depression therapies, both types of pramipexole-related benefit were statistically significant, and the correlation between them was positive.

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Multicentre case-control study on restless legs syndrome in multiple sclerosis: the REMS study

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The existence of a symptomatic form of restless legs syndrome (RLS) secondary to multiple sclerosis (MS) is still controversial. The aim of the study was to assess the prevalence and the possible associated risk factors of the RLS in MS by a prospective, controlled, face to face, multicentre epidemiological survey. Twenty Sleep Centers, certified by the Italian Association of Sleep Medicine, participated to the investigation. Eight hundred and sixty one patients affected by MS and on 649 control subjects were included. Data regarding demographic, clinical, presence of the international criteria for RLS and the severity of RLS, hematological tests and visual analysis of cerebro-spinal MRI were collected. The prevalence of RLS was 19% in MS and 4.2% in control subjects, with a risk to be affected by RLS of 5.4 (CI $\pm$ 95%: 3.56–8.26) times greater for MS patients than for controls. In MS patients the following risk factors for RLS were found to be significant: older age, longer MS duration, the primary progressive MS form, higher global, pyramidal and sensory disability, and the presence of leg jerks before sleep onset. MS patients with RLS more often referred sleep complaints and a higher intake of hypnotic medications than MS patients without RLS. Iron storage indicators, creatinine and folate plasmatic levels did not differ between MS patients with or without RLS. RLS associated to MS was more severe than that of control subjects. RLS is significantly associated to MS, especially in patients with severe pyramidal and sensory disability. These results strengthen the idea that the inflammatory damage correlated to MS, probably involving long cerebro-spinal nervous pathways, may induce a secondary form of RLS. As well as in idiopathic cases, RLS has a significant impact on sleep quality in MS patients, therefore it should be always searched for, particularly in the presence of insomnia unresponsive to the common hypnotics drugs.

P62

Long-term ropinirole therapy for restless leg syndrome

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Introduction: Currently dopamine receptor agonists are the drugs of choice for the management of the restless legs syndrome, but only a few long term trials have been published with these agents. We evaluated in retrospective way the efficacy of ropinirole over 20 months.

Methods: Data from patients with RLS started on ropinirole in our laboratory in 2004 and 2005 were collected and assested retrospectively. From sixten patients, who started ropinirole monotherapy in these two years, ten patients are still receiving ropinirole (all the patients have idiopathic RLS). Six patients discontinued ropinirole because of the lack of efficacy ($n=2$), the occurrence of side effects ($n=5$), or both ($n=1$). Currently, the dose range of ropinirole is between 0.25 mg and 4.5 mg day^{-1}; mean duration of treatment is 24 month (range: 20 to 27 months). Augmentation occurred in 2 cases, switching to another drug was necessary in both. Mean age of male ($n=6$) and of female patients ($n=10$) was 51.2 $\pm$ 11.1 years and 49.9 $\pm$ 10.2 years, respectively. Therapeutic efficacy was monitored using the International Restless Legs Scale (IRLS), actigraphy, and the Forced Immobilization Test.

Results: IRLS scores, actigraphy, and the SIT index revealed more than 80-per-cent improvement of RLS manifestations. Adverse reactions observed during the initial phase of treatment include

nausea ($n = 4$), vomiting ($n = 1$), diziness ($n = 4$), somnolence ($n = 3$) and swelling of the ankles and lower legs ($n = 2$). Currently, 6 per cent of patients reports mild adverse reactions.

Conclusion: Ropinirole was effective and well tolerated on long-term monotherapy, improved the symptoms and associated sleep disturbance in RLS. The efficacy of the drug remained unchanged during treatment for 20 months. Side effects occurred in 37.5% of patients and necessitated discontinuation of dosage in 25% of subjects. Augmentation occurred in 2 cases. As shown by these results, ropinirole monotherapy proves effective for the treatment of RLS on the long-term (i.e. over 20- to 27 months).

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Low normal levels of ferritin is common in patients with restless leg syndrome and periodic limb movement disorder

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Background: Restless Leg Syndrome (RLS) and Periodic Limb Movement Disorder (PLMD) are two conditions characterized by abnormal leg movements during sleep which may disrupt sleep quality. Iron deficiency is a cause of RLS/PLMD. However, low levels of stored iron (ferritin) that are within the normal range may contribute to the development of RLS and PLMD that maybe reversible with iron supplementation. Recent guidelines recommend treatment of RLS with iron supplementation if the ferritin level is less than 50 ug L^{-1} (normal range 11–307 ug L^{-1}). This study aims to investigate the proportion of patients with RLS/PLMD that have a ferritin less than 50 ug L^{-1} and therefore may have reversible disease.

Method: A retrospective case notes review of 100 consecutive patients, aged between 22 and 85 years seen in the Sleep Disorders Clinic, St. Thomas' Hospital, London between 2006 and 2008. Electronic patient records were used to review ferritin results. Data collected included age, gender, co morbidities, treatments and ferritin levels.

Results: Of these 100 patients, 68 were male and 32 were female. Forty two (29 Males, 13 Females) had their ferritin level tested. Of the 42 tested patients, 19 (47.6%) were found to have a ferritin level less than 50 ug L^{-1}. The majority of patients (17 of 19), with ferritin less than 50 ug L^{-1}, were found to have ferritin that was in the low normal range (11–50 ug L^{-1}).

Conclusions: Ferritin in the low normal range is common in patients with restless leg syndrome and periodic limb movement disorder. This may be overlooked as a cause of restless leg and periodic limb movement disorder and maybe reversible with iron supplementation.

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A case of RLS concomitant with liver cirrhosis, successfully treated with levodopa and palliative therapies for liver dysfunction

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A 73-year-old man suffering from liver cirrhosis came to our clinic with a complaint of nocturnal discomfort of the legs. This symptom urged him to walk in and around the bedroom, and his daily sleep was severely interrupted. A video-assisted polysomnography revealed repetitive awakening with fidgety leg movements. He was diagnosis as having restless legs syndrome (RLS), and loading of levodopa initially reduced his nocturnal symptoms. However, those symptoms sometimes exacerbated, coupled with serum NH3 elevation. Addition of lactulose or intensification of branched-chain amino acids (BCAA) administration reduced his nocturnal symptoms coincidentally but more dramatically. By the combination of levodopa and those palliative therapies for liver dysfunction, his RLS symptoms have been well controlled. The etiology and therapeutics of RLS concomitant with chronic liver disease remain unclear. Both levodopa and palliative therapy for liver dysfunction might bring their benefits, by restoring dopaminergic system dysfunction or by eliminating neurocytotoxicity.

P65

Periodic leg movement during sleep: near infrared spectroscopy (NIRS) provides evidence for cerebral hemodynamic changes even in the absence of arousal

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Background: Near infrared spectroscopy (NIRS) non-invasively monitors brain tissue oxygen saturation (StO_2) together with changes in concentration of oxyhemoglobin (O_2Hb), deoxyhemoglobin (HHb) and total haemoglobin (tHb), functionally related to cortical activity. Periodic leg movements during sleep (PLMS) are associated with different degrees of brain activation, from an autonomic response to EEG arousal.

Objective: To test whether cerebral hemodynamic changes are associated with leg movements (LM), even in absence of any EEG correlate.

Methods: Three PLMS patients were investigated by cerebral NIRS, positioning a single sensor on the right forehead. The EEG correlates of leg movements (LM) were visually scored according to the American Sleep Disorders Association (ASDA) criteria for arousal and to rules for the A phases detection within Cyclic Alternating Pattern. Cerebral NIRS data were analysed in order to identify hemodynamic changes associated with cortical activation.

Results: PLMS are constantly associated with a constant triphasic cerebral hemodynamic pattern. Cerebral hemodynamic fluctuations show higher amplitude when occurring together with changes in the EEG activity.

Conclusion: NIRS provides further evidence of cortical response to LM from an unique cerebral hemodynamic perspective, even in the absence of EEG arousal. This is the first report of cerebral hemodynamic alterations associated with LM, further studies are needed to clarify their pattern amplitude and topography.

P66

Restless trunk syndrome – outlines of a putative disorder

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The term restless legs syndrome (RLS) refers to a condition, where the unpleasant crawling or itchy feelings are restricted to the lower extremities or seldom to the upper ones. On the other hand, disorders of peripheral nerve hyperexcitability (PNH) often affect the truncal musculature, but are practically always associated with visible myokymia and in most cases with myokymic electromyographic discharges, too. The authors present the cases of two young male patients suffering from tugging, creepy-crawly sensations, resembling those complained in RLS, quaintly in the

truncal area. Both patients felt as if the sensations were related to fibrillary muscle contractions right under their skin. However, mycloni could never be observed either by the patients themselves, or by the treating medical staff. No pathological electromyographic findings were present, and the disorder did not meet the diagnostic criteria of fibromyalgia syndrome, either. Hamilton Anxiety Scale (HAMA) and Hamilton Depression Rating Scale (HAM-D) scores did not give proof of an anxiety or affective disorder, respectively. Complaints seemed to be related to wakefulness, however tended to emerge or worsen at rest after physical activity. During the 3–10 years of the patients' medical history, neither the administration of any kind of antidepressants, nor benzodiazepine anxiolytics or antiepileptics revealed a complete remission. Finally, based on the similarity of the symptoms to those observed in RLS, a dopamine agonist treatment was introduced. Both patients have been successfully treated over a long period with a low dose of pramipexole, revealing in complete and persistent remission. The effectiveness of the dopamine agonist treatment, in contrast to the failure of serotonergic, antiepileptic, anxiolytic and dopamine antagonist medication, suggests that the underlying pathology is closer to the one responsible for the symptoms of RLS than that of either PNH, or anxiety and mood disorders, respectively. Thus, the presented patients' histories can be considered as cases of an atypical, yet undefined, RLS-like disorder-designated by the authors by the working name ''Restless Trunk Syndrome''. In order to elucidate the problem, however, publishing some similar case reports would be desired.

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Periodic limb movements in patients with chronic thromboembolic pulmonary hypertension (CTEPH)

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Sleep related breathing disorders are described in pulmonary hypertension like a common affection. Presence of periodic limb movements (PLM) was observed through proceeded sleep study in patients with chronic thromboembolic pulmonary hypertension (CTEPH) before pulmonary endarterectomy.

Material and methods: Fourteen patients (8 males, 6 females, average age of group 57.7 ± 12.8 years) with CTEPH (average pulmonary artery systolic pressure-PASP 100.5 ± 37.7 mm Hg) were examined using polysomnography, Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS). Each subject underwent through the laboratory examination, too.

Results: Poor quality of sleep-low efficiency of sleep (69.3 ± 14.2%), decrease in delta and REM sleep with periodic hypoxemia were measured (average oxygen desaturation index-ODI: 28.0 ± 16.8). Obstructive sleep apnea (OSA) on average of mild intensity was present in 7 patients (average respiratory disturbance index-RDI: 12.9 ± 12.8). PLM activity was mentioned in 11 of 14 patients (average periodic limb movement index-PLMI: 46.9 ± 38.2). There were no complaints of restless legs syndrome. The level of ferritin the same way as other laboratory parameters was normal in all patients. Problems with excessive daytime sleepiness were only in one patient with severe OSA. No other sleep related problems according to PSQI and ESS were present. No clear correlations between PLMI and other parameters (laboratory, polysomngoraphic and pneumologic) were measured.

Conclusion: Obvious association between PLM and measured parameters were not found. With regard the mild intensity or absence of OSA, detected PLM could be taken for independent disorder on OSA in patients with CTEPH. We can conclude that higher incidence of PLM in patients with CTEPH means co morbidity between these two disorders.

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Long-term safety and efficacy of rotigotine in idiopathic RLS: 3-year results from a multinational, open-label trial

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Objective: To evaluate safety and efficacy of long-term rotigotine treatment in moderate to severe idiopathic RLS.

Background: Rotigotine is a D3/D2/D1 dopamine agonist formulated as a once-daily transdermal patch. Rotigotine is licensed in Europe for early and advanced Parkinson's disease (PD) and in the US for early PD; it is in clinical development for RLS. These results are from an ongoing, open-label extension (OLEX) of a completed double-blind, placebo-controlled, dose-finding study.

Methods: Rotigotine was titrated to an optimal dose (0.5–4 mg/24 h); subsequent dose adjustments were allowed at any time to maintain optimal treatment. Safety was evaluated by adverse events (AEs), laboratory values, vital signs and electrocardiograms. Efficacy was measured by IRLS, CGI item 1 (severity of illness) and RLS-6 subscales. Data for the 36-month visit (LOCF) are presented here.

Results: Of the 295 patients entering the OLEX, 159 (54%) completed 3 years of maintenance. The mean rotigotine dose was 2.5 mg/24 h at OL baseline and 3 mg/24 h in year 3. The mean IRLS score was 27.8 ± 5.9 at baseline and improved to 13.0 ± 10.6 after 36 months of treatment. The mean baseline CGI item 1 score was 5.1 ± 0.9, which improved to 2.6 ± 1.3 after 36 months. All RLS-6 subscales showed improvement; changes from baseline were: sleep satisfaction (− 3.6 ± 3.4), symptoms while falling asleep (− 3.6 ± 3.3), night-time symptoms (− 4.2 ± 3.3), day at rest (− 2.7 ± 3.2), while active (− 1.2 ± 2.2), and daytime tiredness (− 2.1 ± 3.1). The most common AEs related to the trial medication were all application site reactions (54%), nausea (11%), fatigue (9%), erythema (8%) and pruritus (5%). Most (83%) application and instillation site reactions were mild to moderate in intensity; 18% of subjects discontinued due to these AEs.

Conclusion: Long-term transdermal 24 h treatment with rotigotine was generally well tolerated and efficacious in moderate to severe RLS. Improvement was sustained over 36 months and more than 50% of patients were retained for the duration.

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Objective assessment of efficacy and safety in idiopathic RLS: results from a 7 week sleep lab trial with the transdermal rotigotine patch

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Objective: To evaluate objectively the efficacy and safety of the rotigotine patch in subjects with moderate to very severe idiopathic restless legs syndrome (RLS) using polysomnographic measurements.

Background: Rotigotine is a licensed dopamine agonist for Parkinson's disease in the US and Europe that is under investigation for the treatment of RLS.

Methods: This was a multicenter, randomized, double-blind, placebo-controlled, 2-arm parallel-group trial. Study medication could be individually up-titrated to the optimal dose (1–3 mg 24 h^{-1}), followed by a stable maintenance dose over 4 weeks. The primary parameter was the Periodic Limb Movement Index (PLM/total time in bed), taken in a classic sleep lab setting. Secondary (subjective) parameters included IRLS and CGI scores.

Results: A total of 67 subjects (59 ± 10 years, 73% females) were randomised at 11 sites in 5 European countries (46 rotigotine, 21 placebo). The PLMI decreased from 50.9 at baseline to 8.1 at end of maintenance for rotigotine and from 37.4 to 27.1 for placebo. At end of maintenance, rotigotine was 4.25 times more effective than placebo ($P<0.0001$). The IRLS score in the rotigotine group was reduced from 26.3 ± 6.4 at baseline to 9.7 ± 9.1 at end of maintenance and from 25.4 ± 6.3 to 15.1 ± 8.3 for the placebo group ($P<0.02$). The CGI item 1 (severity of illness) was reduced from 5.0 ± 0.9 to 2.3 ± 1.2 and from 4.8 ± 0.8 to 3.1 ± 1.6 for rotigotine and placebo, respectively ($P<0.02$). A total of 74% rotigotine and 52% placebo subjects reported at least 1 adverse event (AE). The most common AEs were nausea (21.7%, 4.8%), headache (19.6%, 19.0%), application site reactions (17.4%, 4.8%) and somnolence (13.0%, 9.5%) for rotigotine and placebo, respectively. AEs were usually transient.

Conclusion: Based on the objective PLMI, rotigotine doses from 1 to 3 mg/24 h showed the same clear efficacy compared to placebo as in the subjective assessments in patients with idiopathic RLS and was well tolerated.

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Relationship between restless legs syndrome and snoring during pregnancy

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Keywords: pregnancy, snoring, restless legs syndrome.

Objective: To study the development of restless legs syndrome (RLS) during pregnancy, and whether it is related to occurrence of snoring and/or edemas.

Method: 503 pregnant women were consecutively presented a questionnaire concerning snoring, tiredness in the morning, daytime sleepiness and edema. Epworth Sleepiness score (ESS) and symptoms of restless legs syndrome (IRRLS) were included. The questionnaire was presented at 3 regular visits to a maternity clinic in the 1st, 2nd and 3rd trimester, when blood pressure was also recorded. Women snoring often-always at visit 2 and/or 3 are denoted habitual snorers, those snoring never-seldom non- snorers. Data concerning pregnancy and delivery complications were taken from the maternity clinic's standardized antenatal and delivery records.

Results: 22% of the habitually snoring women reported RLS-symptoms already in the 1st trimester, 33% in the 2nd and 32% in the 3rd. For non-snorers the corresponding figures were 14%, 25% and 29%, respectively. Snoring scores were significantly higher among those who suffered from RLS in 1st and 2nd trimester ($P = 0.002$ and 0.003, respectively), but ns. in 3rd trimester. BMI, weight gain during pregnancy and prevalence of edema showed no difference between RLS and non-RLS women. RLS women were more tired in the morning at the 1st and 3rd visit ($P = 0.03$ and 0.003). They presented more daytime sleepiness during the day and had higher ESS-scores at the 3rd visit ($P<0.001$ and 0.005) than non-RLS. In the RLS-group the systolic blood pressure increased in the 3rd trimester more than in non-RLS ($P = 0.02$), but was within normal range. In the whole material ($n = 503$) there were only 18 cases of pre-eclampsia, without any correlation to RLS.

Conclusion: RLS-symptoms progressed most between the first and second trimester. Women with RLS reported significantly more snoring than non-RLS cases. RLS was also significantly correlated to morning and daytime tiredness, higher ESS score and increases in systolic blood pressure in the 3rd trimester. We found no correlation between RLS and edema or weight gain.

P71

Severity but not prevalence of restless legs syndrome is higher in chronic idiopathic axonal polyneuropathy

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An increased prevalence of RLS in patients with polyneuropathy of various causes has been reported. As the underlying condition causing the polyneuropathy may also interact with the development of RLS, we evaluated the prevalence and severity of RLS in patients with chronic idiopathic axonal polyneuropathy (CIAP), a condition where known (metabolic) causes have been excluded. Patients with CIAP and control persons were interviewed by telephone by a trained interviewer. The diagnosis of RLS was established if all four International RLS Study Group criteria were met. The severity of symptoms was evaluated using the International Restless Legs Syndrome Study Group rating scale for restless legs syndrome (IRLS). Ninety-three patients with CIAP (73% men, mean age 69 SD 9 years) and 57 healthy controls (74% men, mean age 69 SD 8 years) were included in the study. The prevalence of RLS in CIAP (17.2%) compared to the prevalence of RLS in controls (17.5%) was comparable (P-value 0.82). The mean IRLS score was significantly higher in CIAP patients (17.4 SD 8.5) compared to control persons (10.7 SD 5.3) (P 0.02). The age of onset of RLS was similar in patients with CIAP and controls. (60.9 SD 13.2 versus 59.9 sd 15.0) Our study shows that the severity but not the prevalence of RLS is increased in patients with CIAP. This is in contrast with previous studies, which included polyneuropathy of various underlying disorders characterized by a disbalance in metabolic factors, but is consistent with the central dopaminergic deficit hypothesis.

Biological Rhythms and Non-Classical Photoreception

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Nurses' night work influences sleep timing for nurses, their partners and children

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Most existing research concerning night work considers disruption to night workers' own circadian timing system and reduced length and quality of sleep. The present study includes simultaneously collected subjective sleep data for whole families including night workers, their partners and children. Twenty families have participated in the study, each including a female nurse working irregular rotating shifts, their male partner and one or more children aged 8–18 years ($n = 74$: 20 female nurses, 20 male partners, 19 male and 15 female children). A wide range of qualitative and quantitative data have been collected including 14 days of actigraphy and subjective sleep diaries. Data from the subjective sleep diaries detailing timing and duration of sleep have been analysed. This includes night time sleep for all family members as well as nurses' daytime recovery sleep after night shifts. During periods of night shift work, nurses' day time recovery sleep was significantly reduced ($P < 0.001$) (mean $\pm$ SD 04:50 $\pm$ 1:46 h:min) compared with their usual night sleep (07:10 $\pm$ 1:25). After the last night shift, all nurses slept significantly less and got up earlier (sleep duration 03:44 $\pm$ 1:06, wake up 13:31 $\pm$ 1:13) compared with the other night shifts (sleep duration 05:22 $\pm$ 1:43 $P = 0.002$, wake up 14:53 $\pm$ 1:46 $P < 0.001$ for first night shifts; sleep duration 05:50 $\pm$ 1:53 $P < 0.001$, wake up 15:38 $\pm$ 01:30 $P < 0.001$ for middle night shifts). Partners and children had significantly later bedtimes (partners 23:54 $\pm$ 0:57 compared with 23:34 $\pm$ 1:00 $P < 0.05$; teenage children 23:24 $\pm$ 1:44 compared with 22:54 $\pm$ 1:26 $P < 0.05$; pre-teenage children 21:43 $\pm$ 1:02 compared with 21:26 $\pm$ 0:54 ns, $P = 0.106$) when the nurse was working night shifts. Qualitative interviews have provided data to interpret the altered sleep timing for all family members during the nurse's night work. For nurses, this includes constraints of school delivery and collection times and pressures of other household tasks. For partners and children, later bedtimes appear to follow relaxed and less structured evenings where there may be more choice than usual concerning bedtimes. Funded in part by EU Marie Curie Research Training Network (MCRTN-CT-2004-512362).

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Spectral composition of daily light exposure in young adults in summer and winter

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Introduction: Circadian photo-entrainment is mediated in part by intrinsically photosensitive retinal ganglion cells that express the photopigment melanopsin. The spectral sensitivity of melanopsin is greatest for blue light at 480 nm. However, at present, there is little information on the time course of the spectral composition of light to which people are exposed over the 24-h period and any seasonal variation thereof.

Methods: 24 subjects aged 18–29 years, 23.8 $\pm$ 3.8 years (mean $\pm$ SD), with mean body mass index (BMI) 22.1 $\pm$ 2.3 $kg\,m^{-2}$ participated during the winter months (Nov-Dec), whilst 5 subjects aged 24–28 years, 27.2 $\pm$ 0.6 years, BMI 21.3 $\pm$ 0.5 $kg\,m^{-2}$ participated in the summer months (Apr–Jun). Subjects wore actiwatch RGB monitors (Cambridge Neurotechnology) for 7 days. These monitors measure activity, light exposure in the blue, green and red spectral regions, in addition to normal broad spectrum white light, with a two minute resolution. Subjects also completed daily sleep diaries to verify the timing of sleep and wakefulness.

Results: Analysis of the relative contribution of blue light to overall light exposure demonstrated a significant variation with time of day ($P < 0.05$). Light during the 9.00–15.00 h period was relatively blue light enriched (41.0 $\pm$ 0.1%, mean $\pm$ SEM), whereas during the evening during 18.00–23.00 h the contribution of blue light was less (30.1 $\pm$ 1.7%). Analysis of light exposure during summer and winter demonstrated that subjects studied in summer were exposed to higher white light levels compared to those studied in winter ($P < 0.002$). This difference was particularly pronounced between 15.00–20.00 h. For this time interval those subjects studied in the summer were exposed to a significantly higher percentage of blue wavelength light between 16.00–20.00 h, 40.2 $\pm$ 1.5% compared to winter 31.0 $\pm$ 1.2% ($P < 0.05$).

Conclusions: The present data show that in addition to overall light exposure, the spectral composition of light varies with time of day and with season. These variations may contribute to inter-individual and seasonal changes in entrainment and its disorders.

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Increased health risk in subjects with high self-reported seasonality

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Introduction: Seasonal variations in mood and behaviour, termed seasonality, are commonly reported in the general population. The severity of these variations varies between individuals, and about a fourth of the population report seasonality to be distressing. To the best of our knowledge this study is the first to report associations between seasonality and subjective health behaviours and objectively measured health risk factors.

Methods: As a part of a larger health survey, 8860 subjects (3,531 men and 5,329 women) between 40–44 years old completed the Global Severity Score (GSS), which is a subscale of the Seasonal Pattern Assessment Questionnaire (SPAQ), investigating to which extent mood and behaviour covary with seasons. The subjects also completed a questionnaire on miscellaneous health behaviours. Height, weight, waist/hip circumference and blood pressure were measured. Additionally, blood samples were taken and analyzed for glucose, triglycerides and cholesterol. The GSS-scores range 0–24, and scores above or equal to 11 is defined as high seasonality. We compared high seasonality to subjective health risk factors, objective health measurements and blood parameters. Data were analysed using logistic regression analyses, and separate analyses were performed for men and women.

Results: High seasonality was significantly associated with daily cigarette smoking, large waist-hip-ratio, obesity, high triglyceride level and high glucose level (women only) in the crude analyses. When adjusting for sociodemographic factors, high seasonality was still significantly associated with daily cigarette smoking (women only, OR = 1.5, 95% CI = 1.3–1.7), large waist-hip-ratio (OR = 1.5, 95% CI = 1.1–2.1 [men], OR = 1.3, 95% CI = 1.0–1.5 [women]), obesity (OR = 1.8, 95% CI = 1.4–2.3 [men], OR = 1.3,

95% CI = 1.1–1.5 [women]), and high triglyceride levels (OR = 1.3, 95% CI = 1.1–1.5 [men], OR = 1.3, 95% CI = 1.1–1.6 [women]).

Conclusions: High seasonality is associated with risk factors for the development of the metabolic syndrome.

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Light at the wrong time: short-term bathroom light influences physiology and behavior

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Although industrial progress and life in a 24-hour society are based on the use of artificial light at night, the endogenous circadian timing system (CTS) in humans is synchronized to the solar day by means of the environmental light-dark cycle. The proper functioning of the CTS is important to health and well-being. Under controlled laboratory conditions, however, the long-term application of bright-white, blue-enriched or blue light suppresses melatonin excretion which, for the human body, is the signal of darkness. The aim of the present study was to demonstrate that light emitted by everyday lamps in a naturalistic setting influences physiology in healthy human subjects. A total of 9 healthy subjects (6 m, 3f, 22–33 years.) kept their average bedtimes ($\pm$ 1 h) during a 7-day entrainment period (monitored by actigraphy). During the following 6-day experimental period, subjects maintained their habitual daytime schedules, attending the laboratory only in the evening hours from 7–12 PM. During lab hours, subjects were exposed to constant dim light (<10lx); at evenings 2 through 6, subjects were also exposed for a total of 30 min to light by everyday lamps (office, bathroom, industry) of different intensity (130–500lx) and spectral distribution (4 with and 1 without blue portions) 1 h before habitual bedtime. Melatonin suppression was measured by saliva samples taken every 30 min during dim-light exposure, as well as 10 min before, every 10 min during, and 10 min after exposure to light from the everyday lamps. Exposure to yellow light (without a blue portion) had no effect on melatonin concentrations (13 pg mL^{-1} versus 13 pg mL^{-1}). In contrast, 30 min of exposure to light from all four of the lamps that included a blue portion significantly reduced melatonin concentrations (13 pg mL^{-1} versus 9.9 pg mL^{-1}, 10.4 pg mL^{-1}, 8.1 pg mL^{-1}, 7.5 pg mL^{-1}). Subjective alertness was significantly increased at the end of three lighting conditions (all of which had a blue portion). Short-term exposure to everyday lamps is sufficient to influence physiology and behavior. It needs to be determined whether everyday lighting conditions during environmental night are involved in disorders that are otherwise known to occur in shift workers, such as cancer, diabetes, obesity, and depression.

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Inconsistency of daytime sleepiness using the standard (10:00–16:00 h) MSLT in healthy sleepers, when extending MSLT, MWT and PVT testing into late evening

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Introduction: The MSLT distinguishes different levels of sleepiness in healthy adults who are subjectively good sleepers without any symptoms of daytime sleepiness. However, this usually only covers 30% of the waking day (10:00 h–16:00 h). We used this standard research MSLT (2 hourly) to sub-divide adults into two groups differing in MSLT scores, and re-tested them (different days), under two conditions: 1. modified MSLT utilising later testing times (four occasions between 15:30 h–23:00 h); 2. the MWT using these later times. Thus we assessed the consistency of standard MSLT findings, when the usual MSLT testing times were shifted from mid-afternoon to late evening, and also when participants were encouraged to remain awake.

Methods: Twenty healthy young adults (25.9 $\pm$ 3.9 y) (Av.TST 7.77 h) were selected following standard research MSLTs and classed as either 'mildly' (MSLT SoL 12–15 min) ($n = 13$) or 'moderately' (SoL 6–9 min) ($n = 7$) sleepy. In the main study, MSLT (20 min duration) and MWT (30 min duration) sessions were performed at: 15:30 h, 17:00 h, 19:45 h, 23:00 h, with 30 min PVTs at 16:00 h, 22:00 h. The KSS was given 2-hourly on all days, from 11:30 h until 23:30 h.

Results: Although the two groups differed significantly in the initial, standard MSLTs, there was nsd for sleep onset latencies (SoLs) between the groups, for conditions 1 and 2. There was a significant increase in SoL in the MWT versus the MWT, as expected. There was nsd between the groups for PVT lapses and subjective sleepiness.

Conclusion: Differences in healthy individuals in terms of objective sleepiness as measured by the standard morning-until-afternoon MSLT, do not persist until late evening and are not supported by PVT performance or subjective ratings of sleepiness. When assessing apparent levels of daytime sleepiness, in otherwise healthy individuals, other measures should be used in addition to the standard research MSLT.

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Is an afternoon nap or a cup of coffee as good as morning sleep extension at reducing afternoon and evening sleepiness?

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Introduction: Sleep extension should alleviate daytime sleepiness as measured by the MSLT. Recent research has suggested that 7.5 h a night is not enough and we should be aiming for up to 90 min more than this to ensure against the build up of a sleep debt and increased sleepiness levels during the day. As the standard MSLT gives little information on evening sleepiness, we compared the effect of extending nocturnal sleep with an afternoon nap or a caffeinated drink on MSLTs administered late afternoon until late evening, in a group of healthy young adults who habitually slept between 7–8 h a night.

Methods: Twenty healthy young adults (25.9 $\pm$ 3.9 y) (Av. TST 7.8 h), selected following standard research MSLTs, were classed as either 'mildly' (MSLT SoL 12–15 min) or 'moderately' (SoL 6–9 min) sleepy. In the main study, MSLT sessions were later: 15:30 h, 17:00 h, 19:45 h, 23:00 h, with 30 min PVT sessions at 16:00 h, 22:00 h and KSS (hourly). Tests were given under 4 counter-balanced conditions: nil intervention (baseline), extended prior nocturnal sleep (up to 90 min), afternoon nap (20 min) and caffeinated drink (150 mg at 14:15 h).

Results: 19 participants were able to extend their nocturnal sleep (84 $\pm$ 30 min) and all were able to sleep in the nap condition (19.5 $\pm$ 2 min). Afternoon and evening MSLTs showed all active treatments significantly reduced the 'afternoon dip', with nap most effective until mid-evening; next effective was caffeine, then sleep extension. Late evening MSLT, PVT performance and subjective sleepiness did not differ between conditions; neither did subsequent night-time sleep (TST or Sleep Efficiency).

Conclusion: A 20 min nap in the afternoon is more effective at reducing objective sleepiness as measured by the MSLT than extending nocturnal sleep by 90 min. In addition, none of the interventions impacted on performance or subjective sleepiness.

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Impact of intense computer use on sleep quality and circadian rhythm: a cross-sectional case-control pilot study on young Swedish adults

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Introduction: There are not many studies investigating the potential impact of intense computer use on sleep, and most of them are based on subjective assessments rather than objective measurements. This is a pilot cross-sectional case-control study aiming to investigate whether intense use of computer affect sleep quality and circadian rhythms in young adults.

Methods: Twenty 20 men and women (aged between 19 and 25 years) were divided in two groups. One group consisting of ten subjects (TS) had a daily computer use of over six hours. The other group consisting of ten control subjects (CS) spent less than two hours a day using the computer. They were investigated with both objective methods measuring their daily activity and their sleep quality (2 weeks actigraph, 24-hours heart rate, one night sleep recording with sensor pad and pulse oxymetry) as well as subjective assessments about their lifestyle (questionnaire), sleep habits (2 weeks sleep diary, Epworth sleepiness scale ...) and psychological health (Beck Youth inventories questionnaire).

Results: TS did not feel as sleepy as CS when going to bed, had poorer sleep quality with longer sleep latency, more awakenings and lower sleep efficiency. They had more difficulty in getting up in the morning, felt less rested when waking up and sleepier during the day. They also used more stimulants, e.g. coffee, soft drinks and hot chocolate, than did the CS. The time of day when the subjects felt most alert and most sleepy was almost inverted between the two groups. There was a trend showing that TS scored lower in self-appreciation and slightly higher in anxiety, depression, disruptive behaviour and anger.

Conclusions: TS had a poorer quality of sleep and their sleep was easily disturbed during the night. The results suggest also that extensive use of computer affects circadian rhythm.

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Daylight saving time influences sleep times in patients with sleep problems

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Daylight saving time (DST) influences the life of all people in the Western world by changing the clock with 1 h twice a year. Poor sleepers may experience problems adjusting to the 1 h time difference. The effect of daylight saving time (DST) on individuals with sleep disorders was studied by means of a web-based questionnaire. 60000 Individuals visited the Somnio web site on sleep disorders on their own initiative. 19000 chose to complete a sleep disorder symptoms checklist. Those with reported symptoms of sleep disorders (6000) were recommended to complete a sleep behavior questionnaire. They were asked to report their ''average'' sleep behavior over the past 4 weeks. The subjects were divided in a 'summertime' group and a 'wintertime' group, depending on the time they reported their sleep behavior. The first month after the change to winter and summertime was excluded. A delay of waking up in the morning in summer (27 min, $P<0.03$) and an advance of going to bed in summer (29 min, $P<0.007$) was reported. As a result the total sleep time was longer in summer (55 min) and mid-sleep time was delayed by 15 min in summer. There was no difference in rise time. This effect was confirmed for a group of 60 insomniacs who completed a detailed daily sleep log. In addition, the insomniacs also reported to sleep better and to feel more refreshed after getting up in the summer than in the winter ($P<0.05$). It is evident that individuals with disturbed sleep can not adjust their sleep schedule to the time change. The net result of this maladjustment, however, was that they slept longer and better in summertime than in wintertime.

P80

Blue-enriched light improves self-reported alertness and performance in the workplace

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Decrements in alertness and performance compromise health and safety in the workplace. Adequate exposure to light can reduce decrements in alertness and performance. These effects are thought to be mediated, in part, by a recently discovered melanopsin dependent photoreceptive system. The spectral sensitivity of this system is shifted towards shorter wavelengths (blue light), compared to the classical visual system. Specifications and standards for existing light installations in the work place, however, are based on the spectral sensitivity of the classical visual system. We investigated the effects of blue-enriched light (17000K), in comparison to standard lighting (4000K), on self-reported measures of alertness, performance and sleep quality. 104 participants (aged 18–60) divided into two groups took part in an 8 week cross-over. After completion of baseline questionnaires, participants completed morning, midday and late afternoon questionnaires during one day per week. These tests measured subjective sleep quality, alertness, mental effort, headaches, eye strain, recovery and mood. The two groups did not differ with respect to demographics (i.e. age, sex and BMI) or sleep characteristic (Karolinska sleep diary). Preliminary analyses of questionnaires completed during the first leg of the trial revealed that the group under blue-enriched light reported enhanced subjective alertness and performance ($P<0.03$) and decreased sleepiness and negative mood. ($P<0.05$). There were no differences in the incidence of headaches or eye strain between the conditions. These preliminary analyses show that blue-enriched light can improve subjective alertness and performance and decrease sleepiness and negative feelings during the normal working day.

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P81

Impact of sustained wakefulness and circadian phase on temporal production and reproduction

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Temporal duration judgments are known to depend on a variety of factors, both cognitive and physiological in nature. Several studies have reported circadian and wake dependent modulations of short-term interval timing i.e., the ability to judge durations in the seconds-to-minutes range. Here, we aimed at investigating the effects of sustained wakefulness and circadian phase on duration production and duration reproduction for multiple time intervals. Since there is evidence that different processes and mechanisms are involved in duration production and reproduction respectively, we hypothesized that the tasks respond unequally to homeostatic and circadian challenges. In order to obtain a differentiated view of the impact of temporal dynamics in physiology on short-term interval timing, we probed production of 5-s, 10-s and 15-s intervals and reproduction of 3.75-s, 5-s, 7.5-s, 10-s and 15-s intervals in parallel at 3-h intervals in 12 young male subjects (mean age 24.9 $\pm$ 2.96 years; age range 21–29 years during 40-h of sustained wakefulness under near-constant routine conditions. The two methods

employed i.e., production and reproduction, yielded antidromic response curves across the 40-h episode. RM ANOVA using factors time (elapsed time into protocol) stimulus (stimulus duration) and task (task type) yielded no significant effect of factor time, but significant effects of factors task and stimulus and significant interactions of factors stimulus×task, stimulus×time and stimulus×task×time. ($P<0.05$) Reproduction displayed wake-dependent changes combined with a general overestimation for shorter (3.75-s, 5-s) and circadian modulation combined with a general underestimation for longer intervals (10-s, 15-s); 7.5-s intervals were reproduced accurately during the entire protocol. In contrast, produced durations were consistently underestimated and did not exhibit consistent wake-dependent or circadian dynamics. The findings reveal a complex interaction between task type, interval length, circadian phase and state of the sleep-wake homeostat, which need to be incorporated into current models of interval timing.

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Habitual sleep length and subjective perception of seasonality are associated with melatonin deficit

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Although the responsiveness to photoperiod is well conserved in humans (Wehr 1993), only some 25% of the normal human population experience seasonal changes in behavior. The aim of the study was to prove that the individual melatonin deficit marker DOC (degree of pineal calcification) is related to the lack of seasonal phenomena in humans. Out of 3000 patients in which cranial computer tomography (cCT) was performed for diagnostic reasons, the DOC score was determined (Kunz 1999) in 99 consecutive "healthy" subjects (44female, 55 male; age 18–68 years, mean 35.3/SD13.4). Exclusion criteria were: pathological finding in cCT, acute/chronic illness, shift-work, alcohol/drug abuse, medication that influence melatonin excretion. The seasonal pattern questionnaire (SPAQ) was performed in a telephone interview. Twentysix subjects fulfilled criteria for seasonal affective disorder (SAD) or sub-SAD. Age was negatively and significantly correlated with seasonality only in females ($r=-0.41$; $P=0.006$). Overall seasonality score was negatively and significantly associated with DOC ($r=-0.224$; $P=0.026$). Controlling for age mean sleep length over the year was negatively and significantly correlated with DOC ($r=-0.372$; $P=0.011$) and even more pronounced in females ($r=-0.51$; $P=0.031$). Data match to an earlier study in which the length of nighttime melatonin excretion was associated with individual sleep length (Aeschbach 2003). Moreover, data prove for the first time in humans, that the lack of seasonality is associated with a reduced individual capacity to produce melatonin. Thus, because among all livings studied today humans show the most pronounced calcified pineal gland, pineal calcification may represent a human adaptation to modern life.

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Day to day variations in cortisol and subjective ratings of sleep and fatigue

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The objective of the study was to examine the day-to-day variation in cortisol among healthy individuals and its relation to ratings of sleep and fatigue. During four consecutive weeks, 15 office workers (mean age 44 ± 12 years) provided saliva samples for each day. Saliva samples were obtained at awakening, fifteen minutes after awakening and at bedtime. Each day they completed a sleep/wake diary reporting their awakening and bed times, sleep quality, fatigue, workload, stress, and self-rated health.

Results: From multiple regression analysis showed that differences between individuals accounted for; 27.7% of the day-to day variation in cortisol at awakening, 25.2% at 15 min after awakening and 18.4% for values taken at bedtime. After controlling for the individual differences, results showed that low cortisol levels in the morning were associated with poor sleep quality, sleepiness at awakening, and exhaustion and poor health the day before. High evening levels of cortisol were associated with symptoms of stress and poor self-rated health. In conclusions, cortisol levels vary both between and within individuals, with largest variations in the morning. Lower cortisol levels in the morning were associated with high levels of sleepiness at awakening, symptoms of exhaustion the previous day, poor self-rated health and poor sleep quality. High levels in the evening were related to stress symptoms and poor self-rated health. We cannot draw any conclusions of the casual relationship but one possible explanation could be that high levels of stress during the day leads to elevated levels of cortisol in the evening, which in turn affects sleep.

P84

Sleep-related and circadian changes of arterial pressure are altered in leptin-deficient mice

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Leptin is a key modulator of the hypothalamic pathways that control food intake and energy homeostasis. Mice lacking leptin are obese and show altered circadian rhythms of sleep and arterial pressure. We investigated the effect of the wake-sleep state on the circadian rhythm of arterial pressure in leptin-deficient mice. Leptin-deficient obese B6.V-Lep^{ob})/OlaHsd (ob/ob, $n=4$) mice and their lean wild-type (WT, $n=5$) littermates were kept on a light-dark cycle of 12-hour periods with ambient temperature of 25 °C and free access to food and water. After a 10-day postoperative recovery, arterial pressure (TA11PA-C10 telemetry transducer, DSI) and electroencephalographic and electromyographic activities (cable transmission) were recorded for 72 h with the mice undisturbed and freely moving in their own cages. The states of wakefulness, non-rapid-eye-movement sleep and rapid-eye-movement sleep were discriminated and the mean value of systolic arterial pressure (SAP) was computed on 4-s epochs. The differences of SAP (ΔSAP) and of the percentage of time spent in non-rapid-eye-movement sleep (ΔNREMS) between the dark and light period were computed for each mouse and compared between groups with *t*-test. SAP was analyzed with a 3-way analysis of variance (ANOVA, with the wake-sleep state, the light-dark period, and the genetic group as factors). Data are expressed as mean ± SEM with significance at $P<0.0^5$ Ob/ob mice showed significantly lower values of ΔSAP (1 ± 1 mmHg) and ΔNREMS (−8 ± 2%) with respect to WT mice (8 ± 1 mmHg and −21 ± 4%, respectively). ANOVA evidenced significant main effects of the wake-sleep state and the light-dark period on SAP as well as significant interaction effects between each of these factors and the genetic group. These data indicate that both sleep-related and circadian factors underlie the altered regulation of SAP, which is associated with congenital leptin deficiency in ob/ob mice. The results suggest that the hypothalamic pathways controlling energy homeostasis are involved in the circadian and sleep-dependent control of arterial pressure.

P85

Comparisons of the VNTR polymorphism in the human Per3 gene, diurnal preferences and sleep start during days off among working college students

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Introduction: In humans the Per3 VNTR polymorphism consists of 4 or 5 repeats of exonic sequence of 54bp. There also seem to be an association between the VNTR and sleep timing affecting circadian rhythmicity.

Objective: To investigate the possible associations between sleep start, the VNTR polymorphism in Per3 gene and diurnal preferences.

Methods: The present study has been conducted on College students working full-time jobs during the day (Monday to Friday) and attending evening classes (19:30–22:30 h) at a public college in São Paulo, Brazil. The study group consisted of healthy males ($n = 38$) and females ($n = 29$), aged 21–26 yrs. Data collection took place in 2007. Participants filled in a questionnaire about sleeping habits and sleeping times, the Horne-Ostberg (HO) questionnaire for diurnal preferences and provided a salivary DNA sample. The length polymorphisms in the hPer3 gene were genotyped using polymerase chain reaction. The Kruskal-Wallis test and the Spearman correlations were calculated.

Results: The data showed that 25 students are homozygous 4-repeat (4/4), 33 heterozygous (4/5) and 9 homozygous 5-repeat allele (5/5). The VNTR polymorphism were not significantly ($P = 0.74$) associated with start of sleep during days-off as well as diurnal preferences. Additionally, start of sleep was correlated with HO (Spearman = 0.55; $P < 0.01$) during days-off.

Conclusion: The lack of association between Per3 polymorphism and diurnal preferences and beginning of sleep might be due to a small sample.

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The internal phase of entrainment between activity, skin temperatures, and melatonin onset differs between women with vasospastic syndrome and controls during a week long ambulatory protocol

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The primary Vasospastic Syndrome (VS) is a functional disorder of vascular regulation in otherwise healthy subjects, whose main symptom is cold hands and feet. These subjects, mainly women, also often suffer from difficulties initiating sleep (DIS). The aim of the study was to determine the internal phase of entrainment (IPE) between diurnal patterns of skin temperatures, wrist activity and dim light melatonin onset (DLMO) in women having both VS and DIS (WVD) compared with controls (CON). Participants were healthy young women (age: 25.4 ± 0.7), 20 with WVD and 21 CON. In a one-week ambulatory study, we measured 11 skin-temperatures (iButtons®; left and right wrist, foot, calf, thigh, infraclavicular region and sternum; 2.5-min intervals) and the sleep-wake cycle (wrist activity, Actiwatch®, and sleep-wake-diary) under real life conditions. On one evening at home under dim light saliva was collected to determine melatonin onset (DLMO). Cross-correlation analyses were used to define internal phase-relationships (e.g. between foot skin temperatures versus wrist activity). Individual time series of CON and WVD were cross-correlated with the mean series of CON. Maximum and minimum lags were extracted from individual cross-correlation curves. In comparison to CON, WVD showed a phase delay in foot skin temperature (CON versus WVD: 2.4 ± 14.8 s.e.m. versus 33.3 ± 14.4 min; $P = 0.043$) but not in wrist activity (11.8 ± 9.2 versus −1.8 ± 15.2 min; n.s.), DLMO (22.04 ± 1.15 versus 21.97 ± 1.21 h; n.s.) and habitual sleep times (24.02 ± 0.21 versus 23.88 ± 0.30 and 7.88 ± 0.27 versus 7.73 ± 0.20 h, n.s.). Intra-individual time series of foot skin temperatures were cross-correlated with wrist activity (31.1 ± 11.0 versus −69.0 ± 42.5 min; $P < 0.0004$) revealing a significant change of IPE in WVD. Taken together, under everyday ambulatory conditions WVD exhibit a phase delay of the thermoregulatory system with respect to their habitual sleep-wake cycle and DLMO, indicating a difference in IPE. Since we have previously demonstrated that adequate distal vasodilatation is a prerequisite for rapid sleep onset, this delay could represent the thermophysiological correlate for DIS. A changed IPE could underlie the prolonged sleep onset latency in WVD.

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Internal phase of entrainment and sleep onset latency are not different in different chronotypes

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Different chronotypes exhibit a different phase angle between sleep-wake cycle and solar cycle (different external phase of entrainment, EPE). However, not much is known about internal phase of entrainment (IPE) in different chronotypes. The aim of this analysis is to show whether different chronotypes exhibit changed IPE between diurnal patterns of skin temperatures, wrist activity and dim light melatonin onset (DLMO) in relation to difficulties initiating sleep (DIS). 41 healthy young women [20 controls and 21 women with vasospastic syndrome and DIS (WVD); age: 25.4 ± 0.7 yr (sem), BMI: 21.0 ± 0.3; luteal phase] were studied for 1 week under ambulatory conditions. Skin temperatures on proximal and distal skin regions were continuously registered using 11 iButton devices (left and right wrist, foot, calf, thigh, infraclavicular region and sternum), and wrist activity using Actiwatches. Daily sleep-diaries were filled out after each night sleep episode. On one evening at home under dim light saliva was collected to determine melatonin onset (DLMO). Following definition has been used for chronotypes: morning-type: $N = 10$, 1.83–3.83 MSFsc; 0-type: $N = 14$, 4.16–4.82; evening-type: $N = 15$, 5.06–7.03. Cross-correlation analyses revealed parallel changes of all registered diurnal patterns according to chronotypes, i.e. later phase position in evening chronotypes (morning-evening -type: DLMO −1.4 hr; foot skin temp. −1.8 hr; activity −1.3 hr; ANOVA, $P < 0.01$). Internal phase angles between DLMO, wrist activity and distal skin temperatures, as well as estimated sleep onset latency (SOL), did not significantly differ between chronotypes (all n.s.). These findings indicate that different chronotypes exhibit a different EPE, but not a different IPE and SOL. Taken together, in contrast to changes in IPE (Gompper et al. this issue) differences in EPE do not influence DIS. However, it remains to be shown whether extreme late chronotypes show different IPE and prolonged sleep onset latency. In conclusion, these analyses reveal that different EPE is not reflected in different SOL. DIS seem to be related to IPE, whereas distal vasodilatation could represent the thermophysiological correlate for a short SOL.

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Subjective and actigraphic sleep in older people with control and 'blue-enriched' white light

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Research has shown that short wavelength light is more effective than other light wavelengths in influencing non-image-forming responses to light e.g. shifting circadian rhythms and affecting sleep structure. The aim of the current study was to assess the ability of 'blue-enriched' white light (colour temperature 17 K) compared to control white light (4 K) to influence subjective and actigraphic sleep in older people ($\geq$ 60 years) with self-reported sleep problems (PSQI $>$5). In a randomised, crossover design, 15 healthy volunteers were exposed to both light conditions (photon density $\sim 3.62 \times 10^{14}$ photon cm^{-2}/s) in their own homes' during an 11 week trial consisting of 1 week baseline, 3 weeks light treatment A or B, 2 weeks washout, 3 weeks light treatment B or A, and 2 weeks washout. During the light treatment weeks light was administered for 2 h in the morning and 2 h in the evening. For the entire study period subjects kept daily sleep diaries and wore an actiwatch-L (AWL) (Cambridge Neurotechnology Ltd., UK) on their non-dominant wrist. Subjective and objective sleep parameters were derived from the sleep diaries and AWLs, respectively. Sleep parameters before, during and after light treatment were compared using repeated measures one-way ANOVA with Bonferroni post hoc analysis. Complete data from 12 participants (mean age $\pm$ SD: 65.3 $\pm$ 4.0 years; 7F, 5M) have been analysed. During and after both light conditions subjective sleep efficiency significantly improved, sleep latency significantly reduced and wake-up time significantly advanced compared to baseline ($P<0.05$). Objective sleep efficiency significantly improved during the 17 K light ($P<0.05$); time awake at night was significantly reduced during both light conditions ($P<0.05$) compared to baseline (4 K) and washout (17). Thus compared to baseline and washout periods, both lights had some significant beneficial effects on sleep. However, there were no significant differences in any sleep parameter between the two light conditions.

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Shift Work

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Chronotypes and shiftwork among nurses: their influence on adaptation

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Introduction: The aim of this study was to explore the interaction between circadian preference and type of shift on measures of stress, sleepiness, fatigue and sleep duration, among a sample of shiftworking nurses.

Methods: Two hundred twenty women (age 39.18 $\pm$ 10.46) participated in a cross-sectional study (response rate 75%) in which a stratified, random sampling among nurses from the 11 sanitary areas of Madrid, Spain, was carried out. Participants were classified in one of two groups: (a) rotating shift ($n = 170$); and (b) night shift ($n = 50$). Self-reported anonymous information was obtained from the Spanish version of the Standard Shiftwork Index (Barton et al. 1995), the Morningness-Eveningness Questionnaire (Horne-Östberg, 1976), and the Epworth Sleepiness Scale (Johns, 1992) which showed acceptable psychometric properties (Cronbach's $\alpha = 0.70$–0.88). Mean differences on all dependent variables for chronotypes and shift-types were analyzed with one-way ANOVA tests. A MANOVA model was carried to study the interaction effect of the above mentioned factors on all dependent variables.

Results: Nurses on a morning-night shift were significantly older, and reported sleeping less on workdays and perceiving higher stress levels than those on an afternoon-night shift or a morning-afternoon-night shift; no significant differences were found in terms of perceived sleep debt (PSD), sleepiness or fatigue between shift-types. In addition, evening types were significantly older and reported a trend towards a higher PSD; no significant differences were found in terms of sleep duration on workdays, perceived stress, sleepiness or fatigue between chronotypes. The MANOVA model, after controlling for age, showed significant differences in measures of sleepiness and PSD for the interaction between chronotype and shift-types, with morning types on a morning-night shift and on an afternoon-night shift reporting both higher levels of sleepiness and PSD, respectively.

Conclusions: These data confirm the importance of taking into account the chronotype of shiftworkers when designing and implementing work shifts. Also, they reveal that some schedules are more efficient in attenuating sleep debt and sleepiness than others.

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The impact of shiftwork on junior doctors' sleep, alertness, performance and well-being

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The implementation of the European Working Time Directive (EWTD), has considerably altered the organisation of junior doctors' work hours. Total hours have been reduced and full shift schedules have replaced traditional on-call rotas. The negative consequences of shiftwork have been extensively documented; effects are reported to include disrupted sleep, impaired vigilance, cognitive impairment, social isolation, as well as negative effects on mood, job performance, mental health and physical health (Issac 2000, Akerdstedt 2003). However, little is known about the effects that the new shift schedules have upon junior doctors. The current study examined the effects of shift work on junior doctor's performance, sleep, alertness, health and general well-being, through qualitative one-to-one interviews. Ten junior doctors, from five NHS Trusts across Wales participated in a semi-structured interview. Participants included doctors from Foundation Level one and two, Specialist Trainees and Specialist Registrars. Inductive Thematic Analysis indicated a complex relationship between work hours and fatigue influenced by shift sequence, career goals and organisational support systems. Three main themes emerged from the data; 'Doctor's schedules' identified specific shift features which were associated with disrupted sleep and intensified fatigue. The impact of working many consecutive night shifts, together with frequent and poorly distributed on-call duties, were discussed in terms of decreased performance, medical error and concern for patient care. 'Work-life balance' depicted an unsatisfactory balance between work and home life, disrupted social and family lives due to anti-social shifts, sleep deprivation and work related fatigue, complicated further by career goals and educational needs. 'Social and organisational support structures' identified a critical role for departmental moral and team spirit. Good support structures in the work place acted as a buffer against the demands of difficult work schedules, and negative role stressors. Implications are drawn for schedule design to reduce fatigue alleviate sleep deprivation and improve welfare of junior doctors.

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The prevalence of disturbed sleep in shift workers: a representative sample

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Shift work sleep disorder has is a diagnostic entity with uncertain prevalence and without a strict quantitative definition. The present study used a national representative sample of shift workers in an attempt to obtain estimate of prevalence. 8000 individuals were interviewed over the phone. 450 of these were shift workers that at least occasionnaly worked nights. This subsample were asked a number of questions on how often fatigue and disturbed sleep occurred in connection with night work (never-each shift). Another question asked whether disturbed sleep was a problem in the respondents life (doesn't occur-occurs but no problem-occurs but a manageable problem, rather great problem, very great problem. The results show that among shift workers disturbed sleep at least half the night shifts occurred in 10%. Fatigue in connection with more than half the night shifts occurred in 23% and either disturbed sleep or fatigue or both occurred in 33%. Disturbed sleep as a rather or very great problem in life was reported by 7.7% of the shift workers. The corresponding value for fatigue was 10.0%. Reports of either fatigue or disturbed sleep as a very or rather great problem occurred in 13%. The prevalence values will depend on whether only sleep is considered or fatigue or both and on whether severity is used as a criterion. The resulting prevalence will vary from 7% up to 25%. It was concluded that disturbed sleep in shift workers may vary from 7% up to 25% depending on definitions.

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Preliminary evaluation of sleep complaints in medical shiftworkers in Armenia (a pilot study)

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Objective: To assess parameters of shiftwork and screen for sleep disorders in physicians and nurses.

Method: A structured screening questionnaire including questions on different aspects of shiftwork was developed and administered to 38 physicians and nurses from different hospitals and departments of Yerevan who have regular shifts including night hours. Monthly frequency and duration of shifts, symptoms during and after shifts, chronic sleep disorders (insomnia, hypersomnia, sleep-disordered breathing-SDB, parasomnias, movements in sleep, 4 criteria for restless legs syndrome-RLS) were screened.

Results: Thirty eight physicians (47,4%) and nurses filled in the questionnaire. Age interval-21–47 years (mean = 28), F-71%. Mean amount of shifts ~8/month, mean duration of a total shift − 22.2 h (16–32 h). Seventy four per cent of respondents were not allowed to sleep during night hours, but 17% of them slept regularly at a mean of 2.4 h. On the day after a nightshift only 2 had no symptoms, the rest mentioned different daytime symptoms: somnolence-84.2%, fatigue-44.7%, loss of initiative-39.5%, decreased working capacity-39.5%, depressed mood-28.9%, irritability-26.3%, memory disturbance-21%. During the nightshift 10 had no symptoms, the rest had: somnolence-52.6%, fatigue-42.1%, loss of concentration-26.3%, loss of initiative-15.8%. Of participants 76.3% consider 12-hour shift as a norm. Respondents consider mean optimal frequency as 6 per month. Disordered sleep out of the shifts was found in 42.1%: hypersomnia-28.9%, insomnia (mostly sleep-onset insomnia)-15.8%, SDB-5.3%, RLS-5.3%, 1 case of sleep-talking (2.6%) and 1-of movements in sleep (2.6%). RLS cases and daytime symptoms (mean of 4) were associated with longer duration of shifts (24 h and >), if < than 24 h-mean symptom count is 1.8. Sleep-maintenance insomnia and SDB cases were associated with higher frequency of shifts (8 and > per month).

Conclusion: From these preliminary data we conclude that in nearly all participants nightshifts lead to serious impairment of performance the next day which is more evident with longer duration of a shift. They also could cause or worsen chronic sleep disorders given longer duration or higher monthly frequency.

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Independent effects of sleep loss and poor sleep quality over daytime well-being in undergraduates

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Aim: To investigate the associations between perceived sleep quality, sleep restriction and well-being of undergraduates in real life circumstances.

Methods: A sample of 1654 (55% F) Portuguese undergraduates (University of Aveiro, Portugal), 17–25 yr old, answered a self-response questionnaire developed for a survey on sleep-wake habits at the university. Sleep Restriction on week nights was computed as the difference between perceived individual sleep needs and sleep length on week nights (hours per night). Items rated on 5-point scales were summed to calculate Sleep Quality (sleep satisfaction, depth of sleep, sleep latency, sleep-onset difficulty, night and early awakenings, whether awakenings are a problem; $\alpha = 0.73$), and four well-being scores: Mood Symptoms (tired, irritable, depressed, nervous; $\alpha = 0.74$); Cognitive Functioning (productive, attentive, motivated, concentrated; $\alpha = 0.73$); Vigour (active; energetic; efficient; alert; happy; relaxed; $\alpha = 0.77$); Somnolence (5 items adapt. Manber et al. 1996. Sleep, 19, 432–441, plus 1 item on somnolence during classes; $\alpha = 0.84$).

Results: Means on well-being measures for Sleep Restriction (none; 1 hr; 2 or+hr/night) and Sleep Quality (Very Poor; Poor; Good; Very Good) groups were compared using bifactorial ANOVAs 3×4. The main effects of both Sleep Restriction and Sleep Quality were significant for all variables studied ($P < 0.001$ in all analyses), whereas interactive effects were not significant. Across increasingly Sleep Restriction groups, there were rises on Somnolence and Mood Symptoms, and diminutions on Cognitive Functioning and Vigour mean scores. This pattern of results were also found across decreasing Sleep Quality groups.

Conclusion: In our sample, sleep restriction on week nights and poor sleep quality, each *per se*, are associated with higher perceived somnolence and with vigour, mood and cognitive impairments. Sleep loss, even in apparently small amounts and accompanied by good sleep quality, is associated with diminished well-being.

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The impact of work hours, sleep and wake on subjective fatigue ratings in Australian doctors

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Hospital doctors routinely work extended hours and are frequently required to be on-call at all times of the day and night. The fatigue arising from sleep and circadian disruption can pose a risk to both patient safety and to the health and well-being of the doctor. Traditionally, fatigue-related risk has been managed indirectly through guidelines around hours of work, without consideration for sleep or time awake. Recent evidence indicates that total work hours however are not the most important factor[1]. This study examined the impact of work hours, sleep and wakefulness on the subjective fatigue of hospital doctors with the aim of more clearly defining the contributing factors. Sleep/wake and duty data was collected from doctors working in two Australian hospitals. Activity monitors were worn for 14–28 days during which time participants also completed daily work and sleep diaries, which included a subjective fatigue assessment [2] at the beginning and end of each work period. To date data from 126 work periods from 2 of the 10 participating hospitals have been analysed using mixed model regression to determine the factors that predict end-of-shift fatigue ratings. Preliminary analyses indicate that work hours do not significantly predict post-shift fatigue ratings. Total sleep in the prior 24-hour period and length of wakefulness however were both found to be significant predictors of post-shift fatigue ratings ($P < 0.05$). In contrast to what might be expected, sleep in the prior 24 h and length of wakefulness were both predictors of end-of-shift fatigue. In light of the widespread use of prescriptive hours of work guidelines, and a push for reduced work hours to manage fatigue-related risk, these findings suggest that prior sleep and wake are critical factors to account for when managing fatigue-related risk. Analyses using the larger 10-site data set will investigate this further in addition to predictions of pre-shift fatigue ratings.

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The impact of shiftwork on junior doctors' sleep, alertness, performance and well-being: a questionnaire survey

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Following the implementation of the European Working Time Directive (EWTD), most junior doctors' work shifts patterns that

include blocks of consecutive nightshifts. In some cases, they are required to work as many as 7 night shifts in a row, while for others this is split into blocks of just 3 or 4 consecutive nights. The circadian rhythms of night-workers do not readily adjust to a nocturnal routine over several successive night shifts (Folkard & Tucker, 2003). Consequently, the sleep that is taken during the day between successive nightshifts continues to be disrupted, as it is taken at an inappropriate circadian phase. Thus fatigue continues to build up with each successive night that is worked, with consequent accumulations in performance impairment and risk of error. The current study assesses the impact of junior doctors' shiftwork arrangements on fatigue and well-being, by means of two questionnaires distributed 6 month apart. The shift features examined include the number of consecutive night shifts before a break; the duration of rest intervals between shifts; the amount of rest breaks and naps taken during night shifts; the frequency of extended shifts; the frequency of weekend shifts; and the frequency of twilight shifts. The main outcome measures are sleep duration; alertness on shift; likelihood of making a minor mistake while on duty; confidence in being able to drive home safely; disruption of work-life balance; job satisfaction; and psychological well-being. The role of a range of moderating factors (e.g. domestic circumstances; job grade; work experience; work load; and circadian type) are also examined. A key focus of the analyses is to examine the accumulation of fatigue across successive shifts and whether the effects of nightworking spill over on to subsequent day shifts (e.g. as a result of circadian disruption). The analyses also considers the impact of napping during the night shift, on circadian disruption and the accumulation of fatigue. Findings are interpreted in the context of the need to optimize the balance between fatigue management and operational requirements (e.g. training, continuity of care), while maintaining compliance with the EWTD.

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Effect of total sleep deprivation on postprandial plasma glucose, triacylglycerol and non esterified fatty acid concentrations in shift workers and non shift workers

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Epidemiological studies have shown that sleep deprived individuals such as shift workers are at higher risk for cardiovascular disease (CVD), accompanied by underlying changes in blood glucose, triacylglycerol (TAG) and non esterified fatty acid (NEFA) concentrations. However, these changes have not been investigated in response to total sleep deprivation in laboratory conditions. Therefore, the aim of the present study was to investigate the effects of one night of total sleep deprivation (TSD), a recovery nap and recovery sleep on fasting and postprandial metabolism under strictly controlled conditions. The responses of shift workers and non shift workers were compared. Six healthy shift workers (33.5 ± 7.8 yrs (mean $\pm$ SD), body mass index (BMI): $28.2 \pm 3.7\,kg\,m^{-2}$ and waist-hip ratio (WHR): 0.93 ± 0.03 cm; shift work history ≥ 5 yrs) were matched with 6 non shift workers (31.5 ± 5.4 yrs, BMI: $25.1 \pm 1.3\,kg\,m^{-2}$ and WHR: 0.91 ± 0.04 cm; shift work history <6 months). Volunteers kept a regular sleep wake cycle (sleep duration 7.5 or 8 h) the week prior to the study and refrained from alcohol, smoking, caffeine and heavy exercise 2 days prior to the study. After an adaptation and baseline night (equal to habitual sleep), volunteers were kept awake for 36.5 h. This was followed by a nap (4 h), recovery sleep (equal to habitual sleep) and another 16 h awake in the laboratory (all procedures in dim light (<8 lux), interventions relative to wake up time, body posture and food controlled between days). Blood samples were taken before and after a standard breakfast on the baseline day, after TSD and after recovery sleep. Plasma glucose ($n = 11$), TAG ($n = 11$) and NEFA ($n = 10$) concentrations were measured by automatic analysis with Ilab 650. Preliminary analysis by two-way ANOVA (within subjects factors: time and day) showed that there was no effect of day on plasma glucose and NEFA concentrations. However, there was a significant ($F_{(2, 9)} = 4.7$; $P < 0.05$) day*group interaction for glucose. There was also a significant effect ($F_{(2, 9)} = 4.2$; $P < 0.05$) of day on plasma TAG levels.

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Paediatrics

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Newborns, sleep and face recognition

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We try to understand the function of sleep in newborns, showing them two different kind of interaction and subsequent face recognition sessions. We match 2 newborns' groups with two different 8′ stimulus, presented by an Adult flexed on the newborn's cradle. The distance between the newborn's face and the Adult's one is about 20 cm. The groups will be named: Communication Group-CG, Still Face Group-SFG. For CG, the newborn's turn taking characterizes the communication. Main communicative behaviors are: imitative cycles of mouth opening, tongue protrusion, vocalization and tactile contact. For SFG the Adult stands still in front of newborn without communicative behavior. After the 8′ period we propose to each newborn a 1st session of face recognition, exhibiting the Communicative Adult-CA or the Still Face Adult-SFA (it depends on the group the newborn belongs to) paired to a New Adult-NA, broadly comparable. Suddenly the first spontaneous awakening, after one cycle of Sleep, at the same newborn is proposed a 2nd session of face recognition. We hypothesize that communication is the crucial process implicated in face recognition, so the newborns of CG will look longer the face of the CA, instead the newborns of SFG will look shorter the face of SFA during the 1st session of face recognition. Concerning the 2nd session we think to find some kind of interaction between Stimulus and Cycle of Sleep. Obtained parents' permission, we videotape 20 full term healthy newborns, in the newborn care division of Policlinico Umberto I, mean age 32 h. Newborns in Quiet Alert, are randomly assigned to the 2 groups. We codify the Gaze Direction in the two sessions of face recognition. Has been used to test hypothesis a mixed factorial design of ANOVA. 1st session: SFG spend more time looking at the NA then CG do ($P > 0.05$). 2nd session: Both groups spend more time looking at the NA. There is an interaction between Stimulus and Cycle of Sleep ($P > 0.05$): there is a significant increase of time spent in looking the NA from the 1st to the 2nd session ($P > 0.01$) for CG, not for SFG. These results suggest, not only for adults, but also for newborns in peculiar context (i.e. communicative one), that sleep produce an effect (unlearning? information storage?) on cognitive tasks.

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The scoring of cyclic alternating pattern in healthy term infants (between 1 and 4 months of age)

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Aim: To evaluate cyclic alternating pattern (CAP) in the sleep of healthy term infants to obtain a standardized database for CAP parameters in this age range (from 1 to 4 months).

Patients and methods: Twenty-three healthy infants with a mean conceptional age (gestational age plus postnatal age) of 47.6 ± 3.8 weeks, age range 42–55 weeks (10 males, 43.47%), were studied by a 3-hour video-polygraphic recording [EOG, EKG, EMG, nasal flow (cannula) respiratory effort, Sa O2 and an extended 13-channel EEG]. More than 1 complete sleep and sleep-wake cycle, including 1 complete period of active and quiet sleep, between 2 feeds, was recorded at the Sleep Unit. The electrodes were attached before feeding and babies were placed in the supine position. General information about the baby's birth weight, Apgar score, and gestational, conceptional, and postnatal ages was collected. Sleep stages, EEG patterns, respiration and CAP were scored according to standard criteria and definitions.

Results: The sample was subdivided in 3 groups according to the age and maturation of quiet sleep EEG patterns from tracé alternant and continuous delta activity sleep to stage 2 NREM sleep: Group 1 was composed of 9 babies (3 males) (tracé alternant and continuous delta activity sleep) with a mean conceptional age of 43.97 ± 1.29 weeks (age range from 42 to 46 weeks); Group 2 included 6 infants (4 males) (continuous delta sleep and rarely immature sleep spindles), with a mean conceptional age of 49.37 ± 3.10 weeks (age range from 46 to 54 weeks); and Group 3 included 8 infants (3 males) (stage 2 NREM), with a mean conceptional age of 50.42 ± 2.86 (age range from 46 to 55 weeks). CAP scoring was performed in Groups 2 and 3. The CAP rate was 6.83 ± 3.58 in Group 2 and increased to 12.91 ± 2.21 in Group 3; the A1 index was lower and A2 index was higher in Group 2 than in Group 3.

Conclusion: We provide preliminary data on CAP analysis in infants from 1 to 4 months of age. We found a transitory period, when tracé alternant disappears and CAP events appear. We suggest that the appropriate time to begin CAP analysis is around 3 months of age, when mature stage 2 NREM appears.

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Moving behavioural sleep work with children into the public health agenda

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The adverse impact of sleep disturbances on the mental health and well being of children and families has been well documented, as has the efficacy of therapies for behavioural problems. Increasing evidence supporting a link between lack of sleep and obesity, is adding weight to move sleep issues into the public health agenda. This poster presentation focuses on the results of a project which has expanded a behavioural sleep service for children, moved it into multidisciplinary and multi agency working, and made progress towards a public health approach for behavioural sleep issues for children. Child psychologists had introduced behavioural sleep clinics to Fife, Scotland. Trained Health Visitors worked in clinics giving individualised behavioural advice to families. Short term funding from the Scottish Executive became available to Change Children's Services and a three pronged co-ordinated approach was developed: 1.) Consolidation and Expansion of the Clinic Service. The referral rate rose from 100 to 300+per annum. Results of parent questionnaires following treatment will be highlighted along with analysis of results from sleep disturbances indices. 2.) Raising the Level of Knowledge of Behavioural Sleep Issues Across Disciplines and Agencies. Multidisciplinary family workers have been given basic strategies to work with families to improve sleep hygiene for children. 3.) Information and Guidance to Parents and Older Children about behavioural issues related to sleep. Leaflets on good sleep routines are distributed to parents of every baby in the county at 2 weeks, 8 weeks, 4 months, & 13 months. Other leaflets for older children and teenagers have been produced. Workshops within schools and community groups have begun.

P100

A professional training programme to address sleep difficulties in children with disabilites

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Background: Children spend half of their lives asleep. Sleep disturbance impairs learning, mood, daytime behaviour and health. Sleep problems are common in children with physical and learning disabilities. UK studies suggest a prevalence of up to 67% in children with significant learning difficulties. Children with physical disabilities, such as cerebral palsy, have confounding problems such as gastro-oesphageal reflux and sleep disordered breathing that may compound their sleep difficulties.

Methods: In 1998 Sleep Scotland developed a service to train sleep multi-professional counsellors in cognitive behavioural intervention for families with children with additional support needs. The Centre for Health and Social Research evaluated the programme alongside continuous evaluation using the General Health Questionnaire 30 (GHQ30), sleep index to rate severity of child's sleep problems and parental and professional feedback forms.

Results: 230 Sleep Counsellors have been trained and have offered this intervention to 1358 families, as well as supporting 3652 parents and 2739 professionals. Sleep Scotland's full evaluation data will be presented in the poster presentation. Sleep Scotland is the only body carrying out this behavioural cognitive intervention work throughout Scotland.

Conclusion: Professionals with diverse backgrounds can be trained and supported to improve sleep problems in children with disabilities. Sleep Scotland is now in partnership with Southampton City Primary Care Trust to develop a similar programme across England.

P101

Relationship between sleep pressure and the slope of slow-waves during puberty

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It was recently suggested that synaptic strength is reflected in slow-wave activity (SWA, 0.5–4.5 Hz), which is commonly used as a measure of sleep pressure in NREM sleep. Particularly, a computer model simulating thalamocortical interactions revealed that alterations of synaptic strength are sufficient to reproduce the SWA decrease over night. Based on the model, the slope of slow-waves is a good indicator of synaptic strength, as it reflects directly changes in synchronization of cortical neurons. Recent data in humans and rats confirm the relationship between sleep pressure and the slope of slow-waves. In the present study we investigated changes in the slope of slow-waves, under low and high sleep pressure in the course of puberty. All night sleep recordings were performed in 8 pre-pubertal children (Tanner 1/2, 11.9 ± 0.3 years) and 6 mature adolescents (Tanner 4/5, 14.3 ± 0.6 years) for a baseline and after sleep deprivation (SD). EEG slow-waves were detected as negative signal deflections between two consecutive positive peaks after visual scoring and bandpass filtering (0.5–4 Hz). Both during baseline and after SD, SWA was higher in pre-pubertal children compared to mature adolescents. We found concurrent differences in the slope of slow-waves between pre-pubertal children and mature adolescents (e.g. first NREM episode; baseline, pre-pubertal children, 580.8 ± 49.0 $\mu V\ s^{-1}$; mature adolescents, 309.7 ± 39.1 $\mu V\ s^{-1}$; $P<0.005$; recovery, pre-pubertal children, 635.8 ± 46.0 $\mu V\ s^{-1}$; mature adolescents, 403.8 ± 46.5 $\mu V\ s^{-1}$; $P<0.005$). Furthermore, even when controlling for the amplitude of slow-waves, pre-pubertal children exhibited steeper slope slow-waves than mature adolescents. A comparison of baseline and recovery sleep revealed an initial significant increase in the slope of slow waves in mature adolescents but not in pre-pubertal children. These findings suggest increased synaptic strength of neurons involved in the generation of sleep slow-waves in pre-pubertal children. Such increased synaptic strength could be due to increased density and/or increased efficacy of synapses. Ceiling effects may prevent a further increase of the slope of slow-waves after SD in pre-pubertal children.

P102

Analysis of sleep cyclic alternating pattern (CAP) in children with Prader-Willi syndrome and effect of growth hormone treatment

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Introduction: Few studies were carried out on sleep in PWS children. Only one study analyzed the sleep microstructure by means of cyclic alternating pattern (CAP) in young adult PWS patients, showing that PWS patients with CAP expression characterized by higher proportion of A1 subtypes presented less severe GH deficiency.

Aims: The aims are to evaluate the sleep microstructure in children with PWS compared to an age-matched control group and to evaluate the differences in PWS children with GH therapy (GH+) and without GH therapy (GH-).

Methods: 30 children with PWS (17 patients were GH- and 13 GH+) were recruited to participate in the study, were underwent to a complete PSG and were analyzing the CAP parameters.

Results: Sleep macrostructure: PWS children had a reduction of sleep efficiency, of 2NREM and of REM. No differences have been found in sleep architecture between GH+PWS and GH- PWS. Sleep microstructure: GH- PWS patients showed a global decrease of total CAP rate, in S1 and in S2 but not in SWS. In GH+PWS patients CAP rate and A1 index in SWS were increased.

Discussion: This study represent the first attempt to evaluate CAP in children with PWS with and without GH therapy and to analyze the effect of GH replacement on sleep. We found a decreased total CAP rate and of all A phases, suggesting a decrease of NREM sleep instability according to the reported generalized hypoarousal state of PWS subjects. CAP rate and A1 index in SWS were significant higher in PWS patients GH+, probably induced by GH.

P103

Sleep architecture in dyslexic children

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Dyslexia is a learning disability that manifests primarily as a difficulty with written language and particularly with reading and spelling. In literature only one study evaluated the sleep parameters in children with learning disabilities showing an increase of stage 4 and a decrease of REM (Mercier et al. 1993). The aims of our study was to evaluate sleep architecture based on conventional parameters and by means of spectral analysis.

Methods: For the purpose of this study, we recruited 9 subjects with Dyslexia and 9 typically developing children. Dyslexic subjects were selected on the basis of a documented history of dyslexia, with defective performances on standard tests for the assessment of reading skills. All the subjects underwent a PSG overnight recording after one adaptation night to avoid the first-night effect. Power spectral (FFT) analysis of the EEG based on the Cz derivation was computed and spindle density was calculated in stage 2 and in SWS.

Results: Children with dyslexia showed differences on macrostructural parameters represented by an increase of Stage 2% (57.6 versus 48.2; $P<0.0001$) and a decrease of Slow Wave Sleep % (15.7 versus 22.2; $P<0.005$). FFT analysis revealed an increase in sigma band in stage 2 in dyslexic children versus control ($P<0.0001$). Dyslexic children showed also a significant increase on spindle density in stage 2 (3.64 versus 1.71; $P<0.0001$).

Conclusions: Our results, although preliminary, showed a significant increase of sigma band and of spindling activity in dyslexic children; this typical sleep pattern could be considered as a characteristic of sleep in these subjects and could be related to the specific cognitive disability of dyslexia. Mercier L, Pivik RT, Busby K. Sleep patterns in reading disabled children. Sleep. 1993 Apr;16 (3):207–15.

P104

Deficits in executive function are associated with shorter sleep duration in normally developing children aged 6–12 years

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Sleep is of fundamental importance to the developing brain and its functioning. Sleep fragmentation and sleep restriction have been associated with deficits in executive functioning in normal healthy children. Lower sleep efficiency and shorter sleep duration have been associated with reduced working memory performance (Steenari et al. 2003). Increased sleep fragmentation has been associated with attentional deficits (Sadeh et al. 2002). This study sought to further examine aspects of executive function (EF) that may be affected by reduced sleep duration, defined as the period from sleep onset to sleep end time.

Method: The sleep patterns of 40 normally developing, healthy children (mean age 9.4) were assessed using actigraphy for 1 week. Children with a history of ADHD or learning difficulties were excluded. A battery of neuropsychological tests was administered that assessed sustained attention, selective attention, and attentional control (TEA-Ch), working memory (digits backward), and planning (NEPSY tower task). Parents completed the Child Sleep Habits Questionnaire (CSHQ), the Strengths & Difficulties Questionnaire (SDQ), and the Behavior Rating Inventory of Executive Function (BRIEF).

Results: Sleep minutes ranged from 336.7–576.1 (mean 465.6). Sleep efficiency ranged from 61.6–97.2% (mean 83.6%). Controlling for age, shorter sleep duration was significantly associated with deficits in processing speed ($r=0.40$, $P<0.05$), working memory ($r=0.47$, $P<0.01$), and planning ($r=0.44$, $P<0.01$). Attention variables did not correlate significantly with shorter sleep duration. Shorter sleep duration was also significantly associated with deficits in executive function as rated by parents. Shorter sleep duration correlated with the total BRIEF score ($r=-0.41$, $P<0.05$) and the planning ($r=-0.41$, $P<0.05$) and working memory ($r=-0.41$, $P<0.05$) subscales. Shorter sleep duration was not significantly associated with parental report of behaviour problems using the SDQ, however, the conduct problems subscale just failed to reach significance ($r=-0.34$, $P=0.07$).

Conclusions: Short sleep duration is not associated with attention as measured using the TEA-Ch. Working memory, processing speed and planning ability may be particularly susceptible to the effects of short sleep duration.

P105

Just: a behavioral-hypnotherapy program for adolescents 11–16 years

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Objectives: Sleep disorders are common in adolescence. About 40% of the children suffer from difficulties to get to sleep or in maintaining sleep, early wakening or insufficient sleep (Vignau et al. 1997). About 35% of the adolescents between 13 and 19 years have insomnia (Bailly et al. 2004). And 67% reports about subjective sleep insufficiency (O'Brien und Mindell, 2005). Treatment for those children is necessary. The objective of the study was to assess a multimodal therapy program for adolescents between 11 and 16 years with insomnia with three months follow up.

Study Design: 11 physical healthy 11 to 16 year old children and their parents participated. The adolescents filled out the Sleep Disturbance Scale for Children (SDSC, Bruni et al. 1996) and the Sleep Hygiene Index (SHI, Mastin, Bryson & Corwyn, 2006) and a questionnaire for Sleep related Cognitions (FB-SK, Scharfenstein, 1995). After two weeks sleep log a psychological behaviour and hypnotherapy training followed. The training consists about 6 sessions group therapy. For assistance they got a manual. The main themes were good sleep hygiene and dealing with daily hassles. The treatment was supported by hypnotherapeutic CDs for each session. The parents got some advices in handling with the adolescents sleep problems. After the treatment and three months later the children and parents were tested again.

Results: As a research hypothesis we first expect significant decrease in sleep disorder symptoms of the adolescents; second, a significant reduction of psychopathological scores in the CBCL/YSR (Child behaviour checklist). First results will be shown.

Conclusions: The multimodal training program for adolescents with insomnia seems to be effectual. The program can decrease the symptoms of sleep disorders of children in age of 11 to 16 years. Looking at the daily effects of these problems such as difficulties to concentrate and behavioural problems as aggression it is important to reduce these symptoms in the early years. Also school problems are often a result of bad sleep. In further studies the school grades should be included and also the effect of the program on medical and physical health.

P106

Incidence and remission of sleep related symptoms in children: The Tucson Childrens Assessment of Sleep Apnea Study (TUCASA)

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Introduction: There is scant evidence related to the incidence and remission of symptoms associated with sleep disorders in children, such as witnessed apnea (WITAP), excessive daytime sleepiness (EDS), habitual snoring (SN), and insomnia (INSOM).

Methods: 503 children aged 6–11 years completed home polysomnograms. A sleep screening questionnaire and sleep habits questionnaire were completed by the parent. Approximately 5 years later, 348 of these families completed the same questionnaires. On both occasions parents were asked to report the frequency of symptoms associated with sleep in their child. WITAP was defined as stopping breathing, struggling to breathe, or having to shake the

child awake while sleeping. EDS was defined as being sleepy in the daytime, falling asleep at school or while watching television. SN was present if the parent reported their child snored loudly. INSOM was present if the child currently experienced trouble falling asleep, staying asleep, or waking too early. The symptom was defined as present if the parent reported it occurred "frequently" or "almost always".

Results: The mean age at first assessment was 9.0 years (range 6–12) while mean age at second assessment was 13.7 (10–18). The mean time between assessments was 4.6 years (2.9–7.3). There were 50.9% males and 49.1% females. Ethnicity was 63.8% Caucasian and 36.2% Hispanic. The incidence rates for key symptoms of sleep disturbance were: SN 3.4%, EDS 10.1%, WITAP 0.9%, and INSOM 12.1%. Remission rates were SN 10.1%, EDS 8.6%, WITAP 6.0%, and INSOM 12.4%. The percent of children who were unchanged between assessments was SN 86.5%, EDS 80.2%, WITAP 93.1%, and INSOM 74.1%, which represents 79.9%, 75.3%, 92.0%, and 60.6% answering "no" both times, and 6.6%, 4.9%, 1.1%, and 13.5% who answered "yes" both times.

Conclusions: In children, the incidence of nocturnal sleep apnea symptoms is relatively low, except for insomnia. Parent reported symptoms associated with sleep disordered breathing are persistent.

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Mini-kiss: a parent training program for children between 0.5–5 years with insomnia

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Objectives: In the first months and years sleep disruptions and irritations are frequent. Behavioral insomnia of childhood, as limit-setting sleep disorder or sleep-onset association disorder, which involves difficulties in initiating or maintaining sleep are common in early childhood. About 20–25% of young children shows sleep disorder-related symptoms. Childhood sleep disturbances may manifest in a variety of ways, including bedtime resistance; refusal to go to bed when requested by parents; sleep onset delay; inability to fall asleep within a reasonable time and prolonged night wakings or inability or unwillingness to return to sleep without assistance after awakening during the night. Treatment for those parents and their children is necessary. The objective of the study was to assess a parent training program for children between 6 months and 5 years with behavioural insomnia with three months follow up.

Study Design: 9 parents with their physical healthy 6 month to 5 year old children participated. The parents filled out a Sleep Disturbance Questionnaire for their children and the Sleep Hygiene Index (SHI, Mastin, Bryson & Corwyn, 2006). Scores of sleep onset Protosyssonia and sleep night waking protodyssomnia were given (Gaylor & Anders, 2001). After two weeks sleep log a parent training which included behaviour and hypnotherapy strategies followed. The training consists about 6 sessions group therapy. For assistance they got a manual. The main themes were good sleep hygiene and dealing with difficult sleep related situations. The treatment was supported by a hypnotherapeutic CD for the parents. After the treatment and three months later the children and parents were tested again.

Results: As a research hypothesis we first expect significant decrease in sleep disorder symptoms of the children; second, a significant reduction of psychopathological scores in the CBCL (Child Behaviour Checklist) and a decrease of the parental stress. First results will be shown.

Conclusions: The parent training program for children with insomnia seems to be effectual. The program can decrease the symptoms of sleep disorders of children in age of 6 months to 5 years.

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Interhemispheric changes in the cortex connectivity in pre term and term neonates during sleep: assessment through EEG phase synchronization measures

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We assess the interhemispheric brain connectivity in preterm and term neonates during sleep from polysomnographic EEG records by means of a recent measure of phase synchronization (PS) between two signals (Stam CJ et al. Human Brain Mapping 28:1178–1193, 2007), called "phase lag index" (PLI), to investigate whether differences in the gestational age result in changes in the interhemispheric coupling.

Methods: Digitised monopolar (256 Hz) EEGs from two groups of 6 healthy neonates of similar postmenstrual age (39 to 41 weeks), one group of preterm (PTER) and another group of term neonates (TERM). The recording electrodes were Fp1, Fp2, C3, C4, T3, T4, O1 and O2 (average as reference). We estimated the PLI magnitude and sign between homotopic electrodes of both hemispheres during active (AS) and quiet sleep (QS) for the EEG delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–13 Hz) and beta (13–8 Hz.) bands. For each pair of electrode, *t*-test was used for comparisons between both groups.

Results: During AS, we found significant differences in the PLI magnitude in delta band between both neonates groups for the pair T3-T4 ($P<0.01$) and O1-O2 ($P<0.05$): PTERM exhibiting a greater coupling than TERM neonates in both cases. However, no phase lag changes were observed in either case. No other significant change were found during AS. During QS, the PLI changed in the beta band for the pair T3-T4, with greater values ($P<0.01$) for the TERM group. Two additional effects were found during QS: phase lag between T3 and T4 in beta band was greater in the TERM neonates ($P<0.001$); also phase lag between O1 and O2 changed the sign from positive to negative ($P<0.001$) although the magnitude of the O1-O2 PLI did not change. We conclude that preterm delivery entails an alteration of the cortex interhemispheric EEG connectivity during sleep that can be assessed using PS measures. According to our results, these alterations become evident either from the magnitude and sign of the PLI of the EEG delta waves between the temporal and occipital areas during AS, or from the PLI of the EEG beta band during QS between the same areas.

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P109

Agreement rates between actigraphy, diary, and questionnaire for children's sleep patterns: recommendations for clinical and research practice

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Background: The evaluation of children's sleep-wake patterns is essential for the identification and management of sleep problems. Sleep-wake patterns can be assessed by different methods. However, none of previous reports about the assessement of sleep-wake patterns provides the clinician or sleep researcher with information about the interchangeable use of the most common used methods in clinical practice (actigraphy, diary, and questionnaire). Do parents accurately report on their child's sleep? How well do

actigraphy, diary and questionnaire data agree? Can these methods interchangeably be used? These questions can only be answered by the statistical approach proposed by Bland and Altman (1986, 1999).

Methods: Cross-sectional study of 50 kindergarten children, age 4 to 7 years. Sleep-scheduled times (sleep start, sleep end, assumed sleep, actual sleep time, and nocturnal wake time) were assessed by different methods. The study included data from 7 nights of actigraph recordings and sleep diary over the same time period, and from a questionnaire, asking about children's normal sleep schedule.

Results: Differences between actigraphy and diary were ± 28 min for sleep start, ± 24 min for sleep end, and ± 32 min for assumed sleep indicating satisfactory agreement between methods, while for actual sleep time and nocturnal wake time agreement rates were not sufficient (± 72 min, ± 55 min, respectively). Agreement rates between actigraphy and questionnaire as well as between diary and questionnaire were insufficient for any investigated variable. Sex and age of children, and SES did not influence the differences between methods.

Conclusions: Actigraphy and diary may interchangeably be used for the assessment of sleep start, sleep end, and assumed sleep, but not for nocturnal wake times. The diary is a cost-effective and valid source of information, while actigraphy may provide useful information about nocturnal wake times. It is insufficient to collect information by a questionnaire asking about children's normal sleep patterns. Therefore, we recommend that the diary should be a standard tool in the assessment of children sleep-wake patterns.

P110

Psychosocial and intellectual functioning in childhood narcolepsy

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This study reports the psychological assessment of twelve children referred to a narcolepsy clinic. The study provides an extra dimension to the current literature through the use of quantitative methods to describe intellectual and psychosocial functioning in childhood narcolepsy. The participants were 6 males and 6 females aged between seven and sixteen years (median age 10 years). All were diagnosed and assessed within a multi-disciplinary regional paediatric neurosciences unit on the basis of clinical history. The diagnosis was supported by investigations including videotape recordings of cataplexy, overnight polysomnography followed by multiple sleep latency testing, HLA status, and in selected cases CSF hypocretin measurement. The psychological protocol included a clinical interview; the Wechsler Intelligence Scale for Children-III-UK; and the Parent version of the Achenbach Child Behaviour Checklist (CBCL). Eleven children obtained an IQ in the average range (mean & median = 100). However, we found a significant difference between verbal and performance scales in 42% of children, compared to WISC-III normative prevalence rates of 24%. CBCL results revealed that 10/12 children scored in the clinically significant range on the Total Score Index, with 9/12 obtaining scores in the significant range on the Internalising Index. The majority of children presented with difficulties in discussing and describing distressing physical and psychological symptoms with parents and others. Our findings suggest firstly, that the psychosocial impact of narcolepsy extends beyond the effects of excessive sleepiness and that symptoms such as hallucinations can lead to significant psychological morbidity. Secondly, whilst most children with narcolepsy have average range intellectual ability, specific cognitive problems may be relatively common.

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Sleep problems and behavior problems in primary school children: is there an association?

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Objectives: Sleep problems are common in children, and they are known to affect emotional, cognitive and social development of children. Pediatric sleep problems are mostly treatable, therefore, early recognition and treatment of sleep problems are important. The aim of the study was to identify the relationship between sleep problems and behavior problems among Japanese school children.

Methods: The study was conducted at a primary school located in the suburbs of the second largest city of Japan. Children's Sleep Habits Questionnaire (CSHQ) and Strengths and Difficulties Questionnaires (SDQ) was given to all students of the school and was filled out by the parents or caregivers. 509 subjects (252 males, 257 females, mean age : 9.0 SD 1.8) who responded to the questionnaire properly (response rate : 86.9%) were included in the analysis. Multivariate logistic regression analyses were performed to examine the sleep problems associated with behavior problems. Six logistic models that use SDQ total and subscale scores as response variables were created. As covariates, CSHQ total and subscale scores were used in common.

Results: Sleep onset delay and daytime sleepiness were shown to be independently associated with conduct problems and elevated total SDQ score. Daytime sleepiness was also associated with hyperactivity/inattention. Sleep anxiety was associated with peer relationship problems. Shortened sleep duration and parasomnias were associated with prosocial behavior. Elevated total CSHQ score was associated with emotional symptoms and elevated total SDQ score.

Conclusion: Sleep problems identified by the CSHQ were related to behavior problems. Early recognition and treatment of sleep problems in children may be important in improving or preventing behavior problems.

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Childhood sleep breathing disorders: neurocognition and behaviour four years after treatment

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Introduction: Sleep breathing disorders (SBD) are common in children and linked with deficits in daytime neurocognitive and behavioural functioning. However, the long-term efficacy of treatment in ameliorating these deficits is unknown.

Methods: This study investigated whether children who had previously been treated by adenotonsillectomy (AT) still had persistent deficits in daytime neurocognition and behaviour, when compared to healthy matched controls. Neurocognitive and behavioural functioning was examined using the Differential Ability Scales (DAS-II), Conner's Parent Rating Scale-Revised (CPRS-R) and the Child Behaviour Checklist (CBCL 4–18). Participants were fifteen healthy children (6 m:9f, 8.9 ± 2.3 yrs) and sixteen children (8 m:8f, 9.2 ± 1.9 yrs) who had undergone AT on average 4.3 ± 0.2 yrs earlier. Current sleep patterns and the presence/absence of snoring were assessed via home oximetry, actigraphy, the Sleep Disturbance Scale for Children (SDSC) and sleep timing questionnaire (STQ).

Results: Four years after surgery, the AT group did not differ significantly from healthy controls in age, gender, socio-economic status or maternal IQ, which are known confounders of neurocognition. The AT group were reported by parents to snore more frequently ($P<0.05$), and had significant deficits in non-verbal ability ($P<0.05$), and somatic behavioural problems ($P<0.01$) relative to controls.

Discussion: Prior treatment of suspected SBD in children by adenotonsillectomy appears not to prevent long-term neurocognitive and behavioural morbidity. This highlights a clear need for earlier detection and improved management of childhood sleep breathing disorders.

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Fast and slow spindles relate inversely to motor skills in primary school aged children

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Although convincing evidence exists for the role of sleep in memory consolidation in adults, there remains a scarceness of studies investigating sleep-dependent learning in children. During childhood, learning abilities are especially high and both macroscopic and microscopic aspects of sleep are clearly distinct from adult sleep features. The current data were obtained during the Great Sleep Experiment, a large-scale project on the relationship between children's sleep and their cognitive performance. These data were acquired in a motor skill learning task: the finger tapping task. Subjects (10.8+0.9 years; mean+SD) performed three versions of the task, each containing a different consolidation period: 12 h containing Wake, 12 h including Sleep, and 24 h containing both Wake and Sleep. Throughout the 12-hour Sleep period, polysomnographic recordings were performed. Besides standard visual sleep scoring, automated detection algorithms were used for spindles and slow oscillations. Interestingly, the behavioural data revealed enormous sleep-dependent improvements, but only for performance accuracy:+49% in the Sleep condition and+47% in the Wake & Sleep condition ($P<0.001$). Performance speed showed large improvements regardless of condition:+32% in the Wake condition,+45% in the Sleep condition, and+33% in the Wake & Sleep condition. Preliminary results of the spindle analyses revealed that baseline performance levels were positively correlated to the density of fast frontal spindles ($r=0.52$, $P=0.01$), and negatively correlated to the density of slow frontal spindles ($r=-0.58$, $P<0.01$). Additionally, results regarding the slow oscillations will be presented. In conclusion, children-comparable to adults-show sleep-dependent consolidation of a motor skill, but-unlike adults-they also display enhanced performance over a period of wakefulness. The thalamo-cortical oscillations apparent during preadolescent sleep appear to relate to general motor skill ability, and may provide an indication of neuronal maturation.

P114

Apneas and blood desaturation according to functional residual capacity during sleep in preterm neonates

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Background: Apneas are frequent in the sleeping preterm neonate, mainly in active sleep (AS), during which the functional residual capacity (FRC) may be decreased. Furthermore, FRC may be inversely correlated with the speed of blood-O2-desaturation. Our purpose was to evaluate the potential involvement of FRC in the mechanisms responsible for the occurrence of blood O2-desaturation during short central apneic events (>3 s) in sleeping "late-preterm" neonates. The specific influence of the sleep states was analyzed.

Material and Method: Apneic events were scored in 29 neonates (postmenstrual age: 36.1 ± 1.2 weeks) during AS and quiet sleep (QS) during a morning nap. FRC was measured during well-established periods of regular breathing with an oxygen wash-in wash-out technique.

Results: Apneas with blood-O2-desaturation (drop in SpO2 >5% from the baseline, mean lowest SpO2 during apneic events: 91.4 ± 1.8% [range 87.8–94.6%]) were more frequent in AS than in QS, whereas no difference was seen for apneas without desaturation. The magnitude of the FRC did not depend on the sleep state. The negative relationship between FRC and the frequency (and proportion) of apnea was observed only in AS ($P<0.05$).

Conclusion: Even in late preterm neonates who do not experience long-lasting apnea, blood O2-desaturation during short apneic events is related to a low baseline FRC, VE and SpO2 values. Sleep stage differences argue in favor of a major role of AS-related mechanisms in these events.

P115

Sleeplessness and creativity in children and adolescents with and without high functioning autism

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Introduction: Childhood sleeplessness problems are common and associated with a number of serious adverse effects including impairment in aspects of daytime functioning such as memory, attention and behavior. However there is only limited work looking at the effect of sleeplessness on creative thinking in typically developing children and there are no studies on how loss of sleep is related to creativity in children with autism.

Objectives: This study aimed to a) assess the association between sleeplessness and creativity of children and adolescents with and without autism and b) compare aspects of creative thinking of children with and without autism.

Methods: 47 children aged 4–16 were divided in three groups. Groups included 21 typically developing children (TDC-S) without sleeplessness; 14 typically developing children with mild sleeplessness problems (TDC+S); 12 children with high functioning autism and mild sleeplessness problems (HFA+S). An intended fourth group of children with high functioning autism and no sleeplessness could not be compiled as most children had sleeplessness problems. Sleeplessness was defined as parent reported settling problems (lasting more than 30 min) or nightwaking occurring more than 1 or 2 times a week. Questionnaire (parent and child report using the Child Sleep Habit Questionnaire), 1 week of sleep diary and 7 nights of actigraphy were further used to describe the children's sleep patterns. The figural version of the Torrance Test of Creativity was administered and scored for originality, flexibility, fluency and elaboration of ideas.

Results: HFA+S performed significantly lower on the total creativity ($P<0.05$), originality ($P<0.01$) and flexibility ($P<0.01$) score than TDC-S but no differences were found on fluency and elaboration scores. No differences for any variables were found between HFA+S and TDC+S nor between TDC-S and TDC+S.

Conclusion: Results confirm existing studies highlighting aspects of impaired creativity in children with HFA and perhaps suggest that mild sleeplessness problems could have an additive effect. A control group of HFA-S would help to explain the relationship further.

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High-density sleep EEG recordings in children and adolescents

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Introduction: In recent years high density (hd) EEG has been proven as a useful tool to investigate different aspects of human sleep. The high temporal and spatial resolution of hd-EEG recordings have revealed task related local changes in slow wave activity (SWA) during NREM sleep (Huber et al. 2004), and allowed a thorough morphological characterization and description of spatiotemporal dynamics of sleep slow waves (Riedner et al. 2007; Massimini et al. 2004). Here we asked whether hd-EEG can also be used to uncover developmental aspects of the sleep EEG in children and adolescents.

Methods: All-night hd-EEG was recorded in eight healthy adults (mean age 28.3 ± 1.6 years) and four children and adolescents (mean age 14.1 ± 2.3 years) using Geodesics Sensor Nets composed of at least 128 electrodes. The EEG recordings were sleep staged, subjected to semi-automatic artifact removal and processed using power spectral analysis (4-s epochs, FFT routine, Hanning window). We calculated power maps for the SWA frequency range (1–4.5 Hz) of the first NREM sleep episode.

Results: As expected from the literature, adult subjects showed highest values of SWA over frontal cortex. This frontal predominance of SWA was lower in all of our children and adolescents. In an initial analysis we computed the age difference in the SWA distribution by the ratio of SWA between a frontal (FPz) and a occipital (Oz) electrode (adult subjects, 3.5 ± 0.3; children and adolescents, 1.2 ± 0.3; $P < 0.005$).

Discussion: To our knowledge these are the first all-night hd sleep EEG recordings in children and adolescents. Our preliminary investigation of SWA topography across age revealed a prominent reduction of the frontal predominance of SWA in children and adolescents compared to adults. Thus, hd-EEG recordings during sleep may represent a promising tool to uncover markers of brain maturation in the sleep EEG.

P117

Sleep disturbances following mild traumatic brain injury in childhood

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Objective: To examine objective and subjective reports of sleep disturbance in school-aged children who had sustained mild TBI at least six months prior to the study.

Methods: Eighteen children aged 7 to 12 years with a history of mild TBI (GCS 13–15. LOC <15 min) were compared to thirty children with orthopaedic injuries using actigraphy and parental and self-report sleep questionnaires.

Results: Parents reported greater sleep disturbance in the mild TBI group. No significant differences were found in parental ratings of daytime sleepiness, child-reported sleep difficulties or objective (actigraph) sleep measures.

Conclusions: The finding of greater parental reports of sleep disturbance following mild TBI 6 months after injury requires greater exploration and future research with a larger sample followed from the point of injury would seem appropriate.

P118

The termination of sleep disordered breathing events in children is associated with autonomic activation

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Objective: Respiratory cessations in adults with obstructive sleep apnea (OSA) are associated with arousals from sleep. In children, however, blunted arousal response to sleep disordered breathing (SDB) has been observed. The Watch_PAT100 device is a tool to detect SDB events predominantly by assessing the autonomic arousals at the termination of events. We have therefore sought to study children with OSA with the Watch_PAT100, to assess whether they experience autonomic activation at the termination of events. We hypothesized that they may not experience cortical arousals, but will demonstrate autonomic activation at the termination of SDB events.

Methods: Thirty three children with OSA (21 m/12f) underwent simultaneous recording of in-lab polysomnography and Watch_PAT100 sleep study. PSG was blindly scored for apneas and hypopneas based on common practice for clinical sleep studies in children. WatchPAT100 was automatically scored for respiratory events based predominantly on autonomic activations.

Results: Children's average age ($\pm$ SD) was 11.3 ± 3.2 years (range 6–17). Their total sleep time was 398 ± 59 min (range 243–475 min). The AHI based on PSG and Watch_PAT100 were 7.4 ± 8.7 and 5.6 ± 7.5, respectively ($P = 0.6$). The correlation between PSG AHI and Watch_PAT100 AHI was 0.88 ($P < 0.001$). Only minority of the SDB events were associated with cortical arousals (defined by adult criteria).

Conclusions: We conclude that utilizing autonomic activation index is an accurate tool in diagnosing sleep disordered breathing events in children. We believe that the previously reported blunted arousal response to respiratory stimuli in children with OSA is applicable for cortical arousals or arousals scored by criteria determined for adults, but not for autonomic responses.

P119

Psychoactive drinks and insomnia symptoms in adolescents

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Aim: This study investigated the association between use of psychoactive beverages (tea, coffee and Colas) and insomnia symptoms in adolescents.

Methods: We evaluated 248 students (120 boys and 128 girls), aged 7 to 16 years old (mean 11-year-old), and enrolled at two public schools of Braga, Portugal (response rate, 96%). Information was obtained using the ''Le sommeil'' validated questionnaire that was self-administrated at school. Adolescents reported theire usual intake of tea, coffee and Colas as mean of diary intake, and we categorized them. The association was estimated as odds ratios and their 95% confidence intervals (95% CI) using unconditional logistic regression, after adjustment for sex and age.

Results: In this sample, 17.0% of adolescents reported sleep onset insomnia, 14.9% sleep maintenance problems, 16.6% reported too early morning awakening, 9.9% had restless sleep and 26.4% went to bed not sleepy. Intake of coffee was reported by 35.0% of adolescents, tea by 18.5% and Coca-Cola by 44.0%. After adjustment, no significantly association was founded with early insomnia. The odds ratio and 95% confidence intervals (95% CI) of sleep onset insomnia was 2.23 (0.91–5.42) for intake 2 or more Colas units per day and was 2.18 (0.79–6.01) for restless sleep. Tea consumption was significantly associated with sleep maintenance problems (OR = 4.71; CI 95%: 2.07–10.69). Both, coffee and Colas

were associated with increasing risk of going to bed not sleepy (OR = 3.29; CI 95%: 1.21–8.95) and (OR = 2.89; CI 95%: 1.29–6.47), respectively.

Conclusion: We found a high intake of coffee and Colas among adolescents and this consumption was associated with high risks estimates of insomnia symptoms. These findings suggest that psychoactive drinks could be an important factor in development of childhood insomnia.

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Prevalence of sleep problems in a community population of children with Down syndrome

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Background: Children with learning difficulties are vulnerable to sleep difficulties and can ill afford the neurobehavioural consequences of sleep deprivation. Previous studies of Down syndrome (DS) have been limited to sleep disordered breathing (SDB) or sleep problems in clinical samples. This study aimed to describe sleep problems in a community sample of DS children.

Methods: DS children were identified from the Southampton children's disability register representing a total child population of 100,000. Parents completed the Children's Sleep Habits Questionnaire (CSHQ). Children were screened with one night of home pulse oximetry (Masimo Radical).

Results: 58/73 (79.5%) DS children were recruited, aged to 0.65–17.9 yrs (mean 8.6). Data were analysed by age category (less than 4 yrs, $n = 18$; 4–12 yrs, $n = 24$ and older than 12 yrs, $n = 16$). As the CSHQ is designed for children aged 4–12 yrs, only children aged 4 years or more are reported for this measure. Compared to normal population data, CSHQ sub-scale scores were significantly higher for bedtime resistance ($P < 0.001$), sleep anxiety ($P = 0.024$), night wakings ($P < 0.001$), parasomnias $P < 0.001$), SDB ($P < 0.001$) and day-time sleepiness ($P < 0.001$). In the teenage group significant differences to population data were retained for all sub-scales other than sleep anxiety and night waking. Of children 4 years and older: 66% rarely fell asleep in their own beds; 55% were always restless during sleep; 40% usually woke at least once in the night and importantly 78% seemed tired during the day at least 2 days per week. 30/40 oximetry studies were adequate for interpretation. Of these 15 (50%) were likely to represent SDB (mean SpO2 < 96%, minimum SpO2 < 82%, more than 4 desaturations > 4%/hour, delta 12s index > 0.4), of whom only 2 had an established diagnosis of SDB. There were no group differences in CSHQ sub-scales between children with abnormal or normal oximetry.

Conclusions: Parents report high rates of sleep problems in a community sample of DS children. Paediatricians should routinely enquire about sleep behaviour in these children. Screening guidelines should take account of the high prevalence of SDB and poor correlation of parental report with objective measures.

P121

Analysis of cyclic alternating pattern in children with obstructive apnea syndrome treated with rapid maxillary expansion for 12 months

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Aim: To assess the outcome of rapid maxillary expansion in the treatment of obstructive sleep apnea syndrome (OSAS) in children, we analyzed microstructure of NREM sleep as measured by the cyclic alternating pattern (CAP), at baseline and after treatment.

Design: Prospective study.

Settings: Sleep laboratory in academic center. Participants: Nine patients (4 female and 6 male; mean age 6.2 ± 1.8) with dental malocclusions treated with of rapid maxillary expansion (RME) for 12 months. They underwent overnight polysomnographic recordings in a standard laboratory setting at baseline and at 12-month treatment. Sleep was visually scored for sleep macrostructure and CAP in a blinded fashion using standard criteria.

Measurements and Results: Participants showed a significant decrease of apnea-hyponea index after 12-month treatment. They showed an higher CAP rate during slow wave sleep, associated with higher A1 index and lower A2 and A3 index than they did at baseline.

Conclusions: The higher CAP rate and A1 index after 12-month follow-up, seem to indicate the persistence of subtle sleep alterations that are not clearly identifiable with other approaches and might provide more robust correlates with outcome of treatment in children with sleep breathing disorder.

P122

Skeletal changes in the sagittal, vertical, and transverse dimensions after rapid palatal expansion in children with OSAS

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Aims: The aim of this study was to evaluate comprehensively the cephalometric features of children with OSAS, with or without adenotonsillar hypertrophy, to elucidate the relationship between cephalometric variables and severity of OSAS and to examine the effect of treatment with Rapid Maxillary Expander (RME) on the sagittal dimensions of the upper airway.

Methods: We studied 15 OSAS patients (mean age 6.2 ± 2.5; 16 males),with deep and/or crossbite. Exclusion criteria were obesity and other cardiorespiratory diseases. Patients were assigned to undergo a 12-mo RME treatment. Each patient underwent to standard overnight polysomnography (PSG): baseline, after six and twelve months of treatment, a cephalometry and orthodontic evaluation. A comparison of cephalometric and polysomnographic findings was made before and after treatment.

Results: After treatment there was an increase of protrusion of the maxilla (from 78.8 ± 2.5 to 80.2 ± 1.2 $P = 0.03$) and mandible (from 74.8 ± 2.9 to 76.2 ± 1.3; $P = 0.03$). The angle from the subspinal point to the nasion to the supramental point did not change (from 4.1 ± 1.7 to 4.1 ± 1.1, $p =$ ns). Cranial base angle and space between the posterior nasal spine and the beginning of the adenoidal protrusion correlated with AHI. The angle formed by the conjunction of the anterior with posterior cranial fossa increased (from 121 ± 5.0 to 124 ± 5.0; $P = 0.013$).

Conclusion: The results indicate that upper airway obstruction during sleep is associated with mild cephalometric and craniofacial modifications in children with OSAS and the institution of early orthodontic therapy in children with OSAS could modify the craniofacial development.

P123

A 6-month open-label study to assess the safety and effectiveness of nCPAP treatment in children < 30kg with obstructive sleep apnea syndrome (OSAS)

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Aim: Nasal continuous positive airway pressure (nCPAP) is the treatment of choice for the OSAS in adults. Over the years there has

been an increasing use in nCPAP in the pediatric age, although it has not been yet approved by the Food and Drug Administration for the use in children who weigh <30 kg. Furthermore, few studies have evaluated the effectiveness of nCPAP in children and no prospective studies have evaluated objective measures of adherence in this age group. The aim of the study was to assess the efficacy and effectiveness of nCPAP therapy in children with OSAS and who weight <30 Kg.

Methods: We performed a prospective study. After baseline sleep studies were performed to assess OSAS severity, nCPAP pressure was titrated. A repeated polysomnogram was performed after 6 months of therapy. Adherence was assessed if the child accepted the nCPAP for more than 5 h per night. Effectiveness was evaluated using polysomnography. Changes in weight, height, BMI and blood pressure were assessed.

Results: Seven children were studied. Adherence to trial was successful in 4/7 children (57%). The efficacy was assessed by a reduction of apnea hypopnea index from 15 ± 8 to 5 ± 3/hour ($P = 0.04$) and by an improvement in average SaO2 from $95 \pm 2\%$ to $98 \pm 1\%$. ($P = 0.02$). Children also had a subjective improvement in daytime tiredness and in the score of questionnaire self reported sleep related symptoms. On the six month trial no side effects were observed.

Conclusion: Although the major drawback was the high dropout rate and even in the adherent children, our study shows that the use of nCPAP was feasible and safe also in children who weigh <30 Kg.

P124

Rapid maxillary expander in the treatment of obstructive sleep apnea syndrome in children

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Aims: Oral appliances and functional orthopaedic appliances have been used for patients who have obstructive sleep apnea syndrome (OSAS) and craniofacial anomalies because they change the mandible posture forwards, potentially enlarge upper airway and increase upper airspace, improving the respiratory function even in childhood. Aim of the study was to evaluate efficacy of a Rapid Maxillary Expander (RME) on 12 months trial in OSAS children.

Methods: We studied 27 OSAS patients (mean age 6.2 ± 2.5; 16 males), with deep, retrusive or crossbite. Exclusion criteria were obesity and other cardiorespiratory diseases Patients were randomly assigned to undergo a 12-mo RME treatment. Each patient underwent to standard overnight polysomnography (PSG): baseline, after six and twelve months of treatment.

Results: Our results showed that apnea hypopnoea index (AHI) decreased at the end of treatment (4.6 ± 5.4 versus 2.8 ± 3.2; $P = 0.007$), together with clinical symptoms. The AHI was lower in children with OSAS and deep or retrusive bite (3.1 ± 2.2 to 0.6 ± 0.4; $P = 0.04$) than in those with crossbite (3.2 ± 2.5 to 2.0 ± 1.9 $p =$ ns).

Conclusions: Rapid Maxillary Expansion may be a useful approach in children with malocclusion and OSAS.

P125

Respiratory muscle endurance in children

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Respiratory muscle weakness resulting in respiratory failure is a feature of many progressive neuromuscular disorders. Single manoeuvres to assess muscle strength such as forced vital capacity have limitations in the evaluation of children with these conditions. The Respiratory Muscle Analyser (RMA) (Micro Medical) is a novel method of measuring respiratory muscle function in clinical practice. It calculates cumulative energy expenditure during incremental inspiratory and expiratory resistance loading. We evaluated the use of the RMA in children to assess its applicability.

Method: 18 healthy children, median age 13.3 years (9.4–15.7 years) and 20 children with progressive neuromuscular weakness (PNW), median age 14.1 years (7.0–17.7 years) were recruited. Height, weight, BMI, body surface area and forced vital capacity (FVC) were measured. Each subject undertook a 6 min test with an initial Rinsp/exp of 0.5KPa and 0.5KPa increments every minute. The test finished after 6 min or at the point of exhaustion. The average flow for the total test, at each resistance and the cumulative energy expended were calculated.

Results: 15 healthy children completed the test and 3 stopped early due to exhaustion. In completed tests, the average flow correlated with height (Spearman rank correlation rs = 0.54, $P = 0.01$), weight (rs = 0.54, $P = 0.04$), body surface area (rs = 0.64, $P = 0.01$) and age (rs = 0.71, $P = 0.003$). Cumulative energy expenditure correlated with height (rs = 0.52; $P = 0.05$) and body surface area (rs = 0.53, $P = 0.04$). Mean flow decreased during the first 3 min of the test but then remained constant despite increasing resistance. In the PNW group, 8 children completed the test and 12 stopped early. There was no clear correlation of RMA outputs with body size or FVC in the PNW group. Although children with PNW had lower FVC (% predicted), this was not predictive of test failure.

Discussion: The RMA produced measurements in healthy children that were positively correlated with body size. The proportion of children with PNW who were unable to complete the test was high indicating that a different test protocol may be needed to obtain results for all children. The method requires further evaluation to determine its utility in the assessment of muscle performance.

P126

Sleep instability and sustained attention in children with attention-deficit/hyperactivity disorder

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Sleep in children with Attention-Deficit/Hyperactivity Disorder (ADHD) is characterized by instability of state control (Labrosse et al. ESRS 2006). The aim of the present study was to find whether sleep organization in ADHD children could be correlated with daytime cognitive functioning.

Method: Twelve boys diagnosed with ADHD (age: 11.0 ± 1.2) were recorded in a sleep laboratory for two consecutives nights. Comorbidity was an exclusion criteria. Methylphenidate was withdrawn for at least 48 h. Cognitive performance was tested between 8:00 and 12:00 the next morning. Results were compared to 15 healthy boys (age: 10.7 ± 1.6) using *t*-tests for independent samples. Pearson's coefficient was used to test the hypothesis of a correlation between sleep and performance. An alpha level of .05 was used throughout.

Results: The sleep macrostructure of ADHD children was not different from controls except for a significantly shorter duration of stage 4. Microstructural analysis of sleep showed that ADHD boys had significantly more stage shifts during slow wave sleep (28.7 ± 13.2 versus 19.6 ± 6.7) and higher microarousal index in the last third of night (6.1 ± 4.3 versus 3.7 ± 2.0). Performance of AHDH boys on the continuous performance test (CPT) was significantly impaired relative to controls, including on the following variables: omissions errors (42.9 ± 8.4 versus 46.6 ± 6.0) and

reaction time variability (59.7 ± 12.5 versus 50.7 ± 9.0). When sleep was correlated with performance, we found that stage shifts during slow wave sleep and the microarousal index during the last third of night were associated to more commission errors and more reaction time variability ($r = 0.61$ and .76, respectively) in ADHD children. These correlation were not found in control participants.
Discussion: The present results show that poor sleep quality correlates with attention deficits in ADHD boys. The fact that the same correlation was not found in control children suggests that the functional relationship between sleep and performance is atypical in ADHD.

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Massage therapy and rest-activity cycle in full-term newborns

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Massage therapy was shown to have pacifying and stress reducing effect on preterm infants. Infants undergoing massage spend more time alert and there is also some evidence of its benefits on sleeping and crying, and on hormones influencing stress levels.The objective of our study was to investigate the effect of short time massage intervention on rest-activity cycle of full-term newborns. Ten full-term and medically stable newborns were included in the study. Massage therapy by standardized protocol was provided by a trained professional for three 15-min periods daily, for three consecutive days. Newborns' rest-activity cycles were measured by actigraphy continuously for 9 days, from three days prior to, until three days after massage intervention. The 24-h recording period was divided into six 4-hour intervals for which the average activity index was calculated and compared before and after massage intervention by a paired *t*-test. In pre and post intervention period maximum activity was observed between 4 pm and 8 pm, while the minimum activity was recorded between midnight and 4 am. For all daytime 4-hour intervals (8 am–8 pm) the activity index after massage was significantly higher in comparison to its baseline values (mean ± SEM; interval 8 am- noon: 70.24 ± 2.08 versus 44.79 ± 2.13; interval noon-4 pm: 53.97 ± 1.95 versus 43.92 ± 1.84; interval 4 pm − 8 pm: 73.26 ± 2.80 versus 59.44 ± 2.19; all $P<0.0001$), providing additional proof for better daytime alertness in infants receiving massage therapy. The reverse was true for the nightime period (8 pm- 8 am) with the activity count being significantly lower after massage therapy than prior to it in every separate 4-hour interval (mean ± SEM; interval 8 pm- midnight: 29.49 ± 1.53 versus 41.78 ± 1.85, $P<0.0001$; interval midnight-4 am: 22.41 ± 0.97 versus 25.84 ± 1.24, $P<0.0300$; interval 4 am-8 am: 33.66 ± 1.31 versus 50.73 ± 1.94, $P<0.0001$), supporting the beneficial effect of massage intervention on sleep quality. Our findings confirm early development of the circadian rest-activity rhythm and beneficial effect of short term massage therapy on better daytime alertness and nightime sleep in full-term newborns.

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Sleepiness and driving performance: a simulator study of the effects of sleep loss and time of day

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The aim of this study was to evaluate driver sleepiness in an advanced, moving base simulator, using an extensive design, in which the drivers are examined during the whole 24-h day during both sleep loss and baseline sleep. The study included 14 randomly selected, healthy, drivers that were examined during two conditions; baseline sleep (BS, 23.00–07.00 h) and partial sleep loss (PSL, 03.00 h–07.00 h). Each condition included 6 one-hour driving sessions. The driving sessions were evenly distributed across the 24-h day. In total, 12 h of driving were recorded for each participant. The simulator includes a large moving base car (Volvo 850). During the experiment, EEG and EOG were continuously recorded and self-ratings of sleepiness (KSS, 1 very alert-9 very sleepy) were given every tenth minute by the driver. Standard deviation of the lateral position (sd lat) was used as a metric for driving performance. KSS was significantly higher during PSL ($P<0.001$) and during nighttime ($P<0.001$), and increased across each driving session ($P<0.001$). Visually scored sleepiness (based on EEG and EOG recordings) and blink duration also increased during nighttime ($P<0.05$) and towards the end of the driving session ($P<0.01$). Many participants reached extreme levels of sleepiness during late night hours. Sd lat and number of incidents (defined as two wheels outside the lane) showed a similar pattern as physiological sleepiness and increased during nighttime ($P<0.01$) and across the driving session ($P<0.01$). The results showed pronounced individual differences, in particular for driving performance and physiological indicators but less so for KSS. The ratio between individual differences (standard deviation of the random intercept) and the fixed effect of PSL were estimated at 2.2 for SD lat, 2.7 for blink duration and 0.7 for KSS. The results showed that driver sleepiness increased during nighttime and with increased time on task. The effect of sleep loss was less robust and only subjective sleepiness increased when sleep was restricted to 4 h. During nighttime "near driving off the road accidents" peaked, in particular towards the end of the (1 h) driving sessions. The study was sponsored by IVSS and carried out within the research project DROWSI.

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A spontaneous bold oscillation specific to REM sleep is associated with rapid eye movements and putative Ponto-Geniculo-Occipital (PGO) waves. Preliminary results in a single human

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REM sleep is characterized by a unique pattern of spontaneous brain activity, classically studied by electrophysiological methods. Recently, new techniques identified reproducible patterns of BOLD fluctuations in resting awake brain. We applied this methodology to characterize brain activity in REM sleep as compared to wakefulness. Seven non sleep deprived subjects were scanned during the second part of the night using a simultaneous EEG-fMRI recording, after having slept 5 h in a normal bed. One subject was selected for presenting sufficiently long periods of both wakefulness and REM sleep. The analysis of these functional time series combined SPM5, using a standard general linear model approach and probabilistic independent component analysis (ICA) as implemented in FSL. A novel component was detected by ICA during REM sleep. Its time course was correlated with an estimate of brain activity elicited by the generation of REM and was used as a regressor in the SPM analysis to reveal its underlying neural correlates. Finally, correlates of spontaneous fluctuations in the EEG power density in the alpha band (8–12 Hz) were computed. ICA identified classical 'resting state networks' including the default network, with similar spatial distribution in REM sleep and wake. In REM sleep, an additional thalamo-cortical network could be identified without any corresponding spatial map in wakefulness. This network showed significant activity in pons, mesencephalon, geniculate bodies and posterior thalamus, visual, sensorimotor and auditory cortices, but any

frontal regions. This pattern of brain activity has been suggested to be involved in the PGO waves in humans. In line with this view, we observed a strong temporal correlation between the time course of this network and ocular saccadic events. Finally, the activity in a very similar set of brain areas was associated with a negative modulation of alpha-EEG-power during REM sleep. This is in line with previous findings of an anti-correlation between alpha activity and REM events during this sleep stage. This is the first report of a REM sleep specific network, using a data driven analysis of spontaneous bold fluctuations. This network reflects a different cerebral organisation between REM sleep and wakefulness.

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Sleep structure modifications during overnight polysomnography in near-term neonates exposed in utero to smoking

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Sleep integrity is of paramount importance in the neurophysiological development of neonates. Disruption of sleep mechanisms by prenatal smoking exposure may predispose neonates to alterations in vegetative functions and neurobehavioral development. We investigated the effects of prenatal smoking exposure on sleep structure in the near-term neonate. Overnight polysomnography (EEG, ECG, eye and body movements) was performed at thermoneutrality in 40 healthy near-term neonates (postconceptional age: 33.9 ± 6.0 wk, study weight: 1.94 ± 0.49 kg). 3 groups were studied according to whether the mothers either did not smoke (NS, control group), or stated having smoked less (S-) or more (S+) than 10 cigarettes per day throughout pregnancy. Sleep was analyzed for stability and structure using frequency, duration and percentage of active (AS), quiet (QS), indeterminate (IS) sleep stages and wakefulness after sleep onset (WASO). Only heavy prenatal smoking exposure (S+group) modified sleep stability and structure. Although the overall frequency of sleep states changes did not change, neonates of the S+group exhibited a decrease in total sleep time (-18.2%, $P<0.001$), as a result of an increase in the frequency of WASO ($P=0.024$) and a decrease in QS duration ($P=0.001$). Compared to controls, neonates of the S+group showed higher percentage of AS ($+14\%$, $P=0.015$), mainly at the expense of the percentage of QS (-31%, $P=0.030$). Sleep structure of near-term neonates is modified by heavy prenatal smoking exposure. This finding raises the question of the repercussions of these sleep disturbances (at what is a critical stage in brain development) on the child's physiological and neurobehavioral outcomes.

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Effect of in utero exposure to smoking on peripheral chemoreception in near-term neonates exposed to warm environment: interaction with sleep stages

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A triple risk hypothesis of Sudden Infant Death Syndrome (SIDS) results from (1) an altered chemoreceptor response to breathing or blood pressure challenge when (2) thermoregulatory and (3) sleep processes interact. Prenatal smoking exposure is a major risk factor associated with SIDS. The aim of the study was to investigate the effects of prenatal smoking exposure as an additional factor on the interaction between peripheral chemoreceptor activity and thermal stress during sleep in neonates. Peripheral chemoreceptor activity was assessed at thermoneutrality (TN) and in a mild-warm environment (TN+2 °C) in 37 near-term neonates (post-conceptional age: 36.1 ± 1.2 wk, study weight: 2.1 ± 0.3 kg) by performing a 30-sec hyperoxic test (HT, 100% O2) during active (AS) and quiet (QS) sleep. The drop in ventilation (ΔVE) measured in response to the HT reflects the strength of the chemoreceptors tonic drive during resting ventilation. The exposed group consisted of 16 infants whose mothers reported smoking during pregnancy (S+), 21 non-exposed neonates formed the control group (NS). At thermoneutrality, the fall in VE in response to the HT was significantly lower in the S+than in the NS group in AS (-25.8 ± 6.2 versus $-33.8 \pm 12.0\%$ respectively; $P=0.031$) but not in QS. The same results were obtained in the mild-warm condition (AS: -27.6 ± 10.2 versus $-36.0 \pm 9.8\%$ for S+and NS respectively; $P=0.017$). The response time to the HT was longer in the S+group but this difference was only significant during QS at thermoneutrality (11.8 ± 1.9 versus 8.8 ± 3.1 sec in NS; $P=0.005$) and during AS in the mild-warm condition (10.7 ± 3.2 versus 8.5 ± 2.5 sec in NS; $P=0.030$). The influence of prenatal smoking exposure on chemoreceptor activity is sleep-state but not thermal dependent. In smoking-exposed near-term neonates, ventilatory drive is decreased in AS and the HT response time is delayed, whatever the thermal environment. This situation could subject this vulnerable population to an increased risk of cardiorespiratory disorders during sleep.

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Sleep body movements in near-term neonates exposed in utero to smoking

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In utero exposure to smoking is known to adversely affect brain regions involved in behavior and motor activation, and could interact with normal sleep processes in neonates. We investigated the effects of prenatal smoking exposure on sleep body movements in the near-term neonate. Sleep was investigated during overnight polysomnography (EEG, ECG, eye and body movements) performed at thermoneutrality. 40 healthy near-term neonates (postconceptional age: 33.9 ± 6.0 wk, study weight: 1.94 ± 0.49 kg) were enrolled according to whether their mothers either did not smoke (NS, control group), or stated having smoked less (S-) or more (S+) than 10 cigarettes per day throughout pregnancy. Sleep motor activity was evaluated by measuring the frequency and the total duration of body movements (TDM), expressed relative to active (AS), quiet (QS), indeterminate (IS) sleep stages and to total sleep time. Whatever the group of neonates, both the TDM and the frequency of body movements kept decreasing from AS to IS to QS ($P<0.001$). Whatever the sleep stage and compared to controls, neonates of the S- and S+groups showed an increase in the TDM ($P<0.001$ and $P<0.001$, respectively) and in the frequency of body movements ($P=0.043$ and $P=0.003$, respectively). Prenatal smoking exposure was found to increase sleep body movements in near-term neonates. This finding raises the question of the repercussions of sleep fragmentation and unstability on the achievement of normal sleep processes, which are of paramount importance in the neurophysiological development of near-term neonates.

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Relationship between carotid body effectiveness and apnea frequency in sleeping preterm neonates

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Chemoreception is frequently involved in the processes underlying apnea in premature infants. An increase in the carotid body activity during the neonatal period can initiate an "overshoot/undershoot" situation. The apnea results from a central depression in inspiratory drive which is mainly due to hypocapnia. This concept has been described in adult animals and extended to newborn. The aim of the present study was to test the hypothese whereby short apneic episode frequency and duration would be correlated with the magnitude of carotid body activity in sleeping neonates. Carotid body effectiveness was assessed at thermoneutrality in 36 premature neonates (term: 30 ± 2 weeks, postnatal age: 38 ± 15 days, weight: 2.12 ± 0.25 kg) by performing a 30-s hyperoxic test (HT, 100% O2) during active (AS) and quiet (QS) sleep as already described (Bouferrache et al. Am. J. Respir. Crit. Care Med., 2002). The drop in ventilation measured in response to the HT reflects the strength of the carotid body drive during resting ventilation. Ventilatory parameters were monitored before and during the hyperoxic test. Frequency and mean duration of short central apneic events (>3 sec) were recorded by thoracic impedance throughout the 3-h interfeeding interval and correlated with the HT response (Spearman's correlation). There is no correlation between the ventilatory response to the HT and the mean or maximal durations of the short apneic episodes. Interestingly, in AS and QS, a higher frequency of short apneic episodes was linked to a greater ventilation decrease in response to the HT ($\text{rho} = -0.32$; $P = 0.01$). This features that increased carotid body effectiveness is correlated with greater apneic event frequency, regardless of the sleep state. Fetal or early postnatal hypoxemia could have increased peripheral chemoreceptor activity. This may initiate a "overshoot-undershoot" situation, which in turn could induce a critical PO2/PCO2 combination and lead to apnea (Cardot et al. Pediatr. Res., 2007).

P134

Restless legs syndrome is a common finding in children with attention-deficit/hyperactivity disorder

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Introduction: Restless legs syndrome (RLS), a common sleep disorder in adults (5–10%), is characterized by urge to move the legs, usually caused by uncomfortable sensation, that worse when sitting or lying. Symptoms are relieved partially by movement and are typically worse at night. 80% of patients with RLS have periodic leg movements in sleep (PLMs). RLS is traditionally believed to be a middle age disorder but 25% of patients report onset of symptoms between 10–20 years old. In children of 8–17 years old, criteria for definitive RLS were met by 2% and up to 44% of subjects with Attention Deficit/Hyperactivity Disorder (ADHD) have been found to have RLS or RLS symptoms.

Methods: A prospective study, which included 73 children with ADHD criteria (DSM-IVR, subtypes distribution similar to those in ADHD population) and a control group (45 children without severe neurological or medical disease), age matched, was made. Each patient underwent a medical history interview, a physical and neurological examination, a self-report ADHD questionnaire and routine EEG in 25 children. RLS was diagnosed using specific criteria for children (International RLS Study Group, IRLSSG, Sleep Med. 2003 Mar;4 (2):101–19).

Results: Among the 73 ADHD children included, 15 subjects (20%) met the specific criteria for definitive RLS. Attention-deficit, PLMs reported by parents, insomnia and daytime fatigue/sleepiness are more frequent in definitive-RLS group compared with non-RLS ADHD children. We have not found differences in parasomnias in both groups. Three ADHD children (5%) met criteria for "probable RLS". In non-ADHD children, RLS symptoms are reported by only 2 children (4.5%).

Conclusion: RLS is quite prevalent in children and adolescents, up to 2%, and RLS symptoms are more likely to be found in ADHD population. This data suggests that RLS may mimic the symptoms of ADHD or it may be comorbid with ADHD. Their association may reflect some shared common pathology.

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Safety and effectiveness of sodium oxybate in a child with severe narcolepsy-cataplexy

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Introduction: Off label treatment of severe childhood narcolepsy-cataplexy with sodium oxybate (SO) has been used successfully, improving sleepiness and cataplexy. In adults, SO is highly effective in treating narcolepsy symptoms, well tolerated and improvements are dependent on the dosage.

Methods: We report a 9 years girl with excessive daytime sleepiness (EDS), unexplained falls triggered by emotions (usually laughter), fragmented nocturnal sleep, irritability and sadness. Neurological examination, IQ, blood and urine examinations and MRI (Magnetic Resonance Imaging) were normal with moderate overweight (BMI:23.6). Severe EDS was shown in Pediatric Daytime Sleepiness Scale. An overnight polysomnography followed by multiple sleep latency tests (MSLT) demonstrated frequent nocturnal awakenings without sleep apneas or periodic leg movements, a mean sleep latency in MSLT of less than 5 min and 5 sleep onset REM periods in 5 tests. Human Leukocyte Antigen typing (HLADQB1*0602) was positive and low CSF hypocretin levels were found (<110 pg mL^{-1}). Modafinil, methyl-phenidate and selective serotoninergic reuptake inhibitors, SSRI (fluoxetine, venlafaxine) were ineffective. SO was recommended and treatment started in April 2007, with very slow titration to ensure a good compliance and control of adverse events, in association with stimulants and very low dose of venlafaxine (recommended by pediatric psychiatrist for comorbid mood disorder).

Results: After 11 months with SO, improvement of symptoms (EDS, cataplexy and night time sleep) was evident and clearly dose-dependent, with no significant side effects. Clinical Global Impression-Severity (CGI-S) and CGI-Change from baseline (CGI-C) demonstrated an improvement in quality of life. Even with SSRI, depression was not totally controlled and, only after SO reached a dose 5 gr d^{-1}, the patient smiled.

Conclusion: In spite of SO is not approved by FDA and EMEA for its use in children and adolescents, this treatment is highly effective in treating severe narcolepsy-cataplexy in children, well tolerated and even useful in comorbid disorders. In our hospital, treatment of narcoleptic children with SO is performed following approval of our institutional investigation and ethical committee and signed informed consent.

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Polysomnographic findings in a newborn with Prader-Willi syndrome

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Introduction: Prader-Willi syndrome (PWS) is a rare genetic disorder, usually sporadic, affecting 1/25,000 births, in which a critical region of chromosome 15 (15q11-q13) is affected. At birth, PWS infants exhibit characteristic facial features, small hands and feet, severe hypotonia with suckling and swallowing troubles and delay in psychomotor development. After this initial phase, hyperphagia and absence of satiety (severe obesity and sleep apneas), growth hormone deficiency (short stature) and incomplete pubertal development are striking signs. Diagnosis is based on clinical criteria confirmed by genetic study. In spite of many sleep studies are made in PWS children, there is no report of polysomnographic recordings in affected newborns.

Methods: A preterm newborn with low-birth-weight, respiratory distress, microcephalia, dysmorphic features, weak reactivity to stimuli and hypotonia with suckling and swallowing troubles was evaluated. Genetic findings confirmed PWS diagnosis. Patient underwent a daily polysomnographic study (EEG, EOG, EMG, ECG, nasal airflow, respiratory movements and oxymetry) and sleep and associated events were scored based on international rules for newborns.

Results: EEG tracing was normal, according to postconceptional age. Sleep onset was identified as active sleep (AS) but the duration of this stage was dramatically low (5%, normal up to 60%). Submental muscle tone was reduced across wakefulness and all sleep stages and no significant respiratory events were recorded. The most surprising finding was a total absence of arousals and behavioural reactivity to stimuli but other sleep parameters were similar to those seen in healthy neonates evaluated in our hospital.

Conclusion: In spite of PWS is well studied in obese children with sleep apnea syndrome, performing polysomnographic recordings, sleep disturbances are already found in newborns, even before respiratory events appear. This data suggests that lack of reactivity to stimuli in newborn may be related to difficulty in regulation of sensory stimuli from the environment, leading to further symptoms of PWS (poor satiety recognition, decreased sensitivity to pain and sleep disorders).

P137

Prevalence of sleep problems in Dutch school aged children: a pilot study

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Prevalence of sleep problems among children in the Dutch population is not known. Especially for children the estimates are wide ranged. This pilot was designed to investigate the prevalence of sleep problems in children and also to develop a good list for prevalence research.

Methods: Two different measures were used: a widely spread internet questionnaire that was completed by parents of 901 children at the time of analyses and a school questionnaire to elaborate on the items of sleep disorders. Both questionnaires were filled out by parents. The internet questionnaire was brought to the attention through direct requests to schools and day care organisations. The items in the school questionnaires were very elaborate and more detailed about sleep and sleep habits, the internet questionnaire was shorter, contained 17 items about sleep.

Results: For a total of 117 children the school questionnaire was completed and 901 children were in the internet database. The ages in the school questionnaire ranged from 3–12, mean 7.03 (SD = 2.38) and in the internet questionnaire (889 children remained in the database for analysis) ranged from 0–18, mean 5.4 years (SD = 4.04). Ratio boy:girl in both questionnaires was 450:439 (internet) and 60:53 (4 missing; school). We found that in the adolescent group (11–18 years) total sleep time (TST) was below the criterion for normal sleep length (9–11 h per night, based on literature); 40% of adolescents in our database slept only 6 to 8 h a night and 5% even less: 0–6 h. This TST differed significantly from healthy sleeping adolescents (MW, $Z = -6.65$; $P = 0.000$). Parents didn't rate problems in daytime functioning to be importantly impaired.

Discussion: It's difficult to determine whether parents can accurately define the TST of their adolescent children and possible problems in daytime functioning in this group. However, even when estimated, TST is much less than is supposed to be needed for this age group. Also, it's interesting to see whether this age group would rate their own daytime performance to be impaired and how the difference could be explained.

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RLS among Dutch children

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This is an observational web based cohort study to investigate sleep problems among Dutch children. The prevalence of RLS among the adult Dutch population is comparable with the prevalence in other western countries (7.1%). Until now, no studies have been performed to estimate the prevalence of RLS in de population of Dutch Children.

Methods: Data was collected from a web based questionnaire for children, aged between 0 and 18 years. The questionnaire consisted of 17 sleep/wake items. The questions could be answered in an ordinal 5 point scale (never-always). Parents filled out the questionnaire. If a child experienced uncomfortable feelings in the legs in combination with irresistible urge to move the legs this was considered as RLS.

Results: Database consisted of 889 children. The mean age of the responders was 5.4 (SD 4.0) years. From the total group 727 children (92.8%) had no RLS, 57 children had probable RLS (6.4%) and 7 children had clinical relevant RLS (0.8%). Spearman tests indicate there was a significant positive relationship between RLS symptom frequency and problems initiating and maintaining sleep and also problems with rising in the morning. Also the frequency of RLS complaints was positively related, but not significantly, to EDS and parental worrying about the negative consequences of sleep loss during the day.

Conclusion: The prevalence of clinical relevant RLS in this cohort is low; 0.8%. Parents of children with clinical relevant RLS notice problems with sleep. No significant disturbances are noticed in daytime functioning. The web based questionnaire is still open and efforts are made to obtain a representative cohort for the Dutch population.

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Language function in young children with sleep-disordered breathing

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Background: Protracted auditory cortex development in pre-school children may underlie age-related gains in language function. In children with sleep disordered breathing (SDB), language develop-

ment may be constrained by hypoxia and/or hearing loss due to secretory otitis media (SOM); both exacerbated by adenotonsillar hypertrophy. We studied language function in children with SDB and controls, and the contribution of hearing loss to impairment.

Methods: 36 snoring children were grouped by apnoea-hypopnoea index (AHI): mild-SDB ($n = 21$: 67% boys; mean age 3.8 y, SD 0.9; median AHI 1.9, range .2–4.7), moderate-severe SDB ($n = 15$: 60% boys; mean age 3.7 y, SD 0.6; median AHI 10.4, range 6.0–41.7). Cases were recruited from ENT surgical waiting lists in the South of England. Non-snoring controls ($n = 22$; 59% boys; mean age 4.2 y, SD .8) had no history of hearing loss and normal overnight oximetry. All children were administered the Clinical Evaluation of Language Fundamentals, Pre-School Version and had pure tone audiometry. Past hearing loss exposure was assessed by the Childhood Middle Ear Disease & Hearing Questionnaire (CMEDHQ).

Results: Children with SDB had sig. lower scores on core measures of Receptive Language (Controls-104.09.7, mild-SDB-96.913.2, moderate-severe SDB-94.011.2, $P = 0.039$) and Expressive Language (Controls-108.712.0, mild-SDB-98.912.7, moderate-severe SDB-96.19.1, $P = 0.007$). The mild-SDB group had sig. lower Receptive ($P = 0.046$) and Expressive ($P = 0.012$) scores compared to controls. The moderate-severe SDB group had sig. lower Expressive scores compared to controls ($P = 0.031$). There was no correlation between language measures and mean/min. SpO2, or time SpO2 $<90\%$. There was no correlation in the SDB group between language score and current hearing loss or CMEDHQ scores.

Conclusion: Language development in preschool children appears to be constrained by even mild SDB. There was no correlation between language scores and severity of SDB, nor with exposure to past or current hearing loss. The mechanism underlying language deficit is likely to be complex. As the ability to communicate is key to cognitive and behavioural development, even a mild constraint of language function in otherwise normally developing children requires further study.

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Do adolescence sleep problems predict persistent sleep maladjustment at adulthood – a population based investigation

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Aims: To investigate the impact of early life sleep difficulties on adulthood sleeping maladjustment using a cohort study.Longitudinal data from the 1958 National Child Development Study were used to examine the association between early life sleep problems with sleep adjustment in adulthood.

Design: Sleep difficulties at ages 16, 23, 33, and 42 were defined as whether cohort members had difficulties in falling/maintaining sleep or waking unnecessarily early in the morning. Multivariate logistic regression analyses were employed to estimate whether early life sleep problems were associated with persistent sleep difficulties at adulthood. In the first estimation models it was predicted whether sleep problems at age 16 were associated with sleep difficulties at ages 23, 33, and 42. Further analyses were performed to examine whether sleep problems in early adulthood (at ages 23 and 33) were associated with subsequent sleep problems (at age 33 and 42). The association between sleep difficulties and depression was also explored.

Results: When conditioning on adolescence and adulthood factors it was found that sleep problems at age 16 was associated with continuity in sleep problems over a period spanning almost three decades. Also, sleep problems in early adulthood were associated with greater likelihood of sleep maladjustment at mid adulthood. With respect to other factors the results have been less consistent, implying both continuity and discontinuity in factors associated with sleep disorders. In particular, depression was consistently associated with sleep problems at adulthood but not adolescence. Further analyses have revealed however that the continuity in sleep disorders was unlikely to be explained by the continuity in depression. Finally, the incidence of sleep disorders has increased with age.

Conclusion: The findings from multivariate longitudinal and nationally representative data have offered convincing evidence that early life sleep difficulties have long-term adverse consequences on sleep adjustment.

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Sleep habits and difficulties in Georgian medical students: preliminary data

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Introduction: Although few studies have been recently made to evaluate prevalence of sleep problems among an young Georgian population, very little is known about sleep-wake schedules in Georgian students. The aim of the present study was to investigate the questionnaire study on sleep habits and difficulties in a group of Tbilisi State Medical University students in the relation to their fitness training habits.

Methods: A total of non-paid volunteer students ($n = 82$) between the ages of 19 and 21 years consisted of 55 males and 27 females. A self-reported questionnaire was developed covering sleep-wake and physical exercise habits as well as sleep difficulties over the last month. The students were asked to answer one additional special question: Do you know anything about associations of lifestyle with sleep problems?

Results: Among subjects with exercise habits (group E; $n = 57$; 43 males and 14 females) the number of students who were found to be suffering from difficulties initiating sleep was 17 (29.8%) and 58.8% out of these students trained at evening time (7:00 pm–8:30 pm); all (except two females) did not take a nap during daytime. 32% of total subjects with no exercise habits (group NE; $n = 25$; 12 males and 13 females) reported sleep complaints and six females usually took a nap between 3:30 pm and 5:00 pm. The prevalence of sleep difficulties varied with gender: they were more prominent in females: 20% in group E and 49% in group NE. 69 students (84.3% out of total subjects) marked ''NO'' along the variants suggested in responses on the special question.

Conclusion: Sleep-related problem is common among students. It is more than possible that sleep onset difficulty is the consequence of poor sleep hygiene, in general, and is probably the principal cause of the late evening exercise, on the one hand, and late napping time, on the other. Georgian students need to be educated about sleep disturbances and better sleep habits.

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Shift work and coronary heart disease: a population-based 22-year follow-up study

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Objectives: Studies on the association between shift-work and coronary heart disease (CHD) have given conflicting results.

Methods: In our prospective study we assessed the association in the population-representative Finnish Twin Cohort in 1982–2003. Self-reports on the working time (present or last job) in 1975 and 1981 (response rates 89 and 84%) were obtained from 20,142 individuals (51.2% women; mean age in 1981 40.2 years), with response alternatives: 1. mainly daytime work, 2. mainly nighttime work, 3. mainly shift work, or 4. I have never been working. Cause-of-death statistics were obtained from Statistics Finland, and the cause of retirement from the Finnish Social Insurance Institution. Cox proportional hazard models were used to obtain hazard ratios (HR) and their 95 percent confidence intervals (CI) for mortality by type of working time. As reference group we used those daytime working both in 1975 and 1981. Adjustments were made for marital status, social class, education, smoking, alcohol consumption, BMI, physical activity, life satisfaction, diurnal type, sleep length, use of hypnotics and/or tranquillizers, working pace, and physical load of work.

Results: Both in 1975 and 1981 76.9% were daytime working and 9.5% shift-working, and 1.7% had night-time work at either point. During the follow-up there were 857 deaths and 721 retirements due to CHD in the cohort. Age-adjusted risk of CHD mortality was non-significantly increased in night-time workers (HR 1.75 in men and 1.38 in women) and in those shift-working both in 1975 and 1981 (1.09 and 1.22, respectively). The results were similar in the fully adjusted model. There was no significant increase in age-adjusted risk of disability pension due to CHD either in males (night-time workers 0.89, and shift-work both in 1975 and 1981 1.15) or females (1.68 and 0.96, respectively). Full adjustment did not change the results.

Conclusion: Our results do not support a significant association between shift-work and coronary heart disease.

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Effects of culture differences on sleep in adolescents

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In adolescents insufficient sleep has been reported across many cultures. Hormonal and social changes during puberty induce a phase delay in bedtime, although the biological need for sleep is increased. In this paper the effect of intercultural differences on sleep is studied in adolescents in a Dutch high school. A group of 300 adolescents between 12 and 18 years were divided in 3 cultural subgroups: Dutch (58.3%), Moroccan (22%) and Middle Eastern (19.7%) and in 3 subsequent age groups. A questionnaire was administered containing questions on situation at home, parental influence on sleep, sleep pattern, sleep behavior, sleep quality, mood and the use of multimedia in the bed room. In addition school grades for Math and English were used to study the relation with school performance. In all 3 cultural groups the expected delay in bedtimes was found with increasing age. However, the youngest children in both the Moroccan and the Middle Eastern group, had significantly later bedtimes (>30 min later) during school days than Dutch children in the same age group ($P < 0.005$ and $P < 0.000$ respectively). Parents from Moroccan or Middle Eastern background who stimulated their children to go to bed early set a time limit which was more than 30 min later than the Dutch parents. Dutch adolescents had less multimedia devices in their bedroom than the other 2 groups. The chatting/internet activities had a negative influence on sleep quality ($P < 0.003$). The adolescents used mobile telephones in bed, but the Dutch group used SMS during the school week more than the other 2 groups ($P < 0.001$). On average the adolescents woke up 0.86 times during the school week and 1.06 times in the weekend due to incoming phone calls or SMS. Girls in all cultural groups used their phones more often in bed than boys. A negative relation was found between the multimedia and telephone activities and grades on Math. It can be concluded that cultural differences do have an influence on the sleep pattern of adolescents.

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Transition into and out of daylight saving time reduces the quality and amount of sleep

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Transition into and out of the daylight saving time (DST) causes a sudden change in the light-dark cycle. Spring transition into the

DST increases the available daylight in the evening and fall transition out of the DST increases the available daylight in the morning. This kind of a circadian rhythm disruption may decrease mood, motivation, attention and alertness. Thus the DST predisposes individuals to physiological as well as to mental health problems. We explored how the DST transitions impact the quality and amount of sleep. The volunteer participants of our study were healthy adults free of any psychotropic medication. Before starting the study the subjects gave a written informed consent. All subjects lived in Helsinki, Finland, and none was a shift-worker nor crossed time zones during the study. The measurements were performed using aktigraphs. The subjects wore the aktigraphs on their non-dominant arm all the time, except when bathing or swimming. The measurement data was gathered for one week before and one after the transition into and out of the DST. Participants filled in a Morningness-Eveningness Questionnaire and a Seasonal Pattern Assessment Questionnaire before starting the study. Participants also kept sleep diaries during the study period. The participants were assigned into subgroups by the preference for daily activity patterns and by the preferred length of sleep. Several changes were observed in sleep variables after transition into and out of the DST. Transition into the DST reduced the duration and efficiency of sleep. Movement and fragmentation index was significantly increased after the transitions into and out of the DST. Moreover the relative amplitude of the daily rest-activity cycles was decreased after the transition out of the DST. According to our results the transitions into and out of the DST disrupt the rest-activity cycles of healthy adults and thus compromise the process of sleep both by depriving sleep and by reducing the efficiency of the deprived sleep. Our findings also indicated that the effects of the transitions might be gender, age and chronotype specific.

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A population based association study of SNPs of DISC1, in Finnish individuals with melancholic depression, early morning waking and fatigue

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Introduction: Allelic variants of the gene DISC1 (Disrupted-in-schizophrenia 1) have been associated to both schizophrenia and bipolar disorder in the Finnish population. We hypothesized that common variants of this gene could play a role in individual susceptibility to major depressive disorder. We also anticipated that the putative genetic risk could be mediated via its effect on sleep that is disturbed in depressive disorders.

Method: The study was performed on a representative population based sample recruited from Finland's general population during the national Health2000 study. All cases with major depression ($n = 385$) and a group of age and gender matched control individuals ($n = 392$) were included. To study the effect of DISC1 on sleep disturbance, cases were divided into subgroups with early morning waking ($n = 170$) or excessive day-time fatigue ($n = 215$). Five SNPs spanning the DISC1 gene were genotyped, overall success rate for the SNP data were 96%. We tested SNPs for association under x2 tests with max (T) permutation by simulating the data set for 10,000 times.

Result: We found evidence for association of the functional variation rs 3738401 (Arg264Gln) at 5′ end of DISC1 in females with major depression ($P = 0.001$). The same variant showed also weak association to cases with fatigue ($P = 0.018$). The variant rs821616 (Ser704Cys) at 3′end of DISC1 was suggestively associated to males with depressive disorder ($P = 0.044$) while same SNP showed nominal association to cases with fatigue ($P = 0.023$).

Conclusion: Our results provide evidence for involvement of DISC1 in major depressive disorder. The findings are consistent to some extent with earlier observations in the Finnish schizophrenia and bipolar families. Our results also indicate that genetic variability may influence on phenotypes of fatigue but not the early morning waking features.

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Changes in marital status and sleep quality among midlife and older women in Italy

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Previous quantitative studies have found an association between marital status and sleep, especially in women over 40, with higher levels of sleep problems reported by the widowed and the divorced. This research further investigates the topic through the analysis of qualitative data, and a biographical narrative approach. A sample of 65 Italian women between 40 and 80 years old was investigated through in-depth semi-structured interviews, and audio-written sleep diaries for seven days. Findings illustrate how changes in marital status and living circumstances are associated with Italian women's sleep quality. Women tend to attribute specific phases and types of sleep to changes in their marital status, which in turn are associated with their family caring roles and living circumstances. Married women with caring roles describe their sleep as characterized by discontinuity and fragmentation. Caring tasks and worries about family members shape and disrupt their night, in proportion to the nature and intensity of their care work for children, partners and elderly relatives. Sleep tends to become more light and alert versus the continuous sleep experienced when they were single. Major sleep alterations, which last long after the caring has ceased, are found among women who provide intensive caring for chronically ill relatives, especially during terminal illnesses. On the other hand, midlife and older women living alone (separated, divorced or widows) are more subject to feelings of loneliness and lack of safety which result in experiencing more awakenings and insomnia. Our study shows the importance of using qualitative research to understand what underlies correlations found in quantitative studies regarding the ways in which sleep quality varies according to marital status. The authors are grateful for funding from the EU Marie Curie Research Training Network on "The biomedical and sociological effects of sleep restriction" (MCRTN-CT-2004-512362).

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Epworth sleepiness scale distribution among 10755 people (aged 40+) in a primary healthcare checkup and 1797 people from sleep clinic

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Epworth Sleepiness Scale is commonly used for Sleepiness screening. We report distribution of response among screening in the Bordeaux and Cenon primary HealthCare Center in Gironde, France and in our sleep lab.

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Occupation, shift work and sleep – the Hordaland Health Study

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Shift workers sleep less than non-shift workers, but it is not clear to what extent type of occupation is important. We studied relations

between sleep, sleepiness and other sleep characteristics, occupation, shift work, and subjective health in a population of 40–45 year olds participating in the Hordaland Health Study 1997–1999. Participation rate was 63%. A randomly selected half of the subjects answered a questionnaire on sleep habits and problems, questions on shift work and occupation, $n = 7782$. Occupations classified were: Leaders, non-personal service workers, personal service workers, farmers and fishery workers, craft-and construction workers, plant-and machine operators, and drivers. Sleep duration in shift workers was 15 min shorter than in non-shift workers. Differences in night sleep duration between occupational groups were present in non-shift workers in particular: Craft workers, plant operators and drivers slept less than leaders, non-personal and personal service workers. Within some occupations (leaders, personal service workers, and plant operators), shift workers slept less than non-shift workers. Rise time was earlier in craft workers, plant operators and drivers than in the other occupations. Risk factors for sleepiness, insufficient sleep, falling asleep at work and insomnia for shift- or non-shift workers and for the different occupations were investigated using logistic regression analyses. Shift workers had increased risk for falling asleep at work and for insomnia. When adjusted for shift work, craft workers, plant operators and drivers had increased risk of daytime sleepiness and of falling asleep at work compared to leaders.

Conclusion: Occupation has separate effects on sleep duration and sleep characteristics in addition to the effect of shift work.

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Sleep disturbance in adolescents: risk factors – results of a representative study

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Sleep problems including difficulties initiating or maintaining sleep as well as unrefreshing sleep are frequent in children and adolescents. However, the role of socioeconomic status, specific behaviour and further socio-demographic variables as risk factors for sleep disturbance has been little explored in research on adolescent insomnia. On the basis of a representative sample (N = 546, average age = 14.7 years) of adolescents of the city of Stuttgart, Germany, eighth and ninth grade school students were evaluated by questionnaires, physical exam and parent questionnaires including the Strength and Difficulties Questionnaire and the Social Class Index by Winkler. Difficulties initiating sleep were reported by 23.3%, while 11.2% complained of difficulties maintaining sleep and 10.4% complained of daytime fatigue and either difficulty falling asleep or maintaining sleep (insomnia). On average the adolescents slept 8.04 ± 1.66 h. Those suffering from insomnia slept shorter than those without insomnia (7.15 ± 1.51 h versus 8.26 ± 2.0 h; $P<0.001$). Females reported substantially more often insomnia ($P<0.001$) and difficulties initiating sleep ($P<0.02$) than male students. Lower social status was associated with a higher frequency of difficulties maintaining sleep ($P<0.02$). Smoking was associated with elevated frequency of insomnia, initiating and maintaining sleep (all $P<0.001$). Daily time spent watching television influenced frequency of insomnia ($P<0.02$) with a prevalence of 6% among the individuals spending less than one hour, 9.6% in those watching TV 1–2 h, and 15.2% in those watching TV more than 2 h. Additionally, frequency of insomnia differed in those using no cellular phone and those using one for more than one hour a day (5.5% versus 13%; $P<0.05$). Significantly increased frequency of sleep disturbance was also observed for experience of violence ($P<0.05$), experiencing pain the last three months ($P<0.02$), and those demonstrating higher levels of hyperactivity ($P<0.03$). A strong effect was observed for emotional problems. Those reporting elevated emotional problems demonstrated two to three times more often disturbed sleep ($P<0.001$). The identified risk factors should be considered in the planning of treatment and prevention programs.

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Sleep disturbance in adolescents: protective resources – results of a representative study

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Sleep disturbance is frequently observed in children and adolescents. A high percentage of the affected youths are chronically impaired and additionally, insomnia is associated with an elevated risk for the occurrence of further disorders such as depression. Therefore, in addition to identifying risk factors for the occurrence of disturbed sleep the identification of protective resources is important for a possible prevention of sleep disturbance and its consequences. On the basis of a representative sample (N = 546, average age = 14.7 years) of adolescents of the city of Stuttgart, Germany, eighth and ninth grade school students were evaluated by questionnaires, physical exam and parent questionnaires. Among a wide range of relevant health and socio-demographic aspects sleep disturbance was registered. Of special interest was the association with resources such as regular physical activity, family coherence, social support, and personal resources. Difficulties initiating sleep were reported by 23.3% of the total sample, while 11.2% complained of difficulties maintaining sleep and 10.4% of the students complained of daytime fatigue and either difficulty falling asleep or maintaining sleep (insomnia). Significantly less frequent insomnia was observed in those students reporting physical activity three or more times a week in comparison to less frequent activity ($P<0.001$). Unaltered family coherence was strongly associated with reduced occurrence of insomnia, difficulties initiating sleep and difficulties maintaining sleep ($P<0.001$; $P<0.01$; $P<0.001$, respectively). Additionally, the presence of personal resources significantly reduced the risk of insomnia ($P<0.02$), difficulties initiating sleep ($P<0.001$), and difficulties maintaining sleep ($P<0.01$). However, no such association between sleep disturbance and social support was observed. The identified resources physical activity, family coherence, and personal resources appear to be of protective value for adolescents in order to reduce the risk for sleep disturbance. These factors should be strongly considered in the treatment of affected subjects and development of prevention programs for sleep disturbance.

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The direction of longitudinal associations between sleep problems and depression symptoms: a study of twins aged 8 and 10 years

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The objective of the study was to establish the direction and etiology of longitudinal associations between sleep problems and depression symptoms in children. Longitudinal prospective data

on twins aged 8 and then 10 years were obtained. At both assessments, parents completed the Child Sleep Habits Questionnaire and twins reported on their own depression symptoms using the Children's Depression Inventory. Participants were interviewed at the Institute of Psychiatry, London, with the exception of a small number of families who were seen in their home. 300 twin pairs initially enrolled in the study and 87% of those asked to return did so. A genetically informative cross-lagged model examined the links between sleep problems and depression. Sleep problems at 8 predicted depression at 10 years (partial regression coefficient [confidence intervals] = 0.10 [0.01–0.18]), but the converse association was not found. The stability of sleep problems across time-points was mainly due to genetic influences (46% of the genetic influence on sleep at 10 was due to genetic influence on sleep at 8). The stability of depression symptoms was mainly due to nonshared environmental influences (19% of the nonshared environmental influence on depression at 10 was due to nonshared environmental influence on depression at 8). The cross-lagged association between sleep problems at 8 and depression at 10 years was largely due to genes, although this latter finding was not significant. This study adds to our understanding of the temporal precedence of sleep problems and depression and the genetic and environmental risks underlying their associations. There are important implications regarding the value of specifying genes linked to sleep problems in children and potential opportunities for informing early intervention strategies in high-risk groups at key points in the developmental progression to developing more serious problems.

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Has sleep a contributing role in diurnal car accidents?

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Several studies have emphasized the role of sleepiness and of different sleep-related factors in nocturnal car crashes [1]. The aim of this study is to examine the role of different sleep risk factors in a sample of diurnal accidents. 253 drivers, between 14 and 90 years old, who had an accident in a region of central Italy between 7 am and 10 pm in year 2007, were interviewed by professional interviewers. In most cases the interview was carried out directly on the accident place (52% of the cases) and the same day of accident (72%). Following to Connor et al. [1], we considered the following sleep-related risk factors: 1) sleep duration <6 h in the night before the accident; 2) difference >2 h between the habitual nocturnal sleep duration and the one in night before the accident; 3) duration of wake >18 h before the accident; 4) retrospective Karolinska Sleepiness Scale score >6 at the moment of the accident [2]; 5) a job with nocturnal shifts; 6) a clinical Sleep Disorders at the Sleep Disorders Questionnaire [3]; 7) an Epworth Sleepiness Scale score >10 [4]. The factors increasing significantly the probability to have a single car accident during the day were: wake duration >18 h before the accident (OR = 46.2), the sleep duration in the night before the accident <6 h (OR = 12.2) and the KSS score >6 (OR = 12.5). The sleep duration the night before the accident <6 increased significantly also the probability for extra-urban accidents (OR = 9.4). Considering novice drivers the significant risk factors were the sleep duration in the night before the accident <6 h (OR = 8.0) and the difference between habitual sleep duration and the sleep duration the night before the accidents >2 h (OR = 9.0).

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Socio-demographic and clinical characteristics, health behaviour and accident in snorers: a population survey

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Introduction and Aim: Increasing evidence suggests that snoring is part of the spectrum of sleep disordered breathing, from simple snoring on one end through loud snoring with breathing pauses to obstructive sleep apnea/hypopnea syndrome on the other. Here we assess the sociodemographic characteristics, pattern of health behaviour and comorbidity associated with snoring in the Hungarian population.

Methods: Data were collected within a framework of the "Hungarostudy 2002" cross-sectional, nationally representative survey of the Hungarian population. The Hungarian National Population Register was used as the sampling frame and a clustered, stratified sampling procedure was employed. The study population represented 0.16% of the population over the age of 18 years according to age, sex and 150 sub-regions of the country. Interviews were carried out in the homes of 12,643 persons. Self-reported information on smoking, alcohol consumption, comorbidity, chronic pain, daytime sleepiness and accidents were also tabulated.

Results: 37% of males and 21% of females reported loud snoring with breathing pauses. There was a significant increasing trend in the prevalence of alcohol and coffee consumption, and smoking among non-snorers, quiet and loud snorers. Depression and chronic pain were reported by 10% and 60% of the loud snorers, respectively. In an ordinal regression model male gender and the presence of smoking, alcohol consumption (two or more times per week) and 3 or more comorbid conditions were the strongest predictors of snoring (Table 6) (OR = 0.55, OR = 1.71, OR = 1.57, OR = 1.47 respectively $P<0.001$) after controlling for multiple sociodemographic and clinical variables. The prevalence of accidents was higher in the loud snoring group than among non snoring individuals (24% versus 17%, $P<0.0001$).

Conclusions: Snoring is frequent in the Hungarian adult population. In contrast to quiet snoring, loud snoring with breathing pauses is strongly associated with high-risk health behaviour, higher number of comorbidity, and higher prevalence of accidents.

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Adolescent sleepiness on a double-shift school system: MSLT, subjective sleepiness and performance on morning and afternoon school week

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Double-shift school system facilitates irregularities of sleep patterns and sleep duration in adolescents, which is inconsistent with sleep hygiene recommendations stating that adolescents should avoid large delay of bedtime and wake time, and large extension of sleep. Our previous studies indicated that the adolescents used the extension of main sleep on afternoon schedule to pay off the sleep debt accumulated during morning shift days. In this study we wanted to examine whether the levels of their sleepiness differed at the end of the school weeks with morning and afternoon schedule. Twenty-two secondary school students (12 females, modal age 16

yrs) participated in the study. They kept sleep-wake diaries, and wore wrist Actiwatch® Score devices for two consecutive weeks. Half of the participants started the study on the morning shift week, and the other half on the afternoon shift week. They were also giving sleepiness ratings seven times a day on a five point Lykert type scale using the actigraph score option. On Fridays of both school weeks they came to laboratory for MSLT and performance measurements, which were taken four times at two-hour intervals. Performance measures used were speed and accuracy on the Search and Memory task with three levels of difficulty and on a 10 min simple reaction time task. None of the sleepiness measures showed statistically significant difference between morning and afternoon schedule. Mean sleep latencies in both situations approximated 13 min, and subjective sleepiness ratings were very low, ranging from 1 to 3.5. Regardless of the school schedule, the sleep latencies showed an expected circadian effect, being shorter on the measurement points at 11:00 h and 15:00 h. The results of this study indicate that daytime sleepiness in adolescents attending school on a weekly rotating morning and afternoon shifts does not seem to differ between school weeks with different sleep opportunities.

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Sleep disorders among the Romani population in Western Hungary

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The number of Romani people in Hungary is disputed. In the 2001 census only 190,000 people called themselves Roma, but sociological estimates give much higher numbers, about 5%–10% of the total population. Since World War II, the number of Romani has increased rapidly, multiplying sevenfold in the last century. Today every fifth or sixth newborn is Roma. Estimates made by the Central Statistical Institute of Hungary, based on current demographic trends project that in 2050, in case the shrinking of the total population continues, 15–20% of the population (1.2 million people) will be Roma. In case the shrinking of the total population continues the share of the Gypsy population may, despite the ongoing assimilation process, far exceed 10% of the total population in 2050. The prevalence of several diseases is markedly different in Hungary's gypsy inhabitants as compared to the Caucasian majority of the population. Besides the ethnic and genetic differences, the lifestyle of the Central European Romani people is, despite the ongoing cultural assimilation process, partially still different, just like their sleep hygiene and attitude to wakefulness, sleep and dreaming. However, the prevalence and characteristics of sleep disorders among the subgroup of the Hungarian population defining themselves as Romani has not been studied yet. For the prevalence of insomnia, excessive daytime sleepiness, morningness-eveningness, restless legs syndrome and some parasomnias, the authors screened a sample of 129 people (male 43, female 86, age range 21–64) living in the area of Northwest Hungary, voluntarily defining themselves as Romani. Insomnia percentage was found to be equal to the previously published data for the Hungarian population. The distribution pattern of morningness-eveningness, however, tended rather towards morningness. The prevalence of Restless Legs Syndrome is known to be relatively high in the Caucasian population, and significantly lower for example in Afro-American, Chinese or Japanese samples. As regard to the Romani sample screened by the authors, surprisingly, the prevalence of Restless Legs Syndrome was found to be 16,8% in female and 10,6% in male probands-somewhat higher than in the Caucasian population of Hungary.

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Impact of caffeine on sleep is underestimated among Japanese population: a preliminary study

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Objectives: Excessive caffeine consumption is known to affect sleep. However, caffeine-containing beverages are often consumed before bedtime mostly due to lack of knowledge about caffeine. Especially, some soft drinks are consumed without the awareness that they contain caffeine. The aim of the study was to identify how much caffeine-containing beverages are actually consumed and the level of knowledge about caffeine-containing beverages among Japanese community population.

Methods: 108 subjects (34 males, 74 females) from the community was given a questionnaire about caffeine-containing beverages. Subjects were given list of beverages and were asked to choose which they consider caffeine-containing. They were also asked to describe the amount of beverages actually taking on daily basis. Percentage of subjects who correctly chose caffeine-containing beverages was calculated and the total amount of caffeine consumption was also calculated.

Results: Mean total amount of daily caffeine consumption was equivalent to 3.3 SD 2.4 cups of coffee. 82.4% of subjects correctly recognized that coffee contains caffeine. English tea and Japanese green tea were correctly recognized as caffeine-containing drinks in 62.0% and 65.7% of subjects respectively, however, only 26.8% of subjects consider that Chinese oolong tea contains caffeine. Cocoa drinks, cola soft drinks and energy drinks are recognized as caffeine-containing drinks in 11.1%, 20.4% and 31.5% of subjects respectively. 33.3% of subjects consider that wake-promoting effect of caffeine lasts only one hour or less.

Conclusion: Caffeine-containing beverages especially Chinese oolong tea, cola soft drinks and energy drinks are often consumed without the knowledge that they contain caffeine. These beverages are also popularly consumed by children and adolescents, therefore, we should be careful if excessive consumption of these caffeine-containing beverages can cause sleep disturbance of children.

P157

Comprehensibility of pictorial images of sleepiness and features of obstructive sleep apnoea syndrome in a Hong Kong and UK population

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Background: We have previously translated the 8 point written Epworth Sleepiness Scale (ESS) into a Pictorial ESS. Subsequently pictorial sleepiness images were reduced from 8 to 4, and four new images developed for potential use in screening for obstructive sleep apnoea syndrome (OSAS). These images have been tested for comprehensibility in a London teaching hospital amongst Sleep and Non-sleep respiratory patients and we were keen to assess whether our images were equally understood in a non-UK population.

Methods: Pictorial sleepiness images of sitting and reading, watching TV or listening to the radio, sitting quietly after a meal,

travelling as a passenger in a bus or car and 4 screening pictograms of body weight, neck size, blood pressure and witnessed apnoea were tested for comprehensibility using guessability and translucency questionnaires in sleep patients attending the Prince of Wales Hospital, Hong Kong. The patients were non English speaking and the study was undertaken with the aid of an interpreter.

Results: 20 patients (18M, 2F, mean age 50.7 yrs ± 5.1) completed the translucency and guessability questionnaires. Comprehensibility of images were comparable to our previous study amongst London sleep patients (n 64, 47M, 17F, mean age 50.7 yrs ± 11.0). Mean translucency scores (the relationship between image and intended meaning, 1 = no relationship and 7 = strong relationship) were all excellent with scores greater than 5 for all images and comparable to those from London. This included scores for a revised image portraying "witnessed apnoea" (mean score Hong Kong 5.8, UK 6.1) which has traditionally been difficult to portray. Of interest was the blood pressure image which depicted an electronic sphygmomanometer in contrast to the traditional mercury sphygmomanometer. This image was fully comprehensible in Hong Kong and achieved a high mean score of 6.7 (London 6.1).

Conclusion: A pictorial sleepiness scale and images for screening OSAS tested in Hong Kong have been shown to be as comprehensible there as in London, UK. These images are currently being validated in the UK against objective measures of sleepiness and presence of OSAS.

P158

Correlates of short and long sleep duration: cross-cultural comparison between UK and US. The Whitehall II study and the Western New York Health Study

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Objectives: To examine a number of socio-demographic variables, lifestyle behaviors, and co-morbidities that could confound or mediate observed U-shaped associations between sleep duration and health, in two populations from the UK and US.

Methods: Participants were 6,472 adults from the Whitehall II Study (WIIS) and 3,027 adults from the Western New York Health Study (WNYHS). Multivariable odds ratios (OR) were calculated for both short (<6 h) and long (>8 h) duration of sleep across several potential correlates [i.e., marital and socioeconomic status (SES), body mass index (BMI) and waist circumference, smoking and drinking habits, physical activity, SF-36 physical and mental scores, depressive symptoms, hypertension, and diabetes).

Results: For short sleep duration, there were several consistent significant associations in both samples: marital status (not married) [ORadjusted1.49 (95% CI 1.15–1.94) in WIIS; 1.49 (1.10–2.02) in WNYHS]; BMI (continuous) [1.04 (1.01–1.07) in WIIS; 1.02 (1.00–1.05) in WNYHS]; SF-36 physical score (continuous) [0.96 (0.95–0.98) in WIIS; 0.97 (0.96–0.98) in WNYHS]; SF-36 mental score (continuous) [0.95 (0.94–0.96) in WIIS; 0.98 (0.96–0.99) in WNYHS]; hypertension among women [1.70 (1.07–2.70) in WIIS; 1.70 (1.13–2.56) in WNYHS]. For long sleep duration, there were fewer significant associations, likely as a result of the small number of long sleepers in both samples ($n = 93$ in WIIS, $n = 173$ in WNYHS). Specifically: age (years) among men [1.08 (1.01–1.14) in WIIS; 1.05 (1.02–1.08) in WNYHS]; low physical activity [1.75 (0.97–3.14), p value = 0.06, in WIIS; 1.60 (1.09–2.34) in WNYHS]; SF-36 physical score [0.96 (0.93–0.99) in WIIS; 0.97 (0.95–0.99) in WNYHS].

Conclusions: Unmarried marital status, overweight, and poor general health are associated with short sleep duration, and may contribute to the observed associations with diseases. Long sleep duration may represent an epiphenomenon of other co-morbid conditions particularly in the elderly.

P159

A 20-year prospective longitudinal prospective study of insomnia in Sweden

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Insomnia is common and may be persistent. The aim of the present study was to examine how many that will continue to have insomnia complaints over a 20 year period. A second aim was to examine if sleeping difficulties in year 1983 predicted "burnout" in year 2003.

Methods: In 1983: 1.687 subjects, aged 30–44 years, answered a sleep questionnaire (USI). In 2003: In a follow-up, 1.192 subjects, aged 50–64 years, answered the same sleep questionnaire. Subjects were asked about difficulties initiating sleep (DIS) and difficulties maintaining sleep (DMS), and not being rested by sleep (NRS). The questions were answered on a five-point scale (1 = no problems, 2 = minor problems, 3 = moderate problems, 4 = severe problems, 5 = very severe problems). At least severe problems (scores 4 and 5) were considered to be a complaint. Insomnia was defined as having at least one complaint. In year 2003 questions about health included a statement about being "burnout".

Results: At baseline insomnia was reported by 12.1%, and of these 64,9% continued to have insomnia twenty years later. In the total population in year 2003, 7,9% of women and 7,8% of men had persistent insomnia. New insomnia was reported by 21,4%. In year 2003 "burnout" was reported by 7,3% of women, and in 3,9% in men. In a logistic regression we examined the risk for "burnout" in relation to DIS, DMS and NRS at baseline. For women DMS (OR 2,8 CI 1,1–8,0) and NRS (OR 3,3 CI 1,2–9.3) were significant, but not DIS which was the only significant association for men (OR 7,3 CI 2,0–25,3).

Conclusion: Insomnia has a high persistence over a twenty year period, and insomnia is predictive of "burnout".

P160

Survey of cervical curve and sleep-onset-posture in Japanese

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Introduction: Bedding is one of the factors affecting sleep. We focused on pillow and reported that the height of pillow influenced sleep quality (Matsuura et al. 2007). It was also suggested that one change sleep-onset-posture according to the height of pillow. An appropriate height of pillow, which control body load while sleeping, may differ with age and sex because of physical differences. In present study, we conduct a survey with questionnaire and anthropometric to clarify the difference of physical features and sleep-onset-posture by age and sex.

Method: Respondent to the survey had interests or needed functional pillows. They were asked about their sleep habits, height, weight, physical symptoms and sleep-onset-posture. Moreover, we measured their depth of cervical curve that is a rough guide for the proper pillow height with measuring equipment. We analyzed the data of the respondents between the ages of 20 and 79 (1,137 male and 1,839 female; 39.0 ± 13.2 years).

Results & Conclusion: Eighteen percent of the respondents had a problem with their neck such as cervical vertebra injury. They were

excluded from following analyses. Depth of cervical curve was deeper in male compared with female ($P<0.0001$). Moreover, younger group showed lower BMI ($P<0.0001$) and depth of cervical curve was shallowest in twenties ($P<0.01$). Most respondents (89%) got to sleep nearly always in the same posture (supine 51%, lateral 46%, prone 3%). Sleep-onset-posture of female changed with age ($P<0.05$); the ratio of lateral position decreased and supine position increased. With the change of physical features depending on sex and age, it was suggested that one's sleep-onset-posture changes. As we showed in previous study, the importance to customize the height of pillow was shown and it is suggested that age and sex should be taken into consideration to decide the height.

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Life style factors and sleep – a population study

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Relations between sleep duration and smoking, alcohol intake, coffee intake and exercise were studied in a population of 40–45 year olds in Hordaland, Norway-the Hordaland Health Study. The study included all individuals in the county born 1953–57 (29.400). Participation rate was 63% (70% women and 57% men). 8860 persons (5329 women and 3531 men), answered a questionnaire with detailed information on sleep habits and problems, and questions on smoking, drinking, coffee use, and exercise. Both male and female smokers had shorter weeknight sleep duration than those who had smoked but quit ≥ 1 year ago ($P<0.0005$) and those who never smoked ($P<0.0005$). In women, those who had quit slept less than those who never smoked ($P<0.01$) but this was not different in men. Sleep duration was shorter with increasing number of cigarettes smoked per day in both genders. In both genders, abstainers from alcohol use slept less than non-abstainers ($P<0.01$ in men and $P<0.001$ in women). In women, but not in men, sleep duration was shorter the more alcohol units per 2 weeks were used. Women who did not drink coffee had shorter weeknight sleep duration than women who drank 1–3 cups per day ($P<0.05$). With increasing amount of coffee, sleep became increasingly shorter in both genders ($P<0.001$). Exercise habits did not affect weeknight sleep duration, except for a tendency for less sleep with high exercise level in women. A stepwise linear regression analysis (adjusting for gender, education, income, marriage/cohabitation and urban/rural living) showed that cigarette smoking accounted for 1.5 per cent and coffee drinking for 0.3 per cent of the sleep duration variance.

Conclusion: Cigarette smoking, alcohol intake and coffee drinking reduce sleep duration in this population.

Sleep Breathing Disorders

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Effect of CPAP use in severe sleep apnoea syndrome on quality of sleep in a developing nation

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Background: CPAP therapy has been shown to improve excess day time sleepiness, and quality of life in western population. But its effect on subjective concepts like quality of sleep in a developing country like India having people with different perceptions remains unadressed.

Setting: Sleep Lab and Chest Clinic of R.M.L. hospital, Delhi.

Method: This study enrolled 20 patients with severe OSAS (AHI >30 per hour on polysomnogram) who took the CPAP treatment and 9 severe OSAS patients patients who did not. Sleep quality was assessed by Pittsburgh Sleep Quality Index (PSQI). Patients were followed at 1 month (m), 3 m respectively.

Results: PSQI and NHP scores of both groups were comparable at start of study. A significant improvement in Global PSQI score was seen in patients using CPAP at 1 m, 3 m respectively. (baseline 7.65+2.96, 1 m 3.20+1.92, 3 m 2.75+1.55.$P<0.002$) compared to a non-significant change in those not using CPAP. (baseline 8.78+3.78, 1 m 7.89+2.89, 3 m 7.56+2.87.$P=0.4$). on comparing the groups there was significant improvement in PSQI scores at 1 m ($P=0.001$) and 3 m ($P=0.02$) in favour of CPAP using group.

Conclusion: CPAP use leads to significant improvement in perception of quality of sleep in our study group.

P163

Prediction of sleep apnoea episodes using nasal airflow

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A sleep apnoea episode prediction system is presented that is based exclusively on the airflow signal. Detection of obstructive sleep apnoea (OSA) is generally carried out using polysomnography, with the data being analysed and a diagnosis formed. Being able to predict when a sleep apnoea episode is going to occur will allow for treatment to be applied before the episode becomes detrimental to the patient. Flow signals was extracted from full polysomnographic data, which was obtained for 39 patients (24 male), mean (SD) AHI 21.4 (31.5) events/hour slept, age 39.3 (13.2) years, BMI 27.9 (7.7) $kg\,m^{-2}$. Apnoeas, hypopnoeas and periods of normal breathing were identified, and the flow signals were epoched about the onset of the apnoea (obstructive, central and mixed). Classification was performed using neural networks and five different inputs: (i) raw flow signal, (ii) normalised flow signal, (iii) inspiratory peak and expiratory trough values, (iv) weights calculated from principle component analysis and (v) intrinsic mode functions. The training set comprised 1200 apnoeas, 1200 hypopnoeas and 2400 normal, and testing 600 apnoeas, 600 hypopnoeas and 1200 normal. Networks were then tested using unseen data from 6 patients (3 male), AHI 20.2 (33.7), age 41.8 (10.7), BMI 30.8 (3.9), 300 apnoeas, 300 hypopnoeas and 600 normal. Classification of the airflow signal processing an apnoea using the raw flow signal produced the best results, with 78% sensitivity and 83% specificity. Normalising the signals and the results from the intrinsic mode functions were of a similar magnitude, sensitivity ~70% and specificity ~80%. Testing the networks with unseen patient data showed improved reliability for normalising, 83% sensitivity and 92% specificity. In conclusion, the classification of inspiratory airflow signal before an apnoea and hypopnoea is possible with high reliability statistics. Funded by EPSRC.

P164

A calibrated snoring sound sensor

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Snoring is usually measured on the trachea or in the nasal cannula. The tracheal sensor is less sensitive to nasal snoring and vice versa. Both can not produce a calibrated sound level. Therefore, snoring and its therapy can hardly be quantitatively assessed. In contrast, a microphone on the forehead measures sound, independent from its source. A calibrated electronic circuit and a logarithmic converter can produce absolute sound level in dBA. Breathing contains frequencies of about 200–2.000 Hz. Snoring is caused by obstructions in the airway that modulate the amplitude of heavy-breathing sound. The modulations have frequencies around 50 Hz. So, we have applied a hi-fi microphone to capture the sound and an electrical circuit to detect the modulations. The 6×6×10 mm dimensions of the WL93 omni-directional microphone from www.shure.com enable unobtrusive mounting on the forehead. Its frequency bandwidth of 100–20.000 Hz suits the measurement of breathing sound. A pre-amplifier minimizes noise. A standard A-weighting filter attenuates frequencies away from 1000 Hz, thus mimicking the frequency-dependent physiological perception of sound intensity. Finally, an rms-converter produces a positive voltage which is proportional to sound intensity. The bandwidth of this converter is DC-75 Hz, so that it tracks the amplitude modulations caused by snoring. The circuit was calibrated in such a way that absolute 90dBA and 50 dBA sound levels result in 1200 mV and 12 mV at the output, respectively. After digitization at 200 Hz, a logarithmic converter in the software computes absolute sound level in dBA. The sensor has been applied in ambulatory PSG for a few months now. Power consumption is only 2 mW. The measurement range is 35 till 90dBA, i.e. very light till very heavy snoring. The microphone is less sensitive to movement artifacts than the tracheal and nasal sensors. Environmental sounds can easily be distinguished from the subject's snoring and are therefore a valuable addition to the diagnosis of sleep disorders.

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Randomised controlled trial of variable-pressure versus fixed-pressure continuous positive airway pressure (CPAP) treatment for patients with obstructive sleep apnoea/hypopnoea syndrome (OSAHS)

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Background: Present treatment of choice for obstructive sleep apnoea/hypopnoea syndrome (OSAHS) in Edinburgh is continuous positive airway pressure (CPAP) set at a fixed pressure determined by a night's titration on variable-pressure machine. This ongoing double-blind, randomised controlled crossover trial seeks to determine whether OSAHS patients on variable-pressure CPAP (AutoSet Spirit) for six weeks have better outcomes over fixed-pressure CPAP.

Method: Consecutive consenting patients admitted for overnight CPAP titration to the unit, had the ideal pressure determined

using the AutoSet Spirit device (95th centile for the titration period). In the morning they were randomised to receive either fixed-pressure mode or variable pressure mode for a period of 6 weeks. At the end of this time, they were crossed over to the alternative arm of the study. All patients completed Epworth Sleepiness Score (ESS), side-effects questionnaire, sleep diary, SF-36 at baseline and the end of each treatment period. Osler and PVT were performed at the completion of each limb. Preference for treatment type were documented at the end of the study.

Results: Of the 158 subjects recruited, 13 dropped out. No difference in baseline ESS was recorded between the fixed and variable groups (15+3 versus 14+3). CPAP use was significantly better in the variable compared to fixed treatment group (4.1 h night^{-1} $\pm$ 2.3 versus 3.9 $\pm$ 2.3; $P = 0.036$) as was the ESS on completion of both limbs (9.4 $\pm$ 4.7; 10 $\pm$ 4.6; $P = 0.03$). There was a time order effect. The group receiving variable CPAP first had a significantly higher ESS at the end of the treatment limb (11+5 versus 8+4; $P = 0.009$) but usage was not significant between both treatments. Baseline ESS was higher in those who had a machine preference compared to those with no preference ($n = 30$) (15+3 versus 13+3; $P = 0.012$). Preference for treatment was determined by machine used in first limb irrespective of setting.

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Driving simulation and obstructive sleep apnea syndrome: the effects of medium traffic density on performance

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Objectives: Many studies have demonstrated that patients with Obstructive Sleep Apnea Syndrome (OSAS), a very common sleep-related breathing disorder, are usually impaired in their driving ability because of decreased sleep quality. However, most of the simulation procedures in laboratories are designed to create monotonic conditions with low traffic density, if any, thereby leading to a dramatic decrease in performance in OSAS patients because of the lack of stimulation. The aim of this study was therefore to evaluate driving abilities in OSAS patients involved in a driving simulation task with medium traffic density, in order to replicate as far as possible real world conditions. The behavioral and physiological attributes likely to predict driving performance in these patients were also investigated.

Methods: After a normal night of sleep, 12 OSAS patients and 8 healthy controls performed 6 driving sessions during a 24-hour period of sustained wakefulness. Driving performances (speed, lateral position, distances ...) were measured and correlated to sleep parameters and to a waking EEG recorded during the task.

Results: Compared to healthy controls, patients showed difficulties in speed adjustment. However, they maintained longer inter-vehicle distances, including during overtaking. Their waking EEG, while driving, showed increased spectral power in theta (3.9–7.8 Hz) but also in beta (12.7–29.2 Hz) activity, alpha power (7.9–12.6 Hz) being increased in both groups due to sustained wakefulness. Poor sleep indices were correlated to increased theta and beta activities, as well as to more cautious behavior.

Discussion: In medium traffic density conditions, driving performance in OSAS patients remained at near normal levels, but with more cautious behavior than controls. This could be the result of a bigger effort to stay awake, as suggested by an increased beta activity in these patients.

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Prediction of risk of sleep-disordered breathing in pregnant women

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Introduction: In non-pregnant adults, sleep-disordered breathing (SDB) is associated with increased weight, Mallampati grades III/IV, and increasing neck circumference. Routine airway assessment in pregnant women may serve as a proxy measure to detect those at risk of SDB. We investigated the association between simple airway evaluations performed routinely by anaesthetists and snoring during pregnancy.

Methods: A retrospective review of a labour and delivery database was performed over an 18 month period. Women are routinely asked about snoring and airway evaluation includes Mallampati grading and measurement of neck circumference. Mallampati I indicates visibility of the entire tonsil, Mallampati II indicates visibility of upper half of tonsil fossa, Mallampati III indicates visibility of soft and hard palate only while Mallampati IV indicates visibility of hard palate only. Mallampati grades I/II are considered low risk for SDB and and grades III/IV are considered high risk for SDB. A neck circumference of $\geq$40 cm in women is considered high risk for SDB.

Results: Data for snoring and Mallampati grades were available in 4,695 women. Mallampati grades III/IV were found in 10% of women while snoring was reported in 13%. Mallampati grades III/IV were independently predictive of snoring after adjustment for Body Mass Index and age (adjusted odds ratio of 2.0, 95% CI 1.3–2.7; $P \leq 0.001$). Snorers had a larger neck circumference (36.3 $\pm$ 3.6 cm versus 34.8 $\pm$ 2.9 cm; $P \leq 0.001$). A neck circumference of $\geq$40 cm was found in 7% of women and was independently predictive of snoring (adjusted odds ratio 3.3, 95% CI 1.6–6.9; $P \leq 0.001$).

Conclusion: Two pre-operative predictors of a difficult intubation routinely used by anaesthetists may have great cost-effective clinical utility in the identification of pregnant women likely to be at high risk for SDB. These simple, non-invasive techniques may have a role in the obstetric clinic such that pregnant women may be screened for SDB. Also will identification of pregnant women with SDB assist in anticipating the unanticipated difficult obstetric airway?

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Restarting CPAP therapy after a previous failure

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Background: Continuous positive airway pressure (CPAP) is the gold standard therapy for obstructive sleep apnoea with adherence rates in CPAP-virgin patients up to 88%. The persistence of symptoms and the failure of the alternative therapies have put pressures on physicians to retry CPAP therapy after a previous failure. We reported the adherence rate after restarting CPAP therapy in obstructive sleep apnoea patients who previously stopped their CPAP therapy.

Methods: We restarted CPAP therapy to 48 (13 females) consecutive patients who stopped CPAP therapy for at least 6 months (previously failed group) and also started therapy to 238 (59) consecutive CPAP-virgin patients. All received optimal treatment to ensure good nasal airflow prior to CPAP. Humidifiers were given when necessary. CPAP usage was calculated as follow: mask-on

time at the last follow-up visit in hours/total days (not total used days) and the adherence: number of patients with CPAP usage ≥ 4 h day^{-1} $\times 100$/total number of patients.

Results: The mean age and body mass index were significantly ($P<0.05$) higher in the previously failed group than in the CPAP-virgin group: mean $\pm$ SD 56 ± 9 years versus 52 ± 11 and 35 ± 8 kg m^{-2} versus 33 ± 6 respectively. No significant difference regarding the severity of their sleep apnoea was found 42 ± 26 events hour^{-1} versus 38 ± 24. The mean follow-up period was 262 days, (range 1–999) and 384 (5–1090) respectively. The mean daily CPAP usage was significantly ($P<0.001$) lower in the previously failed group 2:11 $\pm$ 2:27 (hrs:min) than in the CPAP-virgin group 3:51 $\pm$ 2:35 with the corresponding adherence rate at 27 and 51%. The major reasons for the first CPAP failure were CPAP disrupted sleep for 27 out of 48 patients, lack of motivation for 8, nasal symptoms for 7, and panic disorders for 6 patients. After restarting, the corresponding adherences were at 7%, 63%, 29% and 50% (significant within-group difference $P<0.01$).

Conclusion: The adherence to CPAP therapy in patients who previously experienced CPAP failure is significantly lower than that in the CPAP-virgin group, especially in those who stopped because of disrupted sleep or nasal symptoms. However, patients manifesting motivation to restart CPAP show significantly better adherence.

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Centro-temporal and rolandic spikes associated with OSAHS-UARS in children: a clinical overlap of diurnal and nocturnal symptoms

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Aim: Spikes in centro-temporal and rolandic regions (CTRS) increase in frequency during drowsiness, may induce prolonged cognitive impairment and have been associated with speech dyspraxia. We studied the prevalence of CTRS among a sample of children with snoring and suspected obstructive sleep apnea-hypopnea syndrome (OSAHS).

Patients and methods: 30 children (16 females) with symptoms of snoring, adenotonsillar hypertrophy and difficulty breathing during sleep were referred to the Sleep Unit during 2007. Patients were assessed by clinical history, physical and neurological examinations, including the Pediatric Daytime Slepiness Scale (PDSS)1 questionnaire. A daytime nap polygraphic recording (with an extended 13-channel EEG) was recorded before one night with standard video-polysomnography (VPSG).

Results: We found CTRS in 5 cases (16.6%, 3 males) mean age was 5.6 years (range 4 to 7 years). We also observed snoring (5/5), mouth breathing (5/5), apnea (3/5), daytime sleepiness (3/5), parasomnias (4/5), behavior or learning problems (3/5), enlarged tonsils and adenoids (5/5), allergic diseases (2/5), poor growth (2/5) and family history of epilepsy (1/5). Video-EEG showed left, right or bilateral interictal CTRS and/or partial motor seizures (2/5) during sleep. VPSG showed disturbed sleep structure (5/5), periodic leg movements (1/5), snoring (2/5) and central apneas (2/5) without significant O2 desaturations.

Conclusion: Our cases presented CTRS with or without nocturnal seizures and disturbed nocturnal sleep associated with an upper airway resistance syndrome (UARS). The association between CTRS-OSAHS-UARS may aggravate the prognosis of neurophycological deficits in children: attention span, executive function, and phonological processing. Due to the overlap of diurnal and nocturnal symptoms, an EEG nap recording or a VPSG (with extended EEG leads) is needed for diagnosis.

Reference: 1. Drake C et al. The Pediatric Daytime Sleepiness Scale (PDSS): Sleep habits and school outcomes in middle-school children. Sleep 2003; 26 (4):455–58.

P170

CPAP treatment compliance results in improvement of symptoms and health related quality of life in OSAS patients

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Aim: The purpose of this study was to evaluate the symptoms and the quality of life of OSAS patients after compliant treatment with CPAP.

Methods: A group of 50 patients (41 men and 9 women) with mean age of 50 ± 12 years, mean Apnea-Hypopnea Index 40 ± 25 events h^{-1} and mean BMI 35.1 ± 7.7 kg m^{-2} were diagnosed with full polysomnography study and treated with CPAP for 6 months. The health related quality of life and symptoms were assessed by administering an officially validated (Cronbach's A statistic >0.7) Greek version of the sleep apnea quality of life index (SAQLI). Sleepiness was measured with the Epworth sleepiness scale (ESS) and compliance by electronic monitoring of CPAP usage per night of sleep.The statistical analysis was made by using the statistical program SPSS v.12 for Windows.

Results: Mean value of compliance of treatment was 4.5 ± 0.5 h of CPAP usage per night. Comparisons between quality of life indexes were made before and after CPAP treatment as following: SAQLI (3.8 ± 0.9 before CPAP versus 5.8 ± 0.8 after CPAP, $P<0.01$), daily functioning (4.2 ± 1.4 versus versus 6.0 ± 0.9, $P<0.01$), social interactions (4.8 ± 1.3 versus 6.3 ± 0.7 $P<0.01$), emotional functioning (4.4 ± 1.4 versus 5.7 ± 1.0, $P<0.01$), symptoms (1.6 ± 0.8 versus 5.8 ± 1.2, $P<0.01$), ESS (13.7 ± 6.5 versus 3.9 ± 3.8, $P<0.01$). Regarding the symptoms the higher improvement was noticed for "sleepiness while watching a spectacle" (96%), reading (95%), carrying on a conversation (95%), driving (92.9%), "restless sleep" (87.8%) and "urinate more than once per night" (84.8%). Lower improvements were observed for "dry mouth-throat upon awakening" (36.1%), excessive fatigue (54.5%), decreased energy (55.3%)". The total improvement of the 21 symptoms in the questionnaire was 77.6%.

Conclusion: We conclude that OSAS patients who are compliant to CPAP show significant improvement of their quality of life, daytime sleepiness and other symptoms after six months of treatment with CPAP.

P171

Morning headache in obstructive sleep apnea syndrome

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Introduction: The prevalence of morning headache has been shown to be 18% to 74% in patients with obstructive sleep apnea syndrome (OSAS). Disappearence of headache when OSAS was treated supports the causal role of OSAS for morning headache. However there are some other studies denying this relationship.

Methods: 563 consecutive subjects with the complaint of snoring were included in the study. Morning headache was assessed using a headache questionnaire. OSAS was determined by using 4 AHI cut points (AHI <5, $5<$AHI <15, $15<$AHI <30, AHI >30). Four groups of subjects were compared according to morning headache

and also demographic and clinical variables. OSAS patients with and without morning headache were also compared for demographic, clinical and PSG variables. Comparisons were made by t test, Fisher exact test and chi-square test. Logistic regression analysis was employed to examine the independent predictors of morning headache.

Results: Morning headache prevalance was significantly higher in severe and moderate OSAS groups ($P<0.05$). AHI was significantly higher in OSAS patients with morning headaches compared to patients without morning headaches (38.7 ± 25.7 versus 34.1 ± 24.6, $P<0.05$). Oxygen saturation nadir during REM and NREM sleep as well as mean oxygen saturation value during total sleep time were also found to be significantly lower in morning headaches group ($P<0.05$). None of the sleep parameters were found to be determinants of morning headaches. At the 1. day, 1. week and 1. month of n-CPAP treatment, morning headache was totally disappeared in 72.4%, 84.2% and 92.1% of patients, respectively. More than half of female OSAS patients reported morning headaches while only 27.9% of males with OSAS reported it ($P<0.05$).

Conclusion: Prevalence of morning headache increases with increasing OSAS severity. Hypoxemia and female gender may influence the occurrence of morning headaches.

P172

Spectral analysis of heart rate variability in treated obstructive sleep apnea

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Introduction: Patients with obstructive sleep apnea (OSA) have been found to have an increased sympathetic activity during sleep. Autonomic nervous system dynamics as measured by heart rate variability and respiration vary according to sleep depth and type. OSA is associated with predictable characteristics such as periodic cycling of breathing and heart rate. This study compares heart rate variability (HRV) examining frequency domain indices in the pre and post split periods for assessment of response to CPAP therapy. The frequency domain indices reflect the effects of the sympathetic and parasympathetic systems on the heart, as well as respiration and circadian rhythm.

Methods: Twenty two adults were selected with a primary diagnosis of obstructive sleep apnea and who were treated with CPAP during their initial study. Patients had a baseline and treatment period during their inpatient sleep study. Only those with a respiratory disturbance index (RDI)<10 per hour and nadir oxygen saturation >85% during the ideal CPAP titration period were included. HRV was analyzed by Morpheus® for time domains with a one hour period analyzed for each period being the most representative of stage II sleep in the pre split period and post split period (at the ideal CPAP level). Patients taking beta blockers were excluded. Heart rate variability (HVR) is a collective term for a group of indices obtained from the RR intervals time series. These indices include: Frequency domain Indices: a) VLF-very low frequency power (0.00333–0.040 Hz). b) LF-low frequency power (0.040–0.150 Hz). c) HF-high frequency power (0.150–0.400 Hz)

Results: The pre split mean of VLF was 1452 (1136) and post split was 866 (1088); pre split mean of LF was 371 (460) and post split mean was 43 (18); pre split HF was 169 (114) and post split was 50 (57). *T*-tests comparing pre and post split periods: VLF $P = 0.08$; LF $P = 0.002$; and HF $P = 0.00009$.

Conclusions: HRV showed improvement with CPAP therapy. HRV may be a useful tool for assessment of response to treatment.

P173

Sleep characteristics and OSAS prevalance of the patients who have generalized tonic clonic seizures with treated sodium valproate

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Background: Obesity is a seven fold risk factor for obstructive sleep apnea syndorome (OSAS). Epileptic patients who become obese after sodium valproate (VPA) monotherapy can have a risk of OSAS related to weight gain.

Methods: We have analyzed 98 adult patients who have generalized tonic clonic seizures attending our epilepsy clinic on VPA monotherapy followed over a median of 34 months. The patients who have a history supportive of obstructive sleep apnea and have no seizure during last two months were included in the study. All of the patients were evaluated by an otorhinoloaryngologist. All of them were applied some subjective sleep tests and full night polysomnograph.

Results: We observed that 70% of the patients had weight gain of more than 4 kg during VPA monotherapy and 51% of the patients have OSAS diagnosis as confirmed by polysomnography. There was meaningful relationship between serious of OSAS and period of VPA treatment or dosage of VPA.

Conclusion: Weight gain is a common and frequent undesirable effect associated with the use of VPA. Weight gain is disturbing to general health, with a possible increase in the risk of obesity and obstructive sleep apnea. Potential mechanisms of VPA-associated weight gain are not yet clear. Possible explanation for lowered blood glucose may be a deficiency in carnitine directly caused by the VPA, that would result in a reduction of fatty acid metabolism and an increase in glucose consumption. In addition, an enhancing effect of gamma-aminobutyric acid-mediated neurotransmission may increase appetite for carbohydrates and reduce energy expenditure. Our results indicate that weight gain may be causes to OSAS at the epileptic patients with treated VPA. Therefore, epileptologists must be careful about the patients with treated VPA for risk of OSAS.

P174

Psychiatric diseases related with OSAS (obstructive sleep apnea syndrome)

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In our study, we aimed to look into the variaty of the psychiatric diseases observed in patients with diagnosis of OSAS and to discuss the spectrum of psychiatric diseases accompanied by the typical clinical symptoms and findings in light of literature knowledge. The cases who visited our polyclinic in between 2004–2007 and the clinics of which seemed as OSAS were inspected all night through video-EEG-polysomnography by certificated sleep technicians using devices of Embla A-10, N-7000 in accordance with sleep apnea protocol in order to trace the change in sleep structure and breathing events. All the cases were assessed by a psychiatric expert and those who had the diagnosis of psychiatric disease with respect to the criteria of DSM IV were included in the study. Almost in 23.8 percent of the 235 cases scanned in our study, there found to be at least one psychiatric disease accompanying. In these cases, it was found that the frequency of the depression to be %92.8, Schizophrenia to be % 7.1, OCD as % 3, 5 and Bipolar disorder-depressive episode to be % 1.7. The sleep continuity in OSAS gets broken and is fragmental. In such psychiatric diseases as depression difficulty in falling asleep, destruction in sleep integrity due to the frequent wake-ups are observed. In generalized anxiety disorder and schizophrenia, a fragmental sleep and dicrease in sleep efficiency get observed. When the psychiatric disease get accompanied by OSAS, high rate of AHI are frequently

encountered. Our study examines the variety of the psychiatric diseases observed in patients with diagnosis of OSAS and makes discussions in light of the psychiatric disease spectrum literature data accompanying the OSAS clinic. Similar studies in bigger serials will ensure the psychiatric disease spectrum seen in cases with OSAS to be understood and diversities in approach against these cases to get clarified.

P175

OSAS in RBD patients: reciprocal interaction and mechanisms

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Introduction: REM Behaviour Disorder (RBD) is often comorbid with OSAS whereas OSAS patients often display NREM related nocturnal agitation possibly mimicking RBD episodes. The aim of our study was to evaluate possible correlations between sleep related breathing disorders (SBD) and RBD in a group of patients referred to our Center for nocturnal behavioural agitation.

Materials and Methods: We retrospectively analyzed clinical and polygraphic features of 25 (22 M, 3F) patients referred to our Sleep Medicine Centre over the last 2 years on account of episodes of nocturnal "agitation" during sleep.

Results: 18 patients (15 M, 3F) were diagnosed for RBD (mean age 57.8 ± 15.5). Total number of clinical episodes recorded was 9, total RBD time 90′30″, total REMWA time 497′30″. 13/18 RBD patients were snorers of which 7 had OSAS, 15 had periodic leg movement (PLM) (mean PLMS Index/h 66.6 ± 45.2), preferentially distributed in REM sleep (mean REM PLM Index/min 1.8) without (or with) definite association with apnoeic related arousals; 3/18 narcolepsy/cataplexy, 2 status dissociatus, 1 RLS. SBD precede RBD in 6/13 patients, mean AHI was 23.8 ± 20.1, mean SaO2 87% ± 6. RBD behavioural episodes were preceded by SBD in 7/13 patients (of which 2 by a clear cut obstructive apnoea) mean HR in the whole RBD group was 66.3 ± 8.4, mean highest HR 77.6 ± 11.4, mean lowest HR 55.2 ± 10.7. In particular mean ΔHR on RBD behavioural episodes was 4.2.

Discussion: Our data show a frequent co morbidity of RBD with PLMs and SBD, although the latter is not severe. A respiratory event may promote via transitory hypoxemia an arousal which in turn may precipitate a RBD event. A blunted sympathetic activation is characteristic of RBD subjects who display a reduced HR variability, without the typical sympathetic response upon arousals, especially those preceding clinical RBD. RBD clinical episodes are scanty by comparison with REMWA episodes. RBD is rare in women who display anyway the same clinical behaviour in the absence, at least in our 3 cases, significant SBD pathology.

P176

Sleep time and body mass amongst children with sleep disordered breathing

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Introduction: Sleep disordered breathing (SDB) and shortened sleep time have been independently associated with increased body mass amongst children. It remains unclear as to whether the association between sleep time and increased body mass varies amongst children with SDB. This study assessed the association between body mass and sleep time amongst a group of children with SDB compared to non-snoring controls.

Methods: Children with SDB were recruited from a hospital waiting list for adenotonsillectomy and non-snoring controls from the general community. All subjects completed one-week sleep diaries prior to overnight polysomnography (PSG).

Results: 32 children with SDB (6.6 years ± 2.7; 20 males) and 41 controls (7.6 years ± 2.6; 19 males) completed 1-week sleep diaries and overnight PSG. Groups were matched for age, gender and BMI z-score. SDB children displayed greater obstructive apnoea and hypopnoea index (OAHI), respiratory arousals and hypoxia when compared to controls. All other sleep characteristics as well as time in bed, sleep time and sleep onset latency as determined by sleep diaries was not different between groups. After controlling for age, socioeconomic status and OAHI, sleep time was only mildly predictive of BMI z-score across the total group, explaining 5.8% of the variance, $\beta = -0.32$, $P < 0.05$. When analysed independently, children with SDB showed a stronger association, with sleep time explaining 13% of the variance in BMI z-score, $\beta = -0.50$, $P < 0.05$, compared to only 6% for controls, $\beta = -0.32$, ns. OAHI did not interact with this association.

Conclusion: This is the first study investigating the association of sleep time and body mass amongst children with SDB compared to controls. Consistent with previous reports, a mild effect was present across the total group showing shorter sleep time to be associated with increased body mass. However, this association was much stronger amongst SDB children and not found amongst controls when analysed separately. The difference between groups was not attributable to OAHI severity. Given these preliminary results and large prevalence of snoring reported amongst children in the community, previous estimates of the contribution of sleep time to body mass must be carefully reviewed.

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Evaluation of long-term continuous positive airway pressure therapy in apparent symptom-free obstructive sleep apnoea patients

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Introduction: Continuous positive airway pressure (CPAP) provides an effective treatment for patients with obstructive sleep apnoea syndrome (OSAS). If patients are satisfied with the initial CPAP therapy, they usually are not routinely followed-up. It is not well known, however, if CPAP pressure should be verified in this group of patients, as apnoea's may still persist, even in apparent symptom-free patients.

Methods: We performed a prospective study in which we evaluated CPAP titration and measured body mass index, excessive daytime sleepiness, depression, vigilance and reaction tests, blood pressure and compliance in patients who used CPAP for at least one year. Patients from the outpatient clinic's database, who were diagnosed with OSAS in the past years and used CPAP, were asked to participate.

Results: Of 151 patients who were contacted, 116 responded and filled out the questionnaires and 100 underwent a clinical polysomnography to re-evaluate CPAP titration. Mean pressure level of CPAP was 7.3 (SD 1.8) cm H_2O. In 52 (52%) patients, CPAP pressure was raised during the clinical polysomnography because of still existing apnoea's. In 14 patients (14%), CPAP pressure was lowered and in the remaining 33 (33%) patients CPAP pressure was unchanged. CPAP treatment had a statistically significant favourable effect on subjective symptoms of headache, dry mouth, snoring and sleepiness. Furthermore, after CPAP treatment, scores on Epworth Sleepiness Scale, Multidimensional Fatigue Inventory-20 and Beck Depression Inventory normalized ($P < 0.01$). There was no important effect of CPAP treatment on blood pressure (mean 138/88 versus 138/84), BMI (mean 31.2 versus 33.9), and vigilance and reaction tests.

Conclusion: In OSAS patients using apparent adequate, long-term CPAP, verification of the CPAP pressure seems to be necessary. Re-evaluation should probably include a clinical polysomnography and may be carried out a year after the initial introduction of the CPAP therapy.

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Hepatic function markers in obstructive sleep apnea syndrome (OSAS)

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Introduction: A combination of venous congestion and decreased oxygen transport are considered to be the main factors in liver injury. OSAS is characterized by repeated hypoxemia due to repeated episodes of apnea/hypopnea during sleep.

Aim: The aim of this study was to evaluate serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) levels in patients with OSAS.

Patients-Methods: We examined 130 patients who claimed sleep disordered breathing with polysomnography and blood tests. Patients who reported drinking >1 alcohol unit/day, a history of chronic liver disease or receiving any kind of medication were all excluded from the study. All patients were tested for virus hepatites infection after written consent.

Results: SGOT levels correlated significantly with Apnea/Hypopnea Index ($r = 0.204$, $P = 0.02$), average SaO2 ($r = -0.265$, $P = 0.002$), and percentage of time of sleep spend with SaO2 $< 90\%$ ($r = 0.188$, $P = 0.034$). SGPT levels correlated significantly with Apnea/Hypopnea Index ($r = 0.181$, $P = 0.04$), average SaO2 ($r = -0.260$, $P = 0.003$), and percentage of time of sleep spend with SaO2 $< 90\%$ ($r = 0.227$, $P = 0.01$).

Conclusion: OSAS can lead to hepatic dysfunction as demonstrated by the increase in SGOT and SGPT levels. Hypoxemia during sleep in OSAS seems to be one of the mechanisms responsible for this effect.

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Snoring and daytime functioning in Finnish schoolchildren

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In numerous studies, it has been shown quite clearly that snoring is associated with problems in daytime functioning of schoolchildren. However, in the Finnish population these studies are few. The present questionnaire is the first part of a larger study concerning snoring and its sleep laboratory findings among Finnish schoolchildren. We sent the questionnaire to ordinary primary schools in the Tampere region, where school nurses or teachers handed it over to the pupils to give it to their parents. All the children were chosen from normal classes (pupils in special education classes were excluded). The questionnaire included information about sleep habits, snoring, night-time breathing difficulties, parasomnias, daytime functioning, snoring in the family, and the health status of the child. 190 out of 831 questionnaires were received (23%). Three questionnaires were excluded because of no information about snoring (2) and age out of the scale (1). The mean of age was 7.4 years (SD 4.7 months). Out of the total, there was 55% girls. Those that snored at least in three nights during the week were considered as snorers (12%). They were compared with the ones who snored never or at most one to two times per month (controls, 76%). In statistical analysis, *T*-test (length & height), chi-square (gender), cross-tabulations and Fisher's exact test were used. The snorers had statistically more wake-up time tiredness and headache, daytime sleepiness, difficulties in concentration and over-activeness. During the night-time they suffered more sweating and breathing difficulties, and had more allergic rhinitis. Their mothers and siblings also snored more often. The following parameters did not differ significantly: weight, gender, sleep length, parasomnias, nightwaking, sleeping during daytime, snoring of the father, smoking of the parents, and past adenotonsillectomy. Our findings in the Finnish schoolchildren are similar to the findings in other countries and strengthen the conclusion of the harmfulness of snoring on daytime functioning.

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Undiagnosed obstructive sleep apnoea in schizophrenia

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Aims: The study aimed to examine a series of community based patients of Schizophrenia with undiagnosed Obstructive Sleep Apnoea (OSA) and identify cases where possible and examine associated features.

Background: OSA is a sleep disorder linked with mood related changes, severe cardiovascular morbidity and sudden death. Risk factors include male gender, increasing age, medication, alcohol use, smoking and obesity. This is a neglected area in Schizophrenia despite both sharing common risk factors.

Method: The study was conducted on patients with Schizophrenia, attending County Wicklow Mental Health Services. Fifty-two patients (30 male, 22 female) completed the study. We collected information on clinical and psychosocial variables, followed by a record of their sleep history, Epworth Sleepiness scale (ESS) and Fatigue Severity Scale (FSS). A portable home sleep monitoring device (Embletta TM) recorded sleep variables. Subjects were defined as either normal with no OSA or significant. OSA was classified as mild, moderate or severe. SPSS was used to correlate demographic, clinical and sleep data with the presence or absence of OSA.

Results: Out of 52 cases, 23 (16 male, 7 female) were diagnosed with OSA. Age, body mass index, waist circumference and waist-hip ratio were associated with the presence of OSA. Additional analysis will be shortly available.

Conclusion: Age and obesity were found to be risk factors for obstructive sleep apnoea in our sample. Patients with Schizophrenia should be evaluated for sleep apnoea.

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Impaired memory consolidation during sleep in patients with obstructive sleep apnea

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Introduction: Compelling evidence from animal and human studies indicates that healthy sleep facilitates the consolidation of newly acquired memories. The aim of this study was to test the hypothesis that overnight consolidation of procedural and declarative memory is attenuated in patients with obstructive sleep apnea (OSA) in comparison to healthy subjects.

Methods: General neurocognitive and memory performance (procedural mirror-tracing task, declarative visual and verbal learning task) was assessed before and after one night of polysomnographic monitoring in 15 patients with OSA (10 men, aged 46.4 ± 5.9 years) and 20 sex- and age-matched healthy subjects.

Results: OSA patients showed a significantly reduced sleep period time, increased frequency of micro-arousals, heightened apnea-hypopnoea index, and subjectively disturbed sleep compared to

healthy subjects (MANOVA, $P<0.05$). Memory performance before sleep did not differ between the groups. As a main result, OSA patients demonstrated a significant impairment of overnight procedural memory consolidation compared to healthy subjects (MANCOVA, $P<0.05$, large effect size). Patients with OSA showed a significantly lower improvement of mirror tracing capacity (30.1% ± 9.7) compared to healthy subjects (39.5% ± 12.2). This lower capacity was mainly driven by a significantly lower improvement in mirror tracing draw time in OSA patients (22% ± 13.4) compared to healthy subjects (32.7% ± 13.8). Without reaching significance, OSA patients also tended to show attenuated consolidation of declarative verbal and visual memory consolidation (low to medium effect size).

Conclusion: The results suggest that OSA is associated with a significant impairment of procedural memory consolidation and a less pronounced impairment of declarative memory consolidation during sleep. Future work is needed to determine whether OSA treatment improves or normalizes deficits in memory consolidation during sleep in patients with OSA.

P182

Dentists' and doctors' attitudes to the provision of intra-oral appliances for the management of snoring and sleep apnoea

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Aim: To determine the attitudes and awareness of dental and medical practitioners in Scotland to the provision of oral appliances for the management of snoring and sleep apnoea.

Setting: The questionnaire was completed by dental practitioners randomly selected from across Scotland and by doctors specialising in sleep medicine within Scotland.

Method: A questionnaire was devised and sent to 17 specialists in sleep medicine and 210 general dental practitioners, community dental service practitioners and hospital-based dental practitioners. A reply-paid envelope was included with each questionnaire.

Results: There were 14 replies (82%) from doctors and 105 (50%) from dentists. All the doctors felt that dentists had a role in the management of these patients. Of the replies from dentists, 60 (57%) stated that they provided appliances but their screening for sleep apnoea and discussion of the side effects of appliances varied widely. Seventy eight dentists (74%) expressed an interest in attending a course on the management of sleep apnoea and snoring.

Conclusions: The current practice of doctors and dentists in the management of obstructive sleep apnoea and socially disruptive snoring with oral appliances in Scotland is varied. Whilst doctors are happy for dentists to be involved, dentists need further training in this area.

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Vulnerability to sleep restriction in OSA? Effects on sleepiness and awareness during simulated driving

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Obstructive Sleep Apnea (OSA) is a common disorder with significant neurobehavioural consequences including excessive daytime sleepiness, deficits in sustained attention, and increased motor-vehicle accident risk. Accidents in healthy, young adult drivers are known to be impacted by lifestyle factors including sleep restriction and alcohol, but the vulnerability of OSA patients to these insults has not been systematically studied. Awareness of both sleepiness and performance is of vital importance, as this underpins the decision to drive. This study aimed to use the AusEd driving simulator and subjective ratings to assess severely-affected OSA patients and controls in awareness of sleepiness during driving, as part of a larger study-addressing vulnerability in OSA. We analysed steering deviation, subjective sleepiness and performance ratings from 13 severely-affected OSA patients (mean [sd]: age = 51.3 [15.2] y; BMI = 34.1 [10.6]; AHI = 67.3 [21.7]/hr), and 14 healthy controls (age = 48.5 [12.3] y; BMI = 22.8 [5.8]; AHI = 8.3 [4.2]/hr). All completed 90 min of simulated driving in the mid-afternoon following normal (8 h) and restricted (4 h) sleep conditions. Mixed model analyses demonstrated clear significant effects of group, condition and time ($P<0.01$) on both subjective sleepiness and subjective driving performance. Steering deviation data showed similar differences, with an additional group×condition interaction effect ($P<0.01$). Within-group comparisons showed that sleep restriction causesd significantly higher levels of subjective sleepiness and worse driving performance than normal sleep in both patients and controls, while steering deviation data showed this difference only in patients ($P=0.05$). These data clearly show that severely-affected OSA patients perform worse at baseline than controls at simulated driving in the mid-afternoon. The addition of sleep restriction results in additional impairment to driving performance in OSA, but not controls, suggesting increased vulnerability in OSA. Subjective data suggest that patients are aware of this impairment. Further investigation is needed to determine vulnerability in mildly-affected patients, who may be less aware of sleepiness and/or impairment.

P184

The impact of mandibular advancement splint therapy on quality of life in OSA patients reselected for treatment

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Aim: To evaluate changes in quality of life (QoL) and daytime sleepiness in obstructive sleep apnoea (OSA) patients, selected for mandibular advancement splint (MAS) therapy.

Methods: A prospective non-randomised controlled study was carried out in 85 mild to moderate OSA patients (AHI $>5<30$ events h^{-1}) with favourable sleep nasendoscopy (SNE) findings a body mass index (BMI) $<30\,kg\,m^{-2}$ and Epworth Sleepiness Scale (ESS) score <18. Patients were concurrently allocated to either treatment or control groups. The treatment group received a MAS; the control group remained untreated for 3-months. The medical outcomes short form-36 (SF-36) and ESS questionnaires were administered at baseline and after 3 months. All patients underwent polysomnography at baseline and the treatment group underwent cardiopulmonary sleep studies with the MAS in-situ at 3 months.

Results: Fourty (89%) of the treatment group and 35 (88%) of the control group completed the study. Significant reductions ($P<0.001$) were detected in median [range] AHI (16 [5.2–30] to 4.6 [0.8–17.2]), and oxygen desaturation index (11 [3–16] to 0 [0–5]) at 3 months with MAS therapy. The treatment group had a significant improvement in the energy/vitality ($P=0.03$) QoL domain, and a reduction in daytime sleepiness (median [range] ESS score 10 [1–18] to 6 [1–14]; $P<0.001$) compared to controls.

Conclusion: OSA patients pre-selected for MAS therapy demonstrated significant improvements in AHI, which was associated with concurrent improvements in energy/vitality and daytime sleepiness.

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UPPP is an alternative to OSAS patients who have failed non-surgical treatment

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Objectives: To evaluate uvulopalatopharyngoplasty with tonsillectormy (UPPP) in sleep apnoea patients failing or not accepting CPAP and Mandibular Retaining Device (MRD).

Design: Nonrandomised prospective intervention study.

Material and Methods: One hundred and fifty-eight patients, 139 men and 19 women, median age 45 years, (range 20–75), median Body Mass Index (BMI) 29 (20–48), with OSAS (symptoms and ODI >5), underwent a conservative form of UPPP in general anaesthesia during 2002–2006. Sleep apnoea recordings and questionnaires including Epworth sleepiness scale (ESS) before and one year after surgery. A safety program for peri-operative care was used, for example monitoring at a postoperative care unit.

Results: One hundred and twenty patients underwent sleep apnoea recordings, which showed a significant decrease in oxygen desaturation index (ODI), from median 23 (6–100) to 8 (0–60). Using the criteria of success (ODI <20 and $>50\%$ reduction), 64% were responders. 120 patients evaluating their sleepiness showed a significant decrease in ESS value from median12 (0–21) to 6 (0–22). Postoperative complications in 158 patients were: seven (4.4%) had minor bleedings, two (1.2%) had more severe bleedings and one (0.6%) a temporary tracheostomy due to pharyngeal oedema. There were no deaths, nor sequel of complications. Eighty-eight percent of the patients were satisfied with their operation. Laboratory success factors were female gender, low age and low preoperative ODI, but not large tonsils or low BMI.

Conclusions: UPPP may be safe and effective when using a conservative method and safety program. UPPP should therefore be offered to OSAS patients failing CPAP and MRD.

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Visual cognitive abilities and sleep depth in obstructive sleep apnea syndrome

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Objectives: To clarify whether patients with obstructive sleep apnea syndrome (OSAS) have a decline in verbally or visually based cognitive abilities and whether the possible decline is related to local sleep depth changes. In addition, the effect of continuous positive airway pressure (CPAP) on the possible changes is investigated.

Methods: Fifteen OSAS patients and 15 healthy controls joined two full-night polysomnographies including a computational measure of NREM deep sleep percentage (DS%) bilaterally from the frontopolar and central EEG channels, and a neuropsychological assessment. After a 6-month CPAP treatment the patients joined a full-night polysomnography with DS% analysis and a neuropsychological assessment.

Results: The patient group had poorer performance in the Picture Completion, in the Digit Symbol and in the copy of the Rey-Osterrieth Complex Figure (ROCFT) compared to the control group. Patients also showed reduced DS% in all four EEG channels. During CPAP treatment the patient group still had poorer performance in the Picture Completion and in the ROCFT, and continued to show reduced DS% in the right hemisphere.

Conclusions: OSAS patients have mild visually based cognitive changes and less deep sleep in the right hemisphere even after CPAP treatment.

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Screening for sleep apnea in primary care patients with difficult to control blood pressure

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Background: Screening for obstructive sleep apnea (OSA) is important in high risk groups, like in hypertensive patients. The Berlin questionnaire has been used in several studies but its diagnostic accuracy (sensitivity and specificity) is unknown in hypertensive patients followed in primary care setting.

Aim: To determine the symptoms of OSA in difficult to control hypertensives followed in primary care practices and to compare those symptoms to sleep study results.

Methods: Patients with difficult to control blood pressure (taking >3 antihypertensive medications with clinical blood pressure $>140/90$ mmHg) were selected from 10 rural primary care practices. Subsequent to ethics approval, an overnight sleep study and a daytime multiple sleep latency test (MSLT) was conducted and 24-hour blood pressure, and patient health-related demographics were obtained. Patients also completed the Berlin questionnaire (BQ), the Athens insomnia scale (AIS) and Epworth sleepiness scale (ESS) to measure the symptoms of sleep apnea.

Results: Forty-four patients participated in the study, 27 (61%) were female. The average age, BMI, neck size and 24-hour blood pressure in males and females were: 67 ($\pm$11) and 67 ($\pm$13) years, 32.7 ($\pm$7) and 34.7 ($\pm$ 9) $kg\,m^{-2}$, 43 ($\pm$5) and 37 ($\pm$ 5) cm and 142/79 ($\pm$13/10) and 144/74 ($\pm$21/11) mmHg respectively. Twenty-eight (64%) patients were found to have OSA: 15/17 men and 13/27 women. Patients with OSA had higher average AIS points than those without OSA: 10 (inter quartilis range :10) versus 6 (iqr:10) $p<0.05$. There were no significant differences between the average ESS points: 8 (iqr8) versus 8 (iqr:6) nor did the average MSLT results differ (9, 5 versus 9, 6 min.) between the two groups. The sensitivity (67%) and specificity (45%) of the Berlin questionnaire was low in this population.

Conclusion: OSA is very frequent (64%), especially in males (88%) in patients with difficult to control hypertension who are followed in primary care. The AIS score was higher, but the ESS score and MSLT results were similar in patients with versus those without OSA. The Berlin questionnaire had low sensitivity and specificity in this population, therefore it is not ideal for screening.

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Heart rate variability during obstructive apneas in OSA patients

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Obstructive sleep apnea (OSA) is characterized by episodes of upper airway obstruction during sleep which produces acute and chronic autonomic changes. Heart rate variability (HRV) is an autonomic marker and spectral components of low frequency (LF)

and high frequency (HF) provide measurement of sympathetic and parasympathetic activity.

Objective: To evaluate sympathetic and parasympathetic activation in apneas associated or not associated with cortical arousals.

Methods: In this study we evaluated the HRV (by discrete wavelet transform) in OSA patients. LF, HF and LF/HF were analysed in 2NREM sleep and compared during 1 min of basal sleep, 20 sec before an obstructive apnea (OA), during and 20 sec after this. We analysed OA not followed by a cortical arousal or movement (''pure'') and followed by a cortical arousal (''not pure''). So 50 patients were studied and 10 of them had these characteristics: 8 were male, mean age of 58,50 y, mean BMI of 30,60 kg m^{-2}, mean AHI of 18,45 events/h and all of them had excessive daytime sleepiness.

Results: The difference between LF during 20 sec period before OA (pure and not pure) and that during the same OA was statistic significant. The difference between LF during pure OA and that during 20 sec period after the same OA was statistic significant, but there was no statistic difference in not pure OA for the same period. The difference between LF during basal period and that during 20 sec after pure and not pure OA was statistic significant, and also was the difference between LF and LF/HF during 20 sec period after pure and not pure OA. There was no statistic difference of HF among these different periods.

Conclusion: Sympathetic activation occurs during ''pure'' OA and persists for a little while after its cessation, and then returns to the level which is the basal of that patient. Sympathetic activation persists after the end of ''not pure'' OA, being then related with arousal. So, sympathetic activation occurs even in the absence of an arousal, but in its presence, in case it exists, is more intense. The parasympathetic activity remains almost the same in these periods. These results must be considered carefully because the small group of patients and its heterogeneity with respect of the severity.

P189

Metabolic status and nocturnal respiration is improved by weight reduction in obese obstructive sleep apnoea syndrome (OSAS) patients

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Purpose: To evaluate the effect on metabolic status and nocturnal respiration by a 6 months dietary intervention program on obese OSAS patients.

Background: Approximately 70% of OSAS patients are obese and they have an increased risk of cardiovascular diseases (CVD).

Study design: Prospective intervention study.

Material and method: Thirty-three obese OSAS patients at the Obesity unit were included for an 8 weeks long low calorie diet followed by behavioral modifying group therapy with a follow-up time of 6 months. Twenty-seven suffered from the metabolic syndrome.

Results: The dietary intervention showed a significant reduction of weight (mean 122 to 104 kg) and Apnoea-Hypopnoea-Index (46 to 26). In addition, metabolic parameters were significantly improved: systolic blood pressure (mean 144 to 134 mmHg), diastolic blood pressure (89 to 83 mmHg), fP-Glucos (7.1 to 6.3 mmol L^{-1}), fS-Insulin (133 to 76 pmol L^{-1}), LDL (3.9 to 3.0 mmol L^{-1}) and HDL (1.2 to 1.4 mmol L^{-1}). The numbers of prediabetics were reduced from 14 to 7.

Conclusion: Weight loss induced by low calorie diet and behaviour change support significantly improved metabolic status and respiratory parameters in obese OSAS patients after six months. Practical implications: We recommend treating well motivated obese OSAS patients with weight reduction to reduce risk factors for CVD.

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High flow therapy via nasal cannulae for OSA

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Introduction: OSA is becoming increasingly common. There have been no new effective treatments described for this disorder for over 20 years. Compliance with CPAP therapy is variable, problems with the interface and/or claustrophobia are commonly cited reasons for poor adherence. Recent published work on 12 patients has suggested that high flow, as opposed to high pressure (such as CPAP),therapy may also be an effective treatment1.

Method: 22 patients with OSA were recruited, anthropometric variables including FEV1 and FVC were measured. Each patient underwent full Nocturnal Polysomnography. For the first half of the night they received no intervention, thereafter they received high flow air via nasal cannulae from a Vapotherm 2000i^{TM} device. This device delivers warm (35 °C), humidified air at pre set flow rates of between 10 and 40 L min^{-1}. The initial flow was 10 L min^{-1}, this was steadily titrated throughout the night until the OSA was controlled or until the patient awoke.

Results: Of the patients studied 19 were male, the average age was 53 and the average pre treatment AHI was 33. One patient's data was excluded due to poor sleep pre intervention. Vapotherm was effective in reducing the AHI in 12 patients out of 21 (57%). There was on average a 51% reduction in AHI (29 to 13). There was no difference between the responders and non responders in terms of BMI, initial AHI, FEV1 or FVC, though there was a non significant trend for the responders to have more hypopnoeas (mean 24 h) and less obstructive apnoeas (mean 4 h) than the non responder group who experienced a mean of 13 hypopnoeas and 16 obstructive apnoeas/hour.

Conclusion: It is unknown as to why some patients responded and others did not. In the responders the mechanism may be an increase in end expiratory pharyngeal pressure or may be due to reduction in upper airway surface tension due to the heavily humidified air. In a group of patients with OSA, whose characteristics are not yet completely defined, high flow therapy, via a Vapotherm device, may prove to be a reasonable alternative to CPAP.

1. McGinley BM, Patil SP, Kirkness JP, Smith PL, Schwartz AR, Schneider H. A Nasal Cannula Can Be Used to Treat Obstructive Sleep Apnea. Am. J. Respir. Crit. Care Med. 176: 194–200.

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Interactions of ventilation and arousal oscillations in patients with Cheyne-Stokes respiration

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Objective: Cheyne-Stokes respiration (CSR) is a periodic breathing characterized by alternating central apnoea (or hypopnoea) and hyperpnoea, with a typical pattern of increasing-decreasing of respiratory range. It affect around 40% of patients with stable heart failure with an ejection fraction (EF) < 40%. The apnoic phase is often associated with a desaturation of O2, while hyperpnoeas are accompanied by arousals, which affect normal

sleep pattern. The respiratory oscillation also influences several physiological systems, so that blood pressure, heart rate, cerebral perfusion start to oscillate with the same frequency. These variations are transient (10–40 seconds) and difficut to evaluate with standard sleep scoring. Aim of this study is to evaluete the alteration of EEG power during apnoea-hyperpnoea cycle and to assess the relationship between the respiratory oscillation and cerebral activity.

Materials and methods: Twenty patients aged between 40 and 78 years (60.2 yrs ± S. D.12.6; BMI 28.9 ± S. D. 4.5) with CSR, due to stable congestive heart falilure, with EF < 45% were enrolled in the study. Each patient underwent a polysomnographic recording. Periods of 10 min of 2NREM sleep were selected and analyzed using an algorithm (Generalized Short Time Fourier Trasform-GSTFT), that represents a particular method of multiresolution analysis, in which frequency and time resolution are optimized in relation of separate EEG bands.

Results: The high resolution for low frequency of GSTFT permitted to point out an oscillation component in EEG signals superponable and with a similar frequency of oscillation of periodic breathing, particularly for delta power. Moreover, the peaks of delta power oscillations anticipate the end of the apnoeas.

Conclusions: From our data, we could suppose that in Cheyne-Stokes respiration apnoea, by means of a reduction of cerebral perfusion, can cause a slowing of EEG activity and an increase in delta power. Thus, oscillations of respiratory signals are reflected in the same oscillations of EEG segnals and power.

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A new method for measuring snoring

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Snoring is a repetitive sound caused by vibration of upper airway structures during sleep. It is a common phenomenon occurring habitually in 44% of men and 28% of women. It is the most common clinical feature of obstructive sleep apnea, but snoring definitions and measuring techniques are not standardized. The aim of this study is to describe a new method for measuring snoring, and to quantify this snoring signal in dB. The snoring signal is recorded with a pressure sensor incorporated in an oesophageal catheter commonly used to diagnose patients for sleep related breathing disorders. The catheter contains four sensors that measure flow and pressure in the upper airways and oesophagus. The sensor used for snore recordings is placed in oropharynx. This sensor is also used to measure the pressure differences in the pharynx caused by inspiration. Snoring occurs at higher frequencies than inspiration and a frequency filter is used to separate these two signals. The snoring signals obtained from the internal sensor is compared to an intensity (dB) recording made with a microphone located 0.5 m away from the patient.

Results: Shows close agreement between the two methods, with a mean difference of −3.2 (SD 3.9). The method is easy to use in clinical practice, and can be valuable to evaluate treatment and may be used as a diagnostic tool.

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Improvement in neuropsychological performance following CPAP treatment for obstructive sleep apnea syndrome

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Introduction: Obstructive sleep apnea syndrome (OSAS) is characterized by snoring and apnea during sleep leading to decreased oxygen saturation and disturbed sleep, excessive daytime sleepiness and neuropsychological disturbances. This study investigates cognitive neuropsychological abilities in a group of 31 OSAS patients before and after 6 months treatment with CPAP.

Methods: Our sample consisted of and 31 serious OSAS patients (29 males and 2 females; mean age 51,7 SD 10.0 years). In patient AHI was 47.7 ± 20.6 h, min SaO2: 67 ± 18%, after treatment 5.4 ± 1.9 h, min SaO2: 91.3 ± 3.2%. We compared patients performance on neuropsychological tasks with a load on executive-Wisconsin Card Sorting Test (WCST). The number of perseverative errors (WCST-P), non-perseverative errors (WCST-NP), completed corrected categories (WCST-CC), conceptual level responses (WCST-%CONC) and set to the first category (WCST-1st CAT) were measured.

Results: Serious OSAS patients before CPAP treatment achieved significantly fewer categories (3,06 SD 2,5 versus 5,29 SD 1,5 $P = 0.001$), made a greater number of perseverative errors (25,22 SD 19,41 versus 13,38 SD 15,57 $P = 0.001$), and had a greater number of perseverative responses (29,83 SD 25,11 versus 15,16 SD 20,57 $P = 0.001$). They required more trials to complete the first category (57,84 SD 52,2 versus 22,64 SD 22,00 $P = 0.001$) and gave fewer conceptual responses (46,06 SD 27,15 versus 64,22 SD 12,37 $P = 0.01$) than after treatment.

Conclusions: CPAP treatment seems to improve executive functions in serious OSAS patients.

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Effect of oral appliance on sleep bruxism in obstructive sleep apnea hypopnea syndrome patients

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Objectives: Sleep bruxism (SB) may cause a variety of problems, though its pathophysiology has not been completely elucidated. Inoko et al. have indicated that SB can be linked to apnea and hypopnea episodes. The aim of this study was to test the hypothesis of a direct association between sleep-disordered breathing and SB.

Methods: Seven patients who snored (one woman and six men; mean age, 51.7 ± 15.3 years, mean BMI, 24.6 ± 1.6 $kg\,m^{-2}$) participated in this study. Two night polysomnographic recordings, including masseter electromyography (EMG), were performed; the first night was before treatment and the second was wearing an oral appliance (OA). Several studies have conducted that SB can be analyzed by masseter muscular activity. Therefore, we measured the frequency of masseter muscular contraction (MC) episodes. MC episodes were classified under the phasic and tonic forms. We defined that a phasic MC showed three or more EMG bursts lasting from 0.25 to 2.0s and tonic MC showed an EMG burst of longer than 3.0s. Wilcoxon signed rank test was used to compare the differences between the patients before treatment and wearing OA, on the values of apnea hypopnea index (AHI), arousal index (ArI), a cumulative percentage of time spent at saturations below 90% (CT_{90}), the frequency of MC episode (MCI), the frequency Phasic MC episode (phasic MCI) and the frequency of tonic MC episode (tonic MCI).

Results: Values of AHI, ArI, CT_{90}, MCI and tonic MCI with OA were significantly lower than before treatment ($P < 0.05$). In contrast, a significant difference was not found on phashic MCI.

Conclusions: These results suggest that OA could reduce the value of AHI, ArI, CT_{90}, MCI and tonic MCI on patients with OSAHS. This finding has supported that tonic masseter muscular contraction is significantly associated with apnea hypopnea events.

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Polysomnographic auto-titration using a bi-level PAP device versus manual CPAP/BIPAP titration in sleep-related respiratory disorders

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Introduction: According to results from a number of studies, automated CPAP titration polysomnography is equivalent to manual CPAP titration; however, only meager experience is available with automated BIPAP titration. Our study compared polysomnographic titration with auto-BIPAP to titration using manual CPAP/BIPAP.

Method: Therapeutic RDI, mean O2-saturation and SWS ratio, as well as the arousal index were compared between two groups of patients with severe OSAHS ($n = 60$ each), during one-night titration with an automated BIPAP device or manual CPAP/BIPAP. All measurements were made using ALICE 3/5 polysomnographs along with a Respironics BIPAP Auto M Series Bi-Flex device (as an automated BIPAP). Manual titration was done by starting at low pressure, which was increased gradually in CPAP or BIPAP mode. Automated BIPAP was set to low pressure until the onset of sleep and switched to automatic mode IPAP (4–20 cm H_2O) and maximum EPAP (4–20 cm H_2O) thereafter. One-night manual BIPAP adjustment was performed after manual CPAP or autotitration had failed.

Results: During manual CPAP titration, 8 patients did not tolerate high pressure and central apnea ensued in 6 cases. Automated titration failed on 6 occasions, owing to an insufficient therapeutic effect (RDI >10). Repeated manual BIPAP titration was unsuccessful in 4 cases: therapeutic effect was unsatisfactory owing to central apnea (occurring in 2 cases) or hypoventilation resulting from severe obesity (in 2 cases). Comparison of successful manual CPAP, manual BIPAP, and automated BIPAP titrations revealed a significantly higher amount of SWS (12,9 ± 6,7%, versus 19,1 ± 5,4%, $P<0{,}01$) and significantly lower arousal index (18.5 ± 7.5 h, versus 11.9 ± 6.5 h, $P<0{,}01$). No significant differences were ascertained between RDI (6,1 ± 4,6/hour, versus 5,4 ± 2,4/hour, $P = 0{,}24$) and mean O2-saturation (92 ± 2,4%, versus 92.2 ± 2.5%, $P = 0{,}76$).

Conclusion: Titration with the automated BIPAP device is superior to manual CPAP titration and equivalent to manual BIPAP titration as regards efficacy. Overall, it is surely a more cost-effective alternative.

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OSAS with intermittent hypoxia and reoxygenation is a potent risk factor for silent brain infarction

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Objectives: The aim of this study was to evaluate whether silent brain infarction (SBI) is increased in different subgroups of patients with sleep-disordered breathing.

Methods: The study population comprised four subgroup of patients. Group 1. Severe OSAS N: 250 (AHI more than 30 h^{-1}) and intermittent hypoxia and reoxigenation oxigen level lower than 90% during apnea but higher than 90% during interpnea. Group 2. Severe OSAS N:200 (AHI more than 30 h^{-1}) without hypoxia-oxigen level higher than 90% during apnea and interpnea. Group 3. Sever sleep fragmentation N:80 (arousal index more than 30 h^{-1} due to respiratory effort related arousals) without severe OSAS (AHI: 5–10 h^{-1}) and with normoxemia. Group 4. control patients N: 80 without OSAS, hypoxia or sleep fragmentation (AHI and arousal index less than 5 h^{-1}). Men/age 30–50 years; BMI 26–32 kg m^{-2}/with positive history of treated hypertension were recruited following diagnostic polysomnography. Patients with therapy resistent hypertension, or with other vascular comorbidities were excluded. After the polysomnography testing presence of SBI was assessed by head MRI.

Results: 78 OSAS patients (31.2%) with intermittent hypoxia/reoxigenation, 16 OSAS patients (8%) with normoxemia and 4 patients (5%) with sleep fragmentation without severe OSAS had positive MRI (appearance of one or more lacunar or terriotorial lesions). In he control age,gender, and confounders matched group 7 patients (8.75%) had positive MRI findings.

Conclusion: Sleep-disoredered breathing cases characterised by intermittent hypoxia/reoxigenation were potent risk factor for SBI while cases with normoxemia or cases with sleep fragmentation alone did not represent elevated risk for SBI.This finding should be considered when recruiting OSAS patients for future studies investigating the relation between OSAS and cerebrovascular diseases.

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Two-piece palato-pharyngo-plasty (Two-P4), as a new strategy for OSAS

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Introduction: Two-piece palato-pharyngo-plasty (Two-P4) for OSAS makes two separated scars on both sides of soft palate and reserving middle soft tissue intact. These scars pull the reserved middle soft palate to each side and pharyngeal space becomes wide and deep after several weeks. Two-P4 established high success rate (88% in 25 patients) by 50% decrement of AHI and AHI less than 20.

Materials and Methods: Twenty-five cases of OSAS received Two-P4 during 2002 and 2007. They underwent Polysomnographic evaluation before and 3 month after the surgery. Their age ranged from 17 to 74, average 41.4 ± 13.6 years old, including 24 men and 1 woman. Their average BMI is 27.2 ± 4.0 kg m^{-2}.

Results: The average AHI reduced from 51.1 ± 21.8 to 11.3 ± 10.9 after surgery. The objective success evaluated by 50% reduction of AHI and by AHI less than 20 is obtained in 22of 25 patients (88.0%). The improvement rate of AHI in all 25 patients is 75.9 ± 22.2%. The reduction of AHI is 86.2 ± 12.0% in patients with Friedman's anatomical stage1,78.9 ± 17.9% in patients with stage2, 54.3 ± 28.5% in patients with stage3. Body mass index (BMI) did not change after the surgery.

Discussion: Two-P4 design is effective to make wide and deep nasopharynx, which could establish high success rate. It is impossible to avoid scar formation after soft palate surgery. Reserving middle soft palate is supposed to be effective to prevent nasopharyngeal stenosis or soft palate insufficiency after surgery. None of 25 cases complaint soft palate insufficiency, or stenosis of the nasopharynx. Two-P4 could be a successful surgical procedure for OSAS. According to the Friedman's anatomical classification, we think that stage1 and 2 are preferable for Two-P4.

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The Informational Needs to CPAP Treatment Inventory (INCI): a new tool for assessing subjective informational needs among CPAP-treated patients with OSAS

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Background: Patient education in OSAS is crucial in order to improve adherence. There is little known about patients informa-

tional needs in relation to OSAS and CPAP. A few studies have used interventions based on patient education with various impact on adherence. However, these studies have not used a validated scale to measure informational needs related to CPAP treatment.

Aim: To describe the Informational Needs to CPAP treatment Inventory (INCI) and its use among patients with OSAS.

Design and sample: A cross-sectional descriptive design was used. A postal questionnaire was sent to 453 patients with OSAS from 3 Swedish CPAP clinics (1 metropolitan and 2 provincial cities). Data collection was achieved with INCI, as well as from medical records (clinical variables and data related to CPAP-treatment). Measurements: INC-I was used to measure perceptions about informational needs. INC-I includes 6 different themes; how sleep apnoea arises, how sleep apnoea affects sleep, how sleep apnoea affects health, how own activities and actions can affect sleep apnoea, how the CPAP works and should be used, and how problems related to the CPAP therapy can be fixed. Each of the 6 themes includes 3 dimensions (i.e., items) answered on a five-point Likert type scale, in total 18 items. The dimensions are; importance, possibility to understand and learn, as well as how knowledge improves CPAP use and should be treated as separate scales. Findings: 350 patients with OSAS (77%) with a mean use of CPAP treatment for 55.9 months (2 weeks-182 months) returned the INCI. 5 out of 6 themes in the INC-I were perceived as very important. The patients scored information about how sleep apnoea affects sleep and how sleep apnoea arises to be the themes of least importance. Patients scored the possibilities to learn, as well as the positive effect of information regarding all 6 themes in the INC-I to be high. Face validity for INCI seems to be good. Few missing values were found among the returned questionnaires.

Conclusion: This is the first study to describe a self-rating scale measuring informational needs to CPAP treatment. INCI can be used in a large variety of clinical and research settings. However, this newly developed instrument needs further testing.

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Examination of inter-night variability of apnoea-hypopnoea index estimation from a combined Holter-oximeter

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Significant night-to-night variability in Apnoea-Hypopnoea Index (AHI) has been reported in Obstructive Sleep Apnoea Syndrome (OSAS). Resource limitations have raised interest in portable monitoring systems that can be used by sleep physicians to improve access to the diagnosis of OSAS. However, inter-night variability in AHI may compromise the ability of these systems to exclude a diagnosis of OSAS on a single assessment and this is an important consideration in the prospective validation of novel diagnostic devices. Thus, the aim of this study was to quantify the repeatability of AHI estimation from a combined electrocardiogram and oximetry recorder (Holter-Oximeter) and assess the adequacy of a single-night study with the device in the screening of OSAS. 18 subjects (16 male: 2 female) with suspected OSAS underwent attended PSG in hospital with concomitant evaluation using a Holter-oximeter (Nemon DR180+), and subsequent unattended Holter-Oximeter evaluation at home. An algorithm for estimation of the AHI using only a single leaf of electrocardiograph (ECG) and the oximetry trace had previously been developed using a database of PSG recordings. This algorithm provides minute by minute apnea annotation and per-subject AHI estimation. Paired *t*-tests and intra-class correlation coefficients (ICCs) were calculated for the estimations of AHI from the hospital and home studies. Estimated AHI correlated well with the AHI obtained on concomitant PSG ($r = 0.82$; $P < 0.001$). Estimated AHI on the home evaluation agreed closely with the estimated AHI obtained from the initial in-hospital study, with no significant difference in the values obtained ($P = 0.276$). The ICC gives a measure of how much reliance can be placed on a single measurement and was high indicating good repeatability (ICC = 0.882; P,0.001). The combined Holter-oximeter monitor is potentially a suitable device for home screening of sleep-disordered breathing in a population suspected of having OSAS. The data suggest that a single-night screening with the device is adequate for this role.

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Prospective study assessing the validity of the Kushida Index for screening for sleep apnoea in a west of Scotland population

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Aim: To assess the validity of the Kushida Index as a screening tool for sleep apnoea.

Setting: Sleep Clinic, Gartnavel General Hospital, Glasgow, Scotland.

Method: Ethics Committee approval for the study was obtained. Patients were examined by a sleep specialist (E.L. & S.W.B) and 85 patients were recruited for the study. These patients were then independently assessed by a dentist (S.J.) (who was blinded to their provisional diagnosis and history). The intra-oral measurements required for the Kushida Index calculation were taken. All patients then had limited sleep studies to identify apnoeic episodes.

Results: At present we have data from 39 sleep studies (33 males and 6 females). The mean age = 48 (range 21–75). Oxygen desaturation was classified as follows: 0–10 normal, 11–15 inconclusive, 16–20 mild, 21–30 moderate, 31-severe. Using these criteria, 24 patients had a diagnosis of sleep apnoea. Kushida's study found that a Kushida score of 70 or more correlated with a diagnosis of sleep apnoea. From these data, we found that the Kushida Index has a sensitivity of 71% and a specificity of 67% for the diagnosis of sleep apnoea.

Conclusion: Preliminary results indicate that the Kushida index has potential usefulness as a screening tool for sleep apnoea.

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Personalized telephone coaching program for patients with OSAS treated with CPAP

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Introduction: Treatment efficacy with continuous positive airway pressure (CPAP) is related to its usage duration. But there are compliance issues, especially during the first month.

Objectives: To assess the effect of a telephone coaching program on adherence and compliance at 5 months of CPAP treatment i.e., (1) maintenance of CPAP at 5 months; and (2) the average device usage time by patients still using the device. To assess patients' progressive knowledge and perceived benefits during first treatment month.

Methodology: The patients are randomized into a "with telephone coaching" group (TC) and a "control" group (C). Three telephone contacts took place on D2, D15 and D30 after installation of the CPAP equipment for TC group.

Acknowledgment: Support covers: (1) knowledge of OSAS; (2) knowledge of the principles of CPAP; (3) knowledge about the equipment used by the patient; (4) the perceived benefits of treatment; and (5) daytime alertness.

Results: One hundred and ninety-four physicians included 674 patients. Three hundred and ten patients in TC group, among whom 291 continued the program to term (D30). In the TC group, 86.2% of patients were still using the device at 5 months versus 78.4% in the C group ($P = 0.009$). In patients still under treatment at 5 months, an average use of 5.76 h/24 h was recorded for the TC group versus 5.18 h/24 h in the C group ($P = 0.008$). In addition, a greater number of patients in the TC group used their device more than 4 h per 24 h (79.7% versus 67.4%; $P = 0.002$). All of the parameters of knowledge, perceived benefits and alertness improved up to D30, with a quasi-maximum gain in alertness at D15.

Conclusion: This randomized study demonstrates the efficacy on adherence and compliance of this patient personalized telephone coaching program implemented at CPAP treatment initiation. It would be interesting to verify the lasting nature of this benefits through long-term follow-up of these patients.

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Mandibular advancement appliance for obstructive sleep apnoea: results of a randomised placebo controlled trial using parallel group design

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The aim of this trial was to evaluate the efficacy of a mandibular advancement appliance (MAA) for obstructive sleep apnoea (OSA). Ninety-three patients with OSA and a mean apnoea-hypopnoea index (AHI) of 34.7 were centrally randomised into three, parallel groups: (a) MAA; (b) mandibular non-advancement appliance (MNA); and (c) no intervention. The appliances were custom made, in one piece. The MAAs had a mean protrusion of the mandible of 74% (range 64–85%). Outcome measures, assessed after continuous use for 4 weeks, were AHI (polysomnography), daytime sleepiness (Epworth) and quality of life (SF-36). Eighty-one patients (87%) completed the trial. The MAA group achieved mean AHI and Epworth scores significantly lower ($P < 0.001$ and $P < 0.05$) than the MNA group and the no-intervention group. No significant differences were found between the MNA group and the no-intervention group. Sensitivity analyses, testing the effect of missing outcome values at the patients not completing the trial, confirmed these results. The MAA group had a mean AHI reduction of 14.1 (95% CI 7.4–20.8), and a mean Epworth score reduction of 3.3 (95% CI 1.8–4.8). Eight MAA patients (30%) achieved a reduction in AHI $\geq 75\%$ ending with an AHI < 5, half of them having baseline AHI > 30. MAA had a significant beneficial effect on the vitality domain of SF-36. Four MAA patients (14.8%) and two MNA patients (8%) discontinued interventions because of adverse effects. Our conclusion is that MAA has significant beneficial effects on OSA, including cure in some cases of severe OSA. Protrusion of the mandible is essential for the effect. MNA has no placebo effect. MAA may be a good alternative to CPAP in subsets of OSA patients.

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Epworth score 'adjusted' for collar size in assessing likelihood of obstructive sleep apnoea/hypopnoea syndrome [OSAHS] in chronic snorers

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We reviewed the case notes of 110 patients referred for suspected OSAHS between May and August 2006. One hundred and eight described socially disruptive snoring and 88 mentioned daytime sleepiness [clinic Epworth > 11 in 64 cases]. Sleep clinic referrals continue to increase, in part due to wider appreciation of OSAHS. Both chronic snoring and excess daytime sleepiness [EDS] are common. We speculated that Epworth score modified up or down according to deviation from 'average' collar size might provide guidance as to the likelihood of EDS relating to OSAHS. No statistical difference was evident between mean ESS 13 [9–17] in those with apnoea/hyponoea index [AHI] 0–15, compared to mean ESS 15 [10–17] for patients with AHI > 25 [$P = 0.48$]. By comparison mean adjusted ESS was 9.2 [5.2–16] and 20.4 [11–32], $P < 0.005$.There were 24 instances where adjusted ESS altered designation from negative [ESS < 11] to positive [ESS > 11]. In 15 instances where redesignated as negative there was correct matching with an AHI 0–15 in 12 and incorrect in 3.In 9 instances where redesignated from negative to positive, 4 correct match to AHI > 15 and 5 incorrect [Fishers test 0.078] We feel our data suggests that where OSAHS is considered in chronic snorers with elevated Epworth but below average collar size, a detailed consideration of non OSAHS cause for EDS is merited ahead of sleep study.

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Reliability and validity of the Greek version of the Sleep Apnea Quality of Life Index (SAQLI)

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Aim: The SAQLI is an instrument for measuring the quality of life of obstructive sleep apnea patients. This study aims to validate the Greek version of SAQLI as a tool for measuring the quality of life among OSAS patients.

Methods: The questionnaire was administered to 50 OSAS patients, 41 male and 9 female (mean age 43 $\pm$ 12 years) before and after 6 months of treatment with CPAP. Construct validity was provided through principle component analysis (PCA) with subsequent rotation of the latent factors. Discriminant validity was assessed with the independent *t*-test method of all the SAQLI indexes between the two groups of patients, whose score on the Epworth Sleepiness Scale (ESS) was $< = 12$ or > 12. Response to treatment validity was ascertained through paired *t*-test method of the SAQLI indexes before and after treatment. Reliability was done through computation of Cronbach's alpha coefficient at the pre- and post- measurements and of their differences.

Results: The Greek version of the SAQLI has good construct validity, as PCA reproduced the domains (A, B, C). Significant correlations ($P < 0.01$) in the pre measurement treatment between the SAQLI scores and the ESS scores prove the discriminant

validity of the SAQLI. The questionnaire's ability to detect a clinically important improvement (paired *t*-test of the SAQLI before and after treatment $P<0.01$) ascertains its response to treatment validity. The Cronbach's alpha reliability coefficients at the pre and post measurements and of their differences were for the domain A: 0.804–0.801–0.802, for the domain B: 0.795–0.797–0.809, for the domain C: 0.820–0.819–0.716 (Cronbach's alpha >0.7).

Conclusion: In conclusion SAQLI is a valid and reliable tool not only in estimating the quality of life of OSA patients but also in depicting its improvement as a result of the CPAP treatment.

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Comparison of obstruction site in obstructive sleep apnea with airway pressure monitoring

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Introduction: To investigate the site of obstruction in the patients with obstructive sleep apnea syndrome (OSAS), and the correlation between obstruction site and apnea severity, we performed night polysomnography (PSG) with apnea level test in OSA patients.

Methods: Sixty-five male OSAS patients underwent night polysomnography with upper airway pressure monitoring. The catheter with four sensors was inserted through the patients' upper airway to esophagus. The locations of sensors were nasopharynx, above the uvula, below the uvula, and esophagus. The sites of obstruction were determined by observed pressure pattern, and divided into 4 categories; 1) above the uvula or whole upper airway, 2) below the uvula 3) esophagus, and 4) mixed level. During screenings, we measured body mass index (BMI), head circumference, and abdominal circumference. OSAS patients were divided into three groups according to their apnea hypopnea index (AHI); Mild (AHI 5–15 hr^{-1}), moderate (AHI 15–30), and severe (AHI >30) OSAS groups. The ANOVA test was used to compare the obstruction site of mild, moderate, and severe OSAS groups. We also evaluated the correlation between age, BMI, head & abdomen circumference, and obstruction site.

Results: Mean age of patients was 46.9 ± 12.2 years old, and the mean BMI was 26.2 ± 2.7 (ranged 21.5–33.6). Among the 65 patients, 17 patients were mild, 13 patients were moderate, and 35 patients were severe OSAS. Anova test showed that mild OSAS group had more obstruction above the uvula or whole upper airway level ($P<0.004$), and moderate OSAS group had more obstruction at the mixed level ($P<0.006$). There was no significant correlation between obstruction site level and age, BMI, head & neck circumference.

Conclusion: Our study demonstrates different obstruction site between different apnea severity groups.

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Results of tailor-made multi-level surgery in patients with obstructive sleep apnea

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In increasing severity of OSAS, the likelihood that obstruction is present on both palatinal as well as retrolingual level. This is confirmed by various methods of evaluation techniques. Therefore, the results of unilevel surgery in these patients is usually disappointing and multilevel surgery should be mandatory. In this study, we present our results of multilevel surgery in OSA with subjective and objective aspects. Eighty-six patients who were diagnosed by polysomnography (PSG) and received multilevel surgery for treatment of OSA with more than 6 months follow-up. Multilevel surgery was performed as a tailor-made manner according to obstruction level: septoplasty and/or turbinoplasty for nasal level; modified uvulopalatal flap or lateral pharyngoplasty, and/or tonsillectomy for retropalatal level; tongue base reduction by radiofrequency or genioglossus advancement for retrolingual level. We checked daytime and night-time symptoms with 10 cm visual analogue scale (VAS) on pre- an postoperative 1 and 6 month. Daytime sleepiness was evaluated by Epworth sleepiness scale (ESS). On postoperative 6 months, PSG were checked for objective evaluation. All daytime and night-time symptoms were much improved on 1 month after surgery and continued until 6 months. But daytime sleepiness was still problem even though their sleep apnea were subsided. Objective success rate was 43.3% when success criteria is AHI <5. Multilevel surgery as a talor-made manner shows relatively good results. This manner may be solution for the OSA patients when medical therapy including CPAP is not tolerable. Precise and tenacious evaluation of obstuction site is the key for increasing surgical success because there is no representative evaluation methods for obstruction site.

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Effects of CPAP on cardiovascular risk profile in patients with severe obstructive sleep apnea and metabolic syndrome

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Background: The increased risk of atherosclerotic morbidity and mortality in patients with obstructive sleep apnea (OSA) has been linked to arterial hypertension, insulin resistance, systemic inflammation, and oxidative stress in previous studies. We aimed to determine the effects of 8-weeks therapy with continuous positive airway pressure (CPAP) on glucose and lipid profile, systemic inflammation, oxidative stress, and the global cardiovascular disease (CVD) risk in patients with severe OSA and metabolic syndrome.

Methods: In 32 patients, serum cholesterol, triglycerides, high density lipoprotein (HDL) cholesterol, fibrinogen, apolipoprotein A-I (ApoA-I), apolipoprotein B (ApoB), high sensitivity C-reactive protein (hsCRP), interleukin 6 (IL-6), tumor necrosis factor-α (TNF-α), leptin, malondialdehyde (MDA) and erythrocytic glutathione peroxidase (GPx) activity were measured at baseline and after 8 weeks of CPAP. Insulin resistance index (HOMA-IR) was based on the homeostasis model assessment method, the CVD risk was calculated using the multivariable risk factor algorithm.

Results: In patients who used CPAP for ≥ 4 h $night^{-1}$ ($n=16$), CPAP therapy reduced systolic (from 148.6 ± 19.6 to 129.4 ± 15.6 mmHg; $P=0.001$) and diastolic blood pressure (from 91.7 ± 13.5 to 79.5 ± 8.2 mmHg; $P=0.006$), total cholesterol (from 5.86 ± 1.02 to 5.17 ± 1.09 mmol L^{-1}; $P=0.002$), ApoB (from 1.15 ± 0.29 to 0.99 ± 0.20 g L^{-1}; $P=0.009$), HOMA-IR (from 4.73 ± 3.18 to 2.93 ± 1.77; $P=0.031$), MDA (from 1.73 ± 0.26 to 1.49 ± 0.22 μmol L^{-1}; $P=0.004$), and TNF-α (from 2.13 ± 0.98 to 1.79 ± 0.69 ng mL^{-1}; $P=0.037$), and increased erythrocytic GPx activity (from 29.2 ± 8.1 to 36.3 ± 12.5 U gHb^{-1}; $P=0.015$), in association with reductions

in the global CVD risk (from 18.8 ± 9.8 to $13.9 \pm 9.7\%$, $P = 0.001$). No significant changes were seen in patients who used CPAP for <4 h night^{-1}. Mask leak was the strongest predictor of compliance with CPAP therapy.

Conclusions: In patients with severe OSA and metabolic syndrome, good compliance to CPAP may improve insulin sensitivity, reduce systemic inflammation and oxidative stress, and reduce the CVD risk.

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Snoring during pregnancy and its relation to pre-eclampsia

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Objective: Does snoring during pregnancy influence development of pre-eclampsia?

Method: Five hundred and three pregnant women were presented a questionnaire concerning snoring, daytime sleepiness and edema. Epworth Sleepiness score (ESS) and symptoms of restless legs syndrome were also included. The questionnaire was presented in the 1st, 2nd and 3rd trimester and blood pressure was recorded. Women snoring often-always at visit 2 and/or 3 were denoted habitual snorers, those snoring never-seldom non-snorers and there was also a category occasional snorers. Habitual snorers were offered a sleep respiratory recording (Embletta); 34 volunteered.

Results: 36/503 women (7,2%) snored habitually already at the first visit. At the end of pregnancy the fraction had increased to 19,5%. At the first visit BMI of habitual snorers was 25,3 compared to 22,9 for non-snorers (s.), but there was no difference concerning increase during pregnancy. Habitual snorers reported more edema at visit 2 and 3, higher scores in morning and daytime tiredness and ESS score compared to non-snorers at all visits (s.). Their systolic blood pressure increased more (s.) already between 1st and 2nd visit. Weight and Apgar scores of the newborns showed no difference. Pre-eclampsia developed in 18 women, twice as common among habitual snorers than in those snoring never-occasionally (n.s.). Their snoring scores were higher at all visits; the greatest difference at visit 3 ($P = 0{,}058$). Their diastolic pressure increased more already at the 2nd visit (s.), they had more edema and higher increase in BMI (s.). ESS and tiredness scores did not differ. 9/34 sleep recordings showed supine AHI >5. Two women who later developed pre-eclampsia were recorded; both had supine AHI >5.

Conclusions: Habitual snorers had higher BMI from start, more daytime tiredness, higher ESS scores and their diastolic blood pressure increased more already during early pregnancy. Pre-eclampsia was twice as common among snorers as non-snorers; not significant due to the low number of cases. The relation between pre-eclampsia and snoring therefore remains elusive.

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Comparison of sexual satisfaction between normal and patients with untreated obstructive sleep apnea and after 2 months of treatment with CPAP

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Introduction: The present investigation compares sexual satisfaction in normals to patients with OSA before treatment and after 2 months of CPAP-treatment.

Material and Methods: Study design: Consecutive inclusion of patients with OSA scheduled for treatment with CPAP. After informed consent the patients were asked to fill out a questionnaire before start of CPAP-treatment and after two months of CPAP-treatment. The questionnaires are designed from pilot-interviews and validated questionnaires on sexuality and quality of life: BSFI, FSFI, Fugl-Meyer, SF-36 (visual analogue scales). Results on sexual satisfaction in general from 377 patients, male/female gender, no.311/66, Age 50,9 (SD = 10,4), with untreated OSA and two months into treatment with CPAP are compared to a reference material of 17000 normals (Danish Health and Morbidity Survey. 2000).

Results: Before treatment with CPAP both male and female OSA patients had significantly lower sexual satisfaction than normals. Two months into treatment with CPAP this difference was almost eliminated in male patients. In female patients the highest negative score was almost dobbelt in percentages after two months.

Conclusion: Sexual satisfaction is almost normalized in male patients with OSA, already two months into treatment with CPAP. In female patients there are still after two months of CPAP treatment a large negative score.

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Sleep pressure and subjective fatigue in healthy snorers and non snorers after acute and chronic partial sleep deprivation

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The aim of the present study was to investigate the effects of acute and chronic partial sleep deprivation (SD) on daytime sleep pressure and subjective fatigue in healthy snorers (S) and non snorers (NS). It has been reported that nasal wall closing up disrupts sleep by inducing micro awakenings in S. We hypothesized that sleep fragmentation would enhance sleep pressure and subjective daytime fatigue with lower recovery capacity in S as compared to NS, particularly in the chronic SD paradigm. 18 male subjects (mean age: 22.39 ± 1.65 years) volunteered in this experiment. They underwent two SD paradigms: acute (40 h of sustained wakefulness) and chronic partial SD (5 consecutive 4-hour sleep nights). The consecutive days, 4 multiple sleep latency test (MSLT) sessions were administered. Before each session, fatigue was assessed using a visual analogue scale. The results indicate that, at baseline (i.e. without prior SD), S showed a shorter sleep latency (SL) as compared to NS ($F(1,13) = 12.92$; $P = 0.003$). The same was observed after acute SD ($F(1,15) = 13.67$; $P < 0.002$). However, in the chronic SD paradigm, SL no more differed between the S and the NS. During the recovery nights, S had a shorter SL after acute SD compared to NS ($F(1,15) = 8.33$; $P < 0.01$), but there was no more difference between groups after chronic SD. The subjective assessments showed that S felt more sleepy after chronic than after acute SD, while no significant difference was observed in NS ($F(1,15) = 3.63$; $P < 0.08$). All together, our study suggests that healthy S may suffer permanent sleep debt since sleep pressure was higher in this group even at baseline. However, SD had differential effects on sleep pressure in both groups. NS showed similar decrease of SL after acute and chronic SD, while S showed a drastic decrease in SL after acute SD, but remained almost at their baseline level after chronic SD. The recovery process was similar in both groups, with a return to the baseline level whatever the SD paradigm. However, the subjective assessments of fatigue did not follow the objective measures of sleepiness, since the major decrement was observed in S after chronic SD. This discrepancy suggests that different underlying mechanisms could occur after acute and chronic SD.

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First results of an automatic pilot for NCPAP, using mandible behaviour as driving parameter in OSA syndrome

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Assuming that mouth opening during sleep is part of an impaired CNS control of the upper airway in OSA, a servo-controller was connected to an APAP in order to increase pressure until some correction in mandible position and behaviour were reached.

Method: The movements of the mandible were measured during sleep by a distance-meter (Jawsens®, NOMICS, Belgium). Two magnetometers placed on the midline of the face, one on the forehead and one above the chin fed a servo-controller driving an APAP device (BREAS iSleep 20i). The algorithm included two key features: presence of mandible oscillations in the breathing frequency band (0.16–0.26 Hz) and movements related to respiratory arousals.To evaluate the results, previously diagnosed OSA patients underwent 2 successive randomised polysomnographies with the same APAP, one night with the originally designed system (Flow-Auto), and the other with the new one (Jaw-Auto). Lower and higher levels were set at $\pm$ 5 hPA around a level defined by Stradling's Formula. Statistics: means $\pm$ SD and comparisons between treatments by Student t test ($P<0.05$).

Results: From 32 studied patients, 20 had to be discarded from final analysis because either the Flow-Auto (8 cases), the Jaw-Auto (4 cases), or both (8 cases) reached the upper or lower security limits during more than 20% of the night. For the remaining 12 patients, no difference in 95% Percentile-pressure (in hPa or cm H_2O) could be achieved. The Flow-auto gave 10.8 ± 2.07 and the Jaw-Auto, 10.9 ± 2.86 (P: 0.908). The performances in residual breathing disturbances were not different. AHI (n/1 h) with the Flow-Auto was 8.9 ± 6.9, and with the Jaw-Auto 7.3 ± 4 (P: 0.309). As for ODI, Flow-Auto gave 1.6 ± 2.64 and Jaw-Auto: 1.8 ± 2.76 (P: 0.674). For the Flow Auto, snoring (in minutes), was 29.4 ± 39 and for the Jaw-Auto 50 ± 81 (P: 0.376). The same non significant differences were obtained for total sleep time, sleep efficiency and sleep quality indices.

Conclusions: No difference in 95% Percentile-pressure, in residual breathing neither in sleep qualities could be observed between two different APAP concepts used in a same device: a fluid mechanistic and a CNS behavioural model approaches.

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Comorbities affect CPAP compliance and resolution of sleepiness

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Continuous positive airway pressure (CPAP) is accepted as standard therapy for obstructive sleep apnea-hypopnea syndrome (OSAHS). CPAP therapy requires patient are ''compliant.'' Measures of compliance remain obscure. Comorbities, such as transmandibular joint disease (TMD), Restless Leg Symdome (RLS), and leg movements during sleep (LMDs) may effect both CPAP compliance and resolution of sleepiness. One hundred and seventy-two patients using conventional CPAP therapy after completing Level 1 Polysomnography were surveyed. A standardize questionnaire was provided to patients to codify symptoms of snoring (SnSI), sleep apnea (SASI), myofacial pain (TMJ), RLS, and LMDs. Epworth Sleepiness Scales and Fatigue Severity Scales were also provided. LMD rates were obtained from polysommnograpy evaluation. Change in sleep-wake cycles were derived from CPAP compliance downloads. Questionnaires were given both at CPAP setup and after a 30-day follow-up. One hundred and seventy-two CPAP users were surveyed: 81 patients responders (RESP) which demonstrated reductions in EpwS of 50% or <10, and 39 non-responders nRESP which had $<50\%$ drop in EpwS. Patients with excessive mask leak were excluded. Statistically RESP did not differ from nRESP with respect to age (43.6 versus 46.4), body mass index (37.9 versus 36.0), diagnostic AHI (30.6 versus 31.5), therapuetic pressures (9.7 versus 9.4). RESP had less days sleeping with CPAP<4 h (4.6 versus 7.5; $P=0.003$)and less mask leak (20.3 versus 28.3; P, 0.001). Baseline SASI's were less among RESP (22.3 versus 25.1; $P=0.037$). SnSI's were greater for RESP (21.3 versus 17.4; $P<0.001$). Symptoms associated with TMJ (5.1 versus 7.2; $P<0.001$), RLS (5.6 versus 7.7; $P<0.001$), and LMDs (19.7 versus 27.3; P, 0.001) were less among RESP than nRESP. LMD rates did not significantly alter compliance between RESP and nRESP. TMJ (5.9 nights with <4 h use versus 9.5 nights; $P=0.0002$) and RLS (6.4 nights with, 4 h use versus 12.1 nights; $P<0.001$) adversely effected compliance. In conclusion, sleep-related comorbities adversely effect CPAP compliance the resolution of sleepiness during 30 days of CPAP use. TMJ and RLS also adversely effected compliance with more TMJ users not using CPAP entirely. LMDs did not adversely effect compliance but did worsen sleepiness outcomes among CPAP users.

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Effects of a total and a partial sleep deprivation on performance in healthy snorers and non snorers

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The objective of the present study was to compare performance in healthy snorers and non snorers subjects after one day of total sleep deprivation (TSD) and five consecutive days of chronic partial sleep deprivation (CSD). A second aim was to examine the recovery process of each group after these two paradigms of sleep deprivation.

Methods: A total of 18 young male subjects (range 20–26 years), healthy snorers and non snorers, underwent two sleep deprivation paradigms: an acute (40 h) and a chronic partial (5 consecutive 4-h nights) sleep deprivation. Performance were assessed with 2 PVT (Psychomotor Vigilance Task) sessions (10 min) at 9:30 and 17:30. We compared performance during the day following TSD and baseline in the acute phase, during the 5 days following chronic partial sleep deprivation, as well as performance during the day following recovery night (8-h night) after TSD and PSD.

Results: TSD increased mean Reaction Time (RT) and percent of lapses (RT >500 ms) ($P=0.00001$). As revealed by a Group Í Night interaction, this increase was more pronounced in the snoring group ($P=0.01$). Across the CSD, RT deteriorated and percent of lapses increased, the highest values were found the 5th PSD day ($P<0.005$). A Group I Hours interaction revealed that performance deterioration was the strongest for the snoring group the morning at 9:30 ($P=0.01$). Concerning the recovery process, on the recovery day following the TSD, PVT scores returned to their baseline level, but on the recovery day following the CSD, performance was still over the level observed during the baseline day ($P=0.05$).

Discussion: The present results suggest that the negative effects on performance induced by total and chronic partial sleep deprivation

are enhanced in snoring subjects. However the recovery process is the same in both groups : an 8 h night of sleep is likely to counteract the cognitive decrement induced by TSD but not the decrement caused by an accumulation of sleep debt over 5 days.

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Patient audit of the Sigma sleep centres, South Africa; sleep apnoea/hypopnoea syndrome (SAHS) and relationships with subjective symptom ratings

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Introduction: Patient notes, responses to standardised self-report questionnaires and polysomnography were audited from a network of five South African sleep centres, each providing standardised equipment and technological and clinical protocols for the diagnosis of sleep disorders.

Methods: All centres offer full polysomnography (Alice 5, Respironics) with routine patient assessments including the Epworth sleepiness scale (ESS), sleep impairment index (SII), fatigue severity scale (FSS), restless legs scale (RLS), Beck depression inventory (BDI) and hospital anxiety and depression scale (HADS). Polysomnography was scored by experienced technologists using R&K criteria for sleep staging, ASDA criteria for scoring apnoeas, EEG arousals and periodic limb movements, and Chicago criteria for hypopnoeas (4% desaturation and/or arousal).

Results: Between November 2005 and October 2007, 271 patients (178 male) were assessed (Cape Sleep Centre, $n = 116$; Constantia Centre, $n = 79$; Morningside and Pretoria Centres, $n = 30$ each; Somerset West Centre, $n = 16$). Patients averaged 46 ± SD 13 years of age with mean body mass index (BMI) of $32.8 \pm 7.8\,kg\,m^{-2}$. Two hundred and sixty-three of 271 underwent successful polysomnography. 153 of 250 patients (63%) scored ESS of 10 or more, and in these polysomnography showed an apnoea+hypopnoea index (AHI) of ≥ 5 per hr in 96 (38%), ≥ 10 in 79 (32%) and ≥ 15 or more in 66 (26%), corresponding to minimal criteria for borderline, mild and significant SAHS, respectively. Spearman correlations for the total patient group showed rho-values for AHI of 0.14 with age, 0.44 with BMI, −0.15 with BDI, 0.26 with Epworth score, −0.09 with FSS, −0.18 with HADS, −0.11 with RLS and −0.08 with SII.

Conclusions: These results show a prevalence of SAHS in South African sleep patients similar to that in developed nations, with expected moderate and weak relationships between AHI, demography and symptom ratings.

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Preliminary results of a prospective randomised placebo controlled study to evaluate the effect of radiofrequency surgery of the soft palate

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Objectives: This study is performed to evaluate the effect and long term results of radio frequency surgery in the soft palate.

Methods: Twenty-five patients in an otolaryngology group who searched help for snoring and mild problems with sleep apnoea have so far been included in our study. All patients underwent a nocturnal sleep evaluation showing an AHI less than 15, before being randomized to radiofrequency or sham surgery. Each patient received 1 to 3 treatments or 1 to 3 sham surgery procedures in the soft palate. At follow up 12 months after the last radiofrequency or sham surgery treatment, all patients underwent a new nocturnal sleep evaluation. Questionnaires including SF-36 and ESS were answered before and after treatment. The study protocol and informed consent were approved by the ethics committee of Umeå University.

Results: Preliminary results will be presented from this ongoing study.

P216

Cost-effectiveness of using continuous positive airways pressure in treating severe obstructive sleep apnoea/hypopnoea syndrome in the UK

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Objective: To estimate the cost-effectiveness of using continuous positive airways pressure (CPAP) in managing patients suffering from severe obstructive sleep apnoea/hypopnoea syndrome (OSAHS), compared to no treatment, from the perspective of the UK's National Health Service (NHS).

Methods: A Markov model was constructed using outcomes from published studies and resource use estimates from a panel of sleep clinicians ($n = 19$). The model depicted the management of a 55 year old patient with severe OSAHS as defined by an apnoea-hypopnoea index (AHI) > 30 and daytime sleepiness (Epworth scale score > 12). The model spans a period of 14 years and was used to assess the cost-effectiveness of CPAP compared to no treatment.

Results: According to the model, 57% of untreated patients are expected to be alive at the end of 14 years compared to 72% of patients treated with CPAP. Moreover, 30% of untreated patients are expected to have survived event-free over 14 years compared to 58% of patients treated with CPAP. Untreated patients are expected to cost the NHS £10,645 per patient over 14 years compared to £9,672 per patient treated with CPAP. Treatment with CPAP for a period of one year was found not to be a cost-effective option since the cost per QALY gained is expected to be > £20,000, but after two years of treatment the cost per QALY gained is expected to be £10,000 or less and after 13 years of treatment, CPAP becomes a dominant treatment (i.e. more effective than no treatment for less cost). The cost associated with managing stroke was found to be the primary cost driver in patients with severe OSAHS.

Conclusion: CPAP was found to be clinically more effective than no treatment and the cost-effective strategy, from the perspective of the UK's NHS, after a minimum of 2 years' treatment.

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NPY and increased risk of CVD in OSAS: *in vitro* study

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Obstructive sleep apnea syndrome (OSAS) is a common disease, prevalent in the community with 9% of women and 27% of men.

Several woks have confirmed a connection between OSAS and cardiovascular events. Recent studies have demonstrated that independently of obesity, OSAS is associated with elevated neuropeptide Y (NPY) level. In our experiment we have investigated effect of NPY and modified LDL on endothelial cells inflammatory properties. Culture of human endothelial cells (EA.hy926) was incubated with native LDL (natLDL) or myeloperoxidase modified LDL (moxLDL) in concentration of 100 μg mL^{-1} (48 h, 37 °C, 5% of CO2). In addition medium was supplemented with NPY (100 pg mL^{-1}). After 48 h level of interleukin-8 was assessed. NPY 100 pg mL^{-1}, alone did not induce IL-8 release (289.1 ± 16.4), while moxLDL 100 μg mL^{-1} proved to be potent pro-inflammatory agent (1190.5 ± 59.4; $P<0.05$). Co-incubation of moxLDL with NPY result in unexpected potentiating of interleukin level (3894.5 ± 400.4; $P<0.05$). Our results suggest pro-inflammatory role of NPY, which in presence of moxLDL, well known risk factor, multiplies inflammatory response of endothelial cells. In light of described association between OSAS and NPY as well as CVD development, we propose that interactions between moxLDL and NPY, may be one of the mechanisms responsible for atherogenesis in OSAS patients. Further studies are necessary to investigate relations between NPY, moxLDL and OSAS.

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Objective assessment of snoring reduction using mandibular advancement splints

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Introduction: Reducing or abolishing snoring in patients with no underlying sleep disordered breathing by issuing custom made mandibular advancement splints (MAS) has previously been assessed using subjective reporting from partners. This study utilises objective multi-night pre and post MAS snoring measurement to evaluate snoring index, calibrated sound pressure level and snoring characteristics.

Methods: Twenty subjects (16M, 4F), identified as 'simple snorers' following a multi-channel, home sleep study (Embletta X10) with AHI index < 5 and Epworth < 5, underwent a 7 night home snoring recording. Patients were subsequently fitted with a custom made MAS (Solutions4Snoring). One month after MAS fitting and use, a further 7 night home snoring recording was performed.

Results: MAS use reduced snoring index, snoring level and snoring characteristics. A significant difference (0.002) between pre and post splint use snoring index was found. 99 percentile snoring levels were significantly (0.01) reduced (mean 12.8dBSPL). Changes in snoring characteristics were identified but were not quantifiable. In 6 patients, snoring was completely abolished. Discussion Successful reduction of snoring index and snoring level were achieved using mandibular advancement splints following one month of usage.

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The compliance and effect of CPAP in obstructive sleep apnea syndrome

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Continuous positive airway pressure (CPAP) is effective in the management of obstructive sleep apnea syndrome (OSAS), but poor compliance might be a major limitation of CPAP treatment. The aims of the study were to investigate the compliance and side effects of CPAP, and to evaluate the efficacy of CPAP in patients with OSAS. This study enrolled 106 patients with OSAS (93 men, 13 women, 51.9 ± 12.1 year), who took the CPAP treatment. The severity of daytime sleepiness was measured using Epworth Sleepiness Scale (ESS), and sleep quality and depressive symptoms were assessed by Pittsburgh Sleep Quality Index (PSQI) and Beck Depression Inventory (BDI), respectively. The patients were asked to fill out the questionnaire about side effects of CPAP sent by mail. CPAP compliance was defined as the use of CPAP for more than 4 h per night on 5 days or more in a week. During 29 months of the study period, 41.5% of patients were using CPAP and 38.7% of patients stopped using it. Compared to non-compliant patients, compliant patients had higher PSQI score and obstructive apnea index. Among non-compliant patients, 83% of them discontinued using CPAP within 3 months after CPAP application. Overall, 85.7% of non-compliant patients were discomforted by the CPAP, but much more nasopharyngeal symptoms were reported in the compliant group. ESS ($P<0.01$) and PSQI ($P<0.01$) were improved after CPAP treatment but not BDI ($P=0.86$). Body mass index (BMI) was decreased by 0.5 $kg\,m^{-2}$ with CPAP ($P<0.01$). CPAP can reduce the daytime sleepiness, nocturnal sleep disturbance, and body weight. To increase the compliance of CPAP, we suggest that active education and support are needed at the early stage of the CPAP treatment.

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Cardiac sympathovagal balance during sleep in obstructive sleep apnea patients: effect of fixed and autoadjusting continuous positive airway pressure

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Introduction: We have recently reported that fixed CPAP, but not APAP treatment, was associated with a decrease in arterial pressure and insulin-resistance (Patruno 2007) in OSA patients, and that CPAP and APAP may be differently capable of normalizing the sympathovagal balance during sleep. Aim of this study was to compare the effects of CPAP and a last-generation APAP on the cardiac sympathovagal balance during sleep using a randomized cross-over study.

Methods: Tweleve consecutive patients with severe OSA (AHI > 30) were randomly assigned to Group A that received one-month (T1) treatment with APAP followed by one-month fixed CPAP (T2), while Group B undertook the same treatments but in the opposite order (RemStarAuto, Respironics Inc., set in APAP or CPAP mode). All patients underwent full-PSG before treatment, at titration and at T1 and T2. We applied heart rate variability (HRV) spectral analysis to polysomnographic ECG and respiratory signals. HRV was performed considering the typical Wake (W), 2, 4 and REM sleep stages (S). LF/HF ratio was considered as an index of the cardiac sympathovagal balance.

Results: Eleven patients (9M, 2F; age 52.4 ± 9.9; BMI 31.6 ± 4.4) completed the study. 4 were hypertensive without any treatment change during the study. All patients showed good objectively measured adherence to PAP therapy. AHI, ODI, Mean SaO_2, SaO_2 nadir, time with SaO2 < 90% and ESS were significantly reduced in both groups from BL by both treatment conditions. In both groups, systolic and diastolic blood pressure were similarly affected by the two treatments. As to HRV, the mean HR as well as the LF/HF ratio progressively decreased from W to 4S and went back to W levels during REM, similarly during CPAP and APAP treatments,

without any significant differences between groups. Coherence levels between HRV and respiration were highest with both treatments through all sleep stages.

Conclusion: Our results suggest that in OSA patients, the treatment with a last-generation APAP, has similar effects than CPAP on cardiac sympathovagal balance during sleep.

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Atherosclerotic phenotype of monocytes in obstructive sleep apnea

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Obstructive sleep apnea (OSA), characterized by Intermittent Hypoxia/Reoxygenation (IHR), is associated with cardiovascular morbidity preceded by atherosclerosis. Atherosclerosis is multifactorial, composing of elements of oxidative stress, inflammation and lipid deposition. Exposure of monocytes/macrophages to oxidized low density lipoprotein (oxLDL), promotes inflammation, intracellular cholesterol deposition and lipid-laden foam cell formation. We hypothesized that OSA alters monocyte function towards an atherogenic phenotype via increased production of cytokines, adhesion molecules, oxLDL uptake and its scavenger receptor CD36, all facilitating increased foam cell formation. Monocytes were isolated from co-morbidity free OSA patients ($n = 11$) and controls ($n = 11$) closely matched by age, gender and BMI (38.6 ± 9.6 versus 37.6 ± 8.9 years; 28.3 ± 4.6 versus 28.1 ± 5.1 kg m^{-2}). Membrane expression of CD11b, oxLDL and CD36, and intracellular TNF-alpha and IL-10 levels were analyzed by flow-cytometry. Foam cell formation was followed microscopically by Oil-Red-O staining. The percentage of monocytes expressing TNF-alpha and IL-10 was significantly higher in OSA as compared to controls ($23.1 \pm 12.6\%$, versus $12.3 \pm 7.6\%$, $P<0.01$; $37.81 \pm 12.9\%$, versus $26.2 \pm 10.1\%$, $P<0.01$, respectively). TNF-alpha positively correlated with IL-10 ($r = 0.75$, $P<0.01$). Expressions of CD11b, oxLDL and CD36, determined by mean fluorescent intensity (MFI), were significantly higher in OSA then in controls (219 ± 86, versus 141 ± 57, $P<0.05$; 94 ± 42 versus 62 ± 25, $P<0.05$; 229 ± 116 versus 139 ± 63, $P<0.05$, respectively), and were positively correlated with each other (oxLDL versus CD36 $r = 0.57$, $P<0.01$; oxLDL versus CD11b $r = 0.45$, $P<0.05$; CD36 versus CD11b $r = 0.44$, $P<0.05$). Plasma oxLDL was higher as well (75.82 ± 21 versus 53.29 ± 27, $P<0.05$). Also, spontaneous foam cell formation in culture was higher in OSA then in controls ($17.9 \pm 10.0\%$ versus $6.3 \pm 2.2\%$, $P<0.009$) A pro-atherogenic monocyte phenotype is evident in OSA via increase in inflammatory cytokines, expression of adhesion molecules and oxLDL scavenger-receptor CD36, oxLDL uptake and increased foam cell formation. These atherogenic sequela most likely contribute to the development of cardiovascular morbidity in OSA.

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An European multi-centre long-term observational cohort (ESADA – European Sleep Apnea Database) within the frame of COST action b26

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The project aims to generate a multinational European database containing medical information on patients suspected of OSA referred to sleep centers. Enrolment is consecutive and includes essentially all untreated patients independently of comorbidity, concomitant medication and degree of sleepiness. A web-based data collection format has been constructed for transfer of clinical data to a central database located and coordinated at Gothenburg University. A joint scientific committee including representatives of the different participating centers decides on the use and exploitation of data. The basic dataset (base cohort) will be used for a series of projects related to outcome research, clinical process evaluation as well as dissemination of standards for diagnosis and treatment of OSA. A subsequent step includes sub protocols dealing with pathophysiology, genetic mechanisms, neurocognitive impairment and cardiovascular disease in OSA. The core of the ESADA has been started from the European Union COST action network of nationally appointed sleep apnea experts. To date there are 22 participating centers across Europe and in the excess of 720 patients have been enrolled. Monthly inclusion rate is approximately 100 patients. In some countries national patient registries are used for data generation within the ESADA network. The first cross sectional analysis is planned at approximately 3000 patients. Providing the planned recruitment goals are met, the ESADA may constitute one of the world's largest prospective cohorts including up to 7,000 patients with sleep disordered breathing. Beside the scientific opportunities offered, the action will generate possibilities to achieve local and cross national standardization, improvement of quality of care as well as increased scientific and clinical exchange of ideas between different European sleep centers.

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Health-related quality of life in OSAS patients compared to the general population

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Introduction: The quality of sleep is intrinsically linked to quality life and sleep apnea may in some patients lead to severe impairment. Sleep apnea patients, however, are often obese and suffer from multiple co-morbidities that also can contribute to decreased quality of life.

Material and Methods: SF-12 was administered to OSAS patients before they were placed on CPAP treatment. The control group consists of a simple random sample of 938 Icelanders 40 years and older (www.boldcopd.org).

Results: Among the 395 OSAS patients who have participated so far 370 (94%) responded to the SF-12 and 772 (82%) among the controls. For the OSAS patients the mean $\pm$ 1 SD unadjusted SF-12 Physical Component Summary Score (PCS) was 40.8 ± 11.0, and the mean SF-12 Mental Health Component Summary Score (MCS) was 48.1 ± 11.1, compared to PCS 50.7 ± 8.0 and MCS 51.4 ± 4.8 for the controls. The unadjusted standardized effect size was very large for the physical component score and moderate for the mental health component. Statistical control for age, gender, and BMI did not change the magnitude of group differences. For PCS the estimated effect size is -1.08 (95% CI -1.22 to -0.95). The effect size for MCS is -0.45 (-0.58 to -0.33). Multiple linear regression analysis for the pooled material of OSAS and controls showed that PCS was strongly related to sleep apnea, male gender, age and obesity (R^2 adjusted = 0.302) while much less of the variation in MCS could be explained (R^2 adjusted = 0.074) Estimate St. Error 95% Confidence Limits PCS: Intercept 68.5 1.9 64.7 72.3 OSA -9.9 0.6 -11.1 -8.8 MALE 3.0 0.5 1.9 4.1 AGE (10 years) -1.8 0.2 -2.3 -1.4 BMI (5 units) -1.6 0.2 -2.1 -1.1 MCS: Intercept 42.7 1.7 39.4 45.9 OSA -3.4 0.5 -4.4 -2.4 MALE 0.9 0.5 0.0 1.8 AGE (10 yrs) 1.2 0.2 0.9 1.6 BMI (5 Units) 0.2 0.2 -0.2 0.6.

Conclusion: OSAS patients describe severely impaired quality life compared to controls, especially in the Physical Component Summary Score. Two year follow-up data are also being collected.

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Menopause and cardiovascular risk factors in sleep apnea

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Introduction: Previous data indicate that cardiovascular comorbidity in obstructive sleep apnea (OSA) differs between pre- and postmenopausal women. This study aimed to compare cardiovascular, respiratory and metabolic status in women with menopausal state classified by age.

Methods: Cross sectional study of a sleep laboratory cohort of 2475 consecutive patients (209 female and 2266 male). Pre- and post-menopausal females were defined by age (<45 years, $n = 20$, 34.9 ± 6.9 years and >55 years, $n = 50$, 62.4 ± 5.0 years, respectively). A group of 816 males fulfilling the corresponding age criteria were identified as controls. A level III sleep study was performed, blood pressure, blood chemistry, respiratory function and blood gases were assessed.

Results: The prevalence of severe OSA (RDI ≥ 30) increased from 15% in premenopausal to 34% in postmenopausal women. In contrast, prevalence was essentially identical (36% and 40%) in the corresponding age groups of men. Total cholesterol, triglycerides, LDL-cholesterol, $PaCO_2$ and HCO_3 all increased steeper with age in women than in men. BMI and diastolic blood pressure were unchanged, while systolic blood pressure increased more in women (133 ± 18.9 and 160 ± 29.0 mmHg, $P<0.01$) than in men (143 ± 21.5 and 150 ± 20.2 mmHg, $P<0.03$). Severity of sleep apnea (RDI) correlated with $PaCO_2$, HCO_3, BMI and blood pressures in post- but not in premenopausal women. Conclusions Menopausal transition was associated with an emergence of cardiovascular risk factors including elevated systolic blood pressure and an unfavorable lipid profile. Decreased CO2 chemosensitivity may be a mechanism behind the increased prevalence of severe OSA after menopause. The negative impact of OSA on cardiovascular morbidity may be promoted by risk factors appearing during the menopausal period.

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Effect of PAP treatment on neurocognitive function and quality of life in patients with obstructive sleep apnea

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Introduction: Sleep fragmentation and intermittent ipoxemia from OSA have been shown to have a negative impact of neurocognitive function. Literature data on improvement after treatment are mixed. Aim was to evaluate neurocognitive function and quality of life (QoL) in OSA patients at baseline (BL) compared to age-matched normal controls and to assess changes after 3 months of PAP treatment.

Methods: Fifteen male untreated patients with severe OSA (AHI $>=30$) and 15 normal controls matched on age, education, gender, and hypertension status. Neurocognitive functioning (attention, vigilance, memory, executive function, visuo-constructional abilities), sleepiness (ESS), mood (BDI), QoL (SF-36 and FOSQ) and quality of sleep (PSQI) were assessed at BL and afetr three months fixed PAP with C-flex treatment (T1).

Results: Patient showed significantly lower score than healthy subjects in: short term memory (MBT) (Digit Forward: $P = 0.000$; Corsi's Test: $P = 0.001$); long term memory (MLT) (Rey List Learning: $P = 0.013$; Rey List Recall: $P = 0.008$) and executive function (Digit Backward: $P = 0.001$; PASAT error: $P = 0.000$; Stroop: $P = 0.026$; Error Stroop: $P = 0.000$; Copy's Rey Picture: $P = 0.015$; TrialA: $P = 0.033$; TrialB: $P = 0.006$). Moreover patients also had significantly lower score at ESS, PSQI and QoL ($P<0.05$). Preliminary results on 13 patients assessed at T1 showed significant improvement on cognition ($P<0.010$)and on ESS, PSQI and QoL ($P<0.005$)over time. Moreover patints reached normal subjects scores at neurocognitive tests except for one executive function test (trial B).

Conclusion: Our data showed that cognitive functions impaired when compared to normal controls at BL significantly improved after PAP treatment over time reaching the scores of normal controls.

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Sleep EEG asymmetries in apneic humans

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The respiratory drive is weakened during sleep and the observation of breathing pauses is frequent in sleep apnea patients which must interrupt their sleep to recover the waking breathing drive. However, the cycle apnea-rebreathing is continuously repeated during a sleep episode. As a consequence, gross sleep disturbances occur, and the next day waking behavior is also severely impaired. However, repeated apneic events of long duration are normal in diving mammals in which the presence of asymmetric or unihemospheric sleep has been considered as a mechanism to maintain respiration during sleep The present report aims at searching state related EEG asymmetries in human apneic patients, which, like diving mammals, could show interhemispheric state differences to optimize the opposite drives to maintain sleep and breathing. C3 and C4 EEG samples obtained from six sleep apnea patients were extracted from whole night recordings, distinguishing between periods of sleep with normal breathing and apneic periods. The interhemispheric asymmetry was calculated using the Phase Lag Index (Stam et al. 2007) which can range between zero (no phase coupling between hemispheres and maximal asymmetry) and 1 (maximal phase coupling and no asymmetry). As a result, decreases in the Phase Coupling Index between the two hemispheres were observed in delta, alpha and beta bands during breathing periods and increases during apneas. No changes were observed in theta band. The results show that the interhemispheric asymmetry was increased during breathing periods, suggesting a difference in the working mode of the two hemispheres which may have attained different levels of sleep and wakefulness to procure breathing maintenance.

Stam et al. (2007). Human Brain Mapping, 28:1178-1193.

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Nocturnal cerebral hemodynamics in obstructive sleep apnea patients

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Background: Near infrared spectroscopy (NIRS) non-invasively monitors brain tissue oxygen saturation (StO_2) together with changes in concentration of oxyhemoglobin (O_2Hb), deoxyhemoglobin (HHb) and total haemoglobin (tHb), and has proved the

occurrence of cerebral hypoxia during episodes of nocturnal obstructive apneas in sleep disordered breathing (SDB) patients. Aim of the present study is to investigate cerebral hemodynamic consequences of different types of nocturnal respiratory events (obstructive apneas and hypopneas).

Methods: Nineteen patients with SDB of variable severity (mean AHI = 24 h^{-1}, range 0–93, mean ODI = 21 h^{-1}, range 0–78) were investigated by nocturnal polysomnography coupled with cerebral NIRS. NIRS data associated with different respiratory events were averaged and cerebral hemodynamic corresponding alterations were assessed.

Results: The relative changes of NIRS parameters were significantly bigger in amplitude during obstructive apneas compared to hypopneas (e.g. mean StO_2 change of $-1.65 \pm 0.45\%$ versus $-0.57 \pm 0.14\%$, $P = 0.011$), where they also showed significant relationships with the concomitant peripheral oxygen desaturations (e.g. for StO_2 Pearson correlation coefficient of 0.8, $P < 0.001$, for obstructive apneas, versus 0.2, $P > 0.05$ for hypopneas). During hypopneas the brain showed a secondary increase of O_2Hb and tHb (i.e. focal hyperoxygenation) to counteract efficiently the incoming cerebral hypoxia.

Discussion: This study suggests that cerebral hemodynamic consequences of SDB are modulated by the type of respiratory event. This data support the hypothesis that cerebral perfusion autoregulatory mechanisms to prevent hypoxia fail only in specific conditions (i.e. obstructive apneas) and not in others (i.e. hypopneas) during SDB.

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Sleep disorders and glucose metabolism – a comparison of OSA, RLS and insomnia

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Objectives: There is some evidence that chronic sleep loss may be a risk factor for impaired glucose tolerance (IGT), a metabolic state preceding type II diabetes. A relationship between sleep disordered breathing has been shown earlier, but very little is known on other sleep disorders.

Methods: Using the oral glucose tolerance test (OGTT) we compared patients with an obstructive sleep apnoea syndrome (OSAS; $n = 20$), restless legs syndrome (RLS; $n = 18$) and primary insomnia ($n = 10$). IGT was diagnosed according to American Diabetes Association criteria, i.e. when 2 h after 75 g glucose load, blood glucose levels ranged between 140–200 mg dl^{-1}. The respective diagnoses were confirmed by polysomnography.

Results: Fasting plasma glucose (FPG), 2 h-postload glucose (2 h-PG) as well as BMI differed significantly among sleep disorder groups. However, group differences in glucose levels did not remain significant after controlling for BMI. Additional analysis revealed a significant main effect of BMI on both, FPG and 2 h-PG levels. Despite a considerably different BMI, IGT was as frequent in RLS (44%) as in OSAS (40%) whereas in insomnia the rate of patients with IGT was in the expected range (20%). Therefore we analyzed RLS and OSAS patients separately by comparing subjects with 'normal' glucose levels and levels indicating IGT. RLS patients with IGT showed a significant higher BMI than patients with 'normal' glucose values, while IRLS and Sleep Efficiency were quite similar. An analysis of covariance confirmed the main effect of BMI on 2 h-PG in this group. In the OSAS group, the BMI was comparable in both subgroups. However, patients with an IGT presented significantly higher Apnoea-Hypopnoea-Indices (AHI) and Desaturation Indices (ODI) than patients with 'normal' glucose levels; this finding was confirmed by means of a simple regression analysis. SEI did not influence glucose levels.

Conclusion: In summary we found that in OSAS, despite the high BMI, disease associated parameters predicted IGT; this was not the case in RLS. In the small group of insomniacs only 2 patients showed an IGT.

P229

Objective and subjective daytime sleepiness evaluation in sleep apnea patients

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Objective: Sleep apnea is a disorder commonly associated with excessive daytime sleepiness (EDS). EDS can be evaluated on three levels: subjective, behavioral (performance) and physiological. We analyzed results of three different sleepiness assessments to find out possible associations in sleep apnea patients.

Method: We analyzed data of 199 consecutive patients with confirmed diagnosis of obstructive sleep apnea. The Epworth Sleepiness Scale (ESS) was used for the subjective evaluation of daytime sleepiness. After the first polysomnographic night, the behavioral level of sleepiness was measured by the "Quatember Maly" vigilance test, the computerized version of the Mackworth clock test. A specific decline in performance can be considered as an indicator for the level of sleepiness: the most important variables were reaction time, "false" response (reaction when not requested) and "skips" (no reaction when requested). The global result of the test was scored: 0-normal, 2-pathological, 3-severely pathological. Immediately after the performing of the vigilance test an standard EEG examination was accomplished. The physiological level of sleepiness was evaluated by the presence of lowered vigilance state on EEG. Hypo-vigilance was scored as 0-none, 1-present, 2-pronounced.

Results: The ESS correlated significantly with the global result of the vigilance test. Significant correlations were found among the level of hypo-vigilance on EEG, reaction time and "false" in the vigilance test. The ESS correlated significantly with the ODI. The global result of the vigilance test correlated significantly with lower mean saturation levels and minimal saturation values. To go into details we analyzed different parameters of the vigilance test separately. There were significant correlation among "false" and both saturation parameters.

Conclusion: We found significant correlations among the ESS, vigilance test and lowered vigilance state in standard EEG in our sleep apnea patients.

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Sleep habits and neurobehavioural correlates in young children who snore

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Background: Children with sleep disordered breathing have fragmented sleep, but less is known about other sleep behaviours and their association with neurocognitive function.

Method: Snoring children listed for adenoidectomy and/or tonsillectomy were studied with non-snoring controls. SDB was assessed by polysomnography (PSG). Parents completed the Children's Sleep Habits Questionnaire (CHSQ), Behavior Rating Inventory of Executive Function (BRIEF) and Strengths and Difficulties Questionnaire (SDQ). Objective neuropsychological assessment included the NEPSY visual attention measure (VA).

Results: Sixty-eight snoring children, mean age 4.6 years (SD 1.2), 59% boys, and 39 controls, 4.9 years (SD 1.2), 54% boys, were recruited. Snoring children had higher CSHQ subscale scores: bedtime resistance ($P<0.000$); sleep onset delay ($P<0.01$); sleep duration ($P<0.000$); sleep anxieties ($P<0.002$); night waking ($P<0.000$); parasomnias ($P<0.000$) and daytime sleepiness ($P<0.000$). However, CSHQ subscales did not correlate with apnoea/hypopnoea index, mean or min. SpO_2 in snoring children. Snorers had significantly worse BRIEF subscale T-scores and emotional, hyperactivity and peer problems (SDQ sub-scales) compared to non-snoring children. BRIEF global executive composite correlated with all CSHQ subscales and SDQ total score correlated with all but the sleep anxieties CHSQ subscale. However, neither of these parental assessments correlated with PSG respiratory measures. NEPSY VA was better in controls ($P = 0.03$) but did not correlate with objective or subjective sleep measures.

Conclusion: Parents report diverse sleep problems and neurobehavioural difficulties in young snoring children compared to controls. These parental reports show a high degree of correlation. However, PSG measures fail to correlate with parent reports of sleep problems or neurobehavioural function. This may represent parental reporting bias or temporal dissociation between the origins of neurobehavioural impairment and PSG. Preliminary post-operative assessment of snorers indicates improvement in CSHQ and SDQ sub-scales but persistent executive function difficulties. In support of parent reports, NEPSY VA measures improve in the snoring group with a significant group by time interaction ($F(1.53) = 4.35$, $P = 0.42$).

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Management of obstructive sleep apnoea in bariatric surgery patients

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Aims: We conducted a retrospective analysis of morbidly obese patients assessed for bariatric surgery referred to the sleep service in a district general hospital in 2006–2007. We aimed to confirm prevalence of Obstructive sleep apnoea (OSA) and hypoventilation, attendance rates for polysomnography and CPAP trials and effectiveness of OSA treatment by CPAP and surgery.

Methods: Patients attended inpatient multichannel sleep study unless they exceeded 170kg or requested home study (oximetry). CPAP trials were offered where patients had daytime sleepiness (Epworth score ESS >10) and more than 10 $>4\%$ dips in oxygen saturation per hour (dip rate >10), or had nocturnal hypoventilation (mean saturation $<92\%$). Sleepiness and Oximetry was reassessed following CPAP and within 12 months following surgery.

Results: A total of 70 patients (21 male) were referred, mean (SD) age 47.1 (10.2). The mean BMI was 49.6 (8) and higher in those with OSA 52.98 than those without 46.45. Mean ESS for the group was 12.85 (4.9), but did not differentiate those with OSA 13.7 (4) from those without 12.0 (4). 18 32% did not attend appointments at least once. Oximetry data was available for 63 patients, 33 had dip rate >10, 19 had hypoventilation. Thirty two were offered a trial of CPAP. Of these, 11 (34%) declined/did not attend CPAP setup, 5 (16%) did not tolerate it and 3 declined further follow up. when tolerated CPAP 12.6 (2.5) cm H_2O pressure, was effective in controlling OSA; 4% dip rate pre CPAP 49.6 post CPAP 3.2, ESS pre 13.7 post 7.3, and hypoventilation mean saturation pre 90.04 post 94.85. Of the 21 patients that had trial of CPAP, 11 (52.4%) had surgery (10 RYGBP, 1 Band). The mean BMI before surgery for those on CPAP was 49.6. So far 8 attended follow up and 5 are off CPAP after an average of 6.8 months. The average BMI of those off CPAP is 33.9 (reduction of 15.7 BMI points) an average of 26.8% body weight loss. 4 patients were declined surgery and continue on CPAP.

Conclusions: OSA and hypoventilation are common in those assessed for bariatric surgery. Attendance rates are poor amongst this group but CPAP is effective when tolerated. Weight loss post bariatric surgery allows withdrawal of CPAP in many patients.

P232

Chiari malformation and sleep-related breathing disorders

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The anatomical and functional integrity of both respiratory circuits and lower cranial nerves controlling the upper airway is necessary for breathing control during sleep. These latter structures may be altered in Chiari malformation (CM), and CM-related sleep-disordered breathing (SDB) has been observed in few investigations. The goal of our study was to estimate the frequency, mechanisms, and predictive factors of sleep apnea syndrome (SAS) in a large group of children and adults affected with type I and II chiari malformation (CM). The influence of curative surgery of CM on SDB has also been evaluated in a subgroup of patients.

Methods: Forty-six, consecutive, unrelated CM patients (40 CMI, 6 CM II), 20 children (8 male, 12 female) and 26 adults (12 male, 14 female), underwent physical, neurological and oto-rhino-laryngoscopic examination, magnetic resonance imaging, and polysomnography to assess sleep and SDB. Eighteen patients have also been evaluated after surgery.

Results: SDB was present in 31 (67.4%) of all CM patients (70% of CMI patients, 50% of CMII including mainly children). Sixty percent of children with CM exhibited SDB, including 35% with obstructive (OSAS) and 25% with central (CSAS) sleep apnea syndrome. SDB was observed in 73% of adults affected with CM (57.7% OSAS, 15.4% CSAS). Severe SDB was found in 23% of adults with CM. Multiple regression analysis revealed that age, type II Chiari and vocal cord paralysis predicted the central apnea index. Polysomnographic analysis after surgery indicates a possible benefit from surgery on SDB.

Conclusion: SDB is highly prevalent in all age groups of patients suffering from CM. CSAS in particular, extremely rare in the general population, is a common finding among CM patients in our study. CM-associated SDB might explain the relatively high frequency of respiratory failures observed during curative surgery of CM. Finally, our results suggest that SDB should be systematically screened in CM patients, especially before surgery. These findings raise the question whether the treatment of SDB may improve the risk of respiratory failure during surgery and mortality associated with CM.

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Factors influencing subjective sleepiness in patients with obstructive sleep apnea syndrome

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Aim: We aimed to clarify the factors influencing subjective daytime sleepiness in patients with obstructive sleep apnea syndrome (OSAS).

Methods: Subjects included 230 adult male OSAS patients aged 20 to 73 years. Single and multiple linear regression analyses were

performed to estimate the association between the Epworth Sleepiness Scale (ESS) and the following variables, i.e., Minnesota Multiphasic Personality Inventory (MMPI), Self-Rating Depression Scale (SDS), age, body mass index (BMI), sleep duration during the preceding month and apnea-hypopnea index (AHI).

Results: Single linear regression analysis revealed that age had negative association with ESS score, while BMI, AHI, SDS, Hs, Hy, Pd, Pt, Sc and Ma on MMPI had positive association with ESS score. However, the other remaining parameters such as nocturnal sleep duration during the preceding month, D, Mf, Pa, Si on MMPI showed no statistical association with ESS score. Multiple linear regression analysis with stepwise elimination method was applied to choose the significant factors associated with ESS. It was shown that three variables including age, AHI and Hs scores were independent factors influencing ESS score. The R2 for the model was 0.14, suggesting that these factors account for 14% of possible variance of subjective daytime sleepiness of OSAS patients.

Conclusions: These results suggest that subjective daytime sleepiness in patients with OSAS may be influenced not only by the severity of respiratory disorder indices but also by a certain personality characteristics affecting Hs score and by age.

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Desaturation index and AHI as predictors for clinical consequences in OSA patients

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Aim of this study was to explore the correlations of Apnea/Hypopnea Index (AHI), Desaturation Index (DesI), and other sleep parameters with clinical symptoms such as excessive daytime sleepiness and anthropometric variables in the patients with obstructive sleep apnea who underwent the polygraphy recordings in the Sleep Laboratory in Split. The data were collected from 120 patients tested between the years 2005 and 2007. AHI, DesI, and other standard sleep parameters were determined with the use of the same diagnostic device PolyMESAM (MAP, Germany). To determine clinical symptoms, extensive questionnaires including the standard Berlin Questionnaire, Stanford Sleepiness Scale, and Epworth Sleepiness Scale were used. The results showed significant correlations of both AHI and DesI with clinical symptoms, however, DesI appeared to exhibit stronger correlations than AHI. In conclusion, both the AHI index and the Desaturation Index are useful tools for predicting the relevance of clinical symptoms like excessive daytime sleepiness in the patients with obstructive sleep apnea.

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Functional MRI activation changes after PAP treatment in obstructive sleep apnea (OSA) patients

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Introduction: OSA is associated with cognitive and functional deficits that improve after PAP treatment. Neuropsychological tests and fMRI were used to investigate whether improvement in cognition reflects a change in cerebral activity underlying these functions.

Methods: Eleven males OSA patients (AHI >30 h) were evaluated before treatment and after 3 months of PAP. During fMRI-scanning participants a 2-back working-memory task was used.

Results: The longitudinal neurocognitive evaluation showed a significant improvement after the treatment in tests of short and long-term memory, attention and executive-functioning, ESS and quality-of-life. Behavioral results during fMRI-scanning showed an improvement in 2-back performance after treatment ($P = 0.068$). Paired *t*-tests on fMRI data showed increased cerebral activations after treatment in occipital and parietal regions (calcarine gyrus, ventral medial precuneus and middle occipital gyrus), right temporal pole and middle cingulate cortex. Decreased activations after treatment were observed in the left inferior frontal gyrus (pars triangularis and opercularis), anterior cingulate cortex, right thalamus and hippocampus bilaterally.

Conclusion: Longitudinal neurocognitive tests confirmed the partial reversibility of cognitive dysfunction in OSA patients after PAP. The stronger occipital and parietal activity might reflect an enhancement of visual attention following treatment. The decrease in frontal and hippocampal activity likely reflects the reduced need for additional resources which characterize pre-treatment OSAs. These changes reverse some of the compensatory activation seen at baseline compared to normal controls.

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Decreased arterial stiffness in CPAP treated patients as measured by augmentation index (AI) derived from peripheral arterial tone (PAT) signal

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Introduction: CPAP treatment has been shown to reduce apnea events and improve cardiovascular outcome. Peripheral Arterial Tonometry (PAT) is derived from the finger tip arterial pulse wave amplitude. We have previously shown that OSA patients have increased arterial stiffness as measured by Peripheral Arterial Tone (PAT) signal derived augmentation index (PAT-AI). This study investigated the effect of long term treatment with CPAP on PAT-AI.

Methods: PAT-AI was compared between CPAP treated and non treated OSA patients. CPAP group comprised 10 male OSA patients treated for at least 3 months who had RDI >20 at the initiation of treatment and RDI <5 during the night of measurement. OSA group comprised 10 age, height and BMI matched males with RDI >20. Mean age was 55 ± 15 and 54 ± 16 years, height 175 ± 6 and 173 ± 8 cm and BMI 30 ± 5 and 30 ± 6 in the CPAP and non treated OSA groups respectively (all $p = $ ns) All subjects underwent a full PSG study in the sleep laboratory with simultaneous recording of the PAT signal (Watch_PAT 100, Itamar Medical, Caesarea, Israel). The AI, an established measure of arterial stiffness, was calculated from the PAT waveform.

Results: Mean all night PAT-AI was significantly lower in the CPAP treated group versus the OSA group (25 ± 25 versus $39 \pm 20\%$; $P = 0.023$). Adjustment of PAT-AI for age and heart rate slightly increased the significance (25 ± 18 versus $39 \pm 13\%$; $P = 0.013$)

Conclusion: Arterial stiffness assessed by calculation of the augmentation index from the PAT signal is decreased in male OSA patients receiving effective long term treatment with CPAP as compared to non treated OSA patients of similar body habitus and similar OSA severity.

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The long term effects of mandibular advancement splints in the treatment of sleep disordered breathing

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Objective: To investigate and quantify the longer term side-effects of mandibular advancement splint (MAS) wear.

Design and Setting: A longitudinal follow-up study undertaken at the Royal London Hospital.

Materials and Methods: Thirty eight patients previously diagnosed with sleep disordered breathing, with pre-treatment cephalograms and study models, who had been wearing a Herbst MAS consistently over a minimum of 3 years, were recruited. A new lateral cephalogram and study models were obtained to investigate occlusal and skeletal changes and identify risk factors for these changes.

Results: A statistically significant ($P<0.001$) reduction in both the horizontal overlap (overjet) and the vertical overlap (overbite) of the incisors was found, with the median cephalometric values (overjet 1.5 mm and overbite 1.7 mm) being greater than the median study model values (0.9 mm for both overjet and overbite). Lower incisors proclined by a median 3.4 degrees and upper incisors retroclined by a median 3.6 degrees ($P<0.001$ for both). In the vertical dimension, lower face height & the maxillary-mandibular plane angle also increased ($P<0.001$ and $P<0.01$, respectively). There were no antero-posterior skeletal changes. Risk factors for reduction in overjet: appear to be: an increased starting overjet, proclined lower incisors and a reduced overbite. For overbite reduction, a deep pre-treatment overbite and a longer duration of MAS therapy seemed to be implicated.

Conclusions: For patients wearing MAS, minor occlusal change is the norm. Patients must be warned pre-treatment and should be regularly monitored.

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Obstructive sleep apnea syndrome (OSAS) and their neuropsychiatric consequences

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Introduction: OSAS lead to physical problems like hypertension and arrhythmias and mostly to neuropsychiatric consequences like Brain atrophy, Depression, Anxiety and Insomnia. Considering the poor knowledge of reliable facts of etiology in neuropsychiatric diseases could show unusually clean-cut conditions of interference with the mechanism of mental and sensory-motor plasticity.

Methods: In our study we used neuropsychological and neuropsychiatric methods in different patient groups in a sleep laboratory. Over the past five years we have been testing more than 2000 patients. During admission to the clinic, all patients were selected according to their clinical diagnosis (ICD-10) and all patients were examined neurologically, neuropsychologically and psychiatrically. All test persons must not suffer from any severe psychiatric disorders. The study was carried out involving all groups of randomly selected patients with OSAS on a number of neuropsychiatric parameters.

Findings: Testing of neuropsychiatric diseases and difficulties and quality of life revealed a highly significant difference between healthy persons and OSAS patients ($P<0.05$). Examination of specific domains of neuropsychiatric diseases and quality of life showed significant differences in patients with OSAS. In all dimensions of neuropsychiatric diseases and quality of life, untreated OSAS patients had inferiority scores than those who had undergone therapy. After more than 6 weeks nCPAP therapy, the neuropsychiatric diseases of the OSAS patients, and quality of life improved to a significant degree ($P<0.05$). Analysis of the degree of severity showed for OSAS that on the whole, there is a significant difference concerning neuropsychiatric diseases and quality of life.

Discussion: The study revealed that a lot of OSAS patients show neuropsychiatric problems and deficits, concerning their quality of life. The degree of severity of the OSAS is relevant. In summary, based on our results, it is to be said that although a continuous nCPAP therapy improves the OSAS symptoms; neuropsychiatric consequences and the quality of life require longer-term degeneration.

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Out patient based OSAHS diagnostic service in NHS Dumfries and Galloway, Scotland

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NHS Dumfries and Galloway is a remote and rural region serving a population of 150,000 people across 2500 square miles. The Respiratory medicine department receives 300 new referrals annually requesting limited channel sleep studies. Level 111 and IV studies can be offered at this facility and requests for Polysomnography (PSG), (<10 in 2007) are referred to the Royal Infirmary of Edinburgh sleep medicine department which is a 190 mile round trip. The service currently manages 358 patients on home CPAP and home NIV and anticipated predicted growth is approximately 80 new patients per annum up to 2010. Current bed capacity permits approximately 150 in-patient studies per year, however bed pressures have resulted in many cancellations, thereby increasing waiting times and inability to meet government targets. As a result the respiratory team has been obliged to seek innovative ways to increase the number of out patient diagnostic studies. In 2007 approximately 270 limited chanel sleep studies were conducted of which, 180 were home tests, 50 were in-patient tests, and 25 were hotel based outpatient tests. Only 6 of these tests had to be repeated due to poor quality of data for analysis purposes. Where there was diagnostic uncertainty, patients were asked to attend clinic review in 6 months for consideration of repeat testing or referral for full PSG. A questionairre of patient views of the service has demonstrated overall satisfaction with service provision and a preferance for a home based test where possible. In economic terms, in 2007-approximately 206 bed days were saved by conducting out patient based testing which equates to a net saving of £71,500 for the organisation. Our experience to date with expanding clinical demand for this service coupled with limited funding is that outpatient based limited chanel sleep studies are an appropriate and acceptable model of service delivery for the majority of patients referred to our region. Where there is diagnostic uncertainty, individuals are referred for full polysomnography.

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More severe sleep apnea syndrome at patients with COPD (overlap syndrome)

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Introduction: COPD (chronic obstructive pulmonary disease) and OSA (Obstructive sleep apnea) are two diseases with a prevalence of 4–6%, increasingly in the general population.

Aims and objectives: We search for significant differences among patients overlap syndrome.

Material and Methods: 427 consecutive patients were investigated in the Sleep Laboratory, June 2005- June 2007. We performed clinical examination, anthropometric measurements (height, weight, BMI-body mass index, neck circumference, abdomen circumference), the Epworth somnolence scale, polysomnographies (Alice 5). We compared two groups, with and without COPD and used t Student test with equal variances and the Welch correction for inequal variances.

Results: The average age of diagnosis was 51,99 years, 314 men (73%) and 113 women (27%), $X^2. < 0.001$, smokers 30%. 69 patients (16.35%) had overlap syndrome and presented more severe forms of OSA: oxygen desaturation ($P < 0.001$), abdominal circumference ($P < 0.001$), BMI ($P < 0{,}001$), age ($P = 0.004$), desaturation index ($P = 0.0049$), neck circumference ($P = 0.0091$), diurnal somnolence ($P < 0.01$). There were no significant differences for apnea hypopnea index (AHI) ($P = 0.055$), central apnoeas ($P = 0.277$). According to AHI (0–9 versus ≥ 10) there are no significant differences regarding COPD ($P = 0.453$).

Conclusions: The patients suffering from the overlap syndrome (16.35% similarly to the percentage in literature) present more severe forms, especially more severe night desaturations, BMI, abdominal and neck circumference, age, excesive daytime somnolence. In 2020, COPD will be the third cause for mortality in the world. Therefore, the association of the two disorders is of great importance.

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Preference for bilevel continuous positive airway pressure (Bi-CPAP) and breathing pattern in patients with obstructive sleep apnoea syndrome (OSAS) at out-patient CPAP set-up

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Bi-CPAP is reported to improve adherence to treatment in OSAS. In our centre, in common with many centres in the UK, initiation of CPAP therapy is performed in a single visit in an out-patient setting. We asked newly diagnosed OSAS patients to express a preference for conventional CPAP or Bi-CPAP after 10 min periods of use of both techniques and investigated if the preference was related to pattern of breathing and reduction in expiratory PAP (EPAP). Sixteen adult patients with newly diagnosed OSAS were randomly allocated to receive CPAP/Bi-CPAP or Bi-CPAP/CPAP using the Respironics CFLEX system, with the device set to provide either conventional CPAP or maximum reduction in EPAP (Comfort Level 3). Patients were informed that there might be a difference in the sensation of breathing but were not informed of the order of testing. Rib Cage and Abdominal excursion and Mask Pressure were monitored continuously. 62% of patients preferred Bi-CPAP. Overall, breathing pattern on CPAP and Bi-CPAP was the same. In the patients preferring Bi-CPAP there was a small but significant increase in respiratory frequency from 13 min^{-1} on CPAP to 14 min^{-1} on Bi-CPAP ($P < 0.05$).The reduction in EPAP achieved by the CFLEX device was very variable (Mean EPAP (CPAP, 9.48 cm H_2O)-Mean EPAP (Bi-CPAP, 8.71 cm H_2O) = 0.7 cm H_2O (range -0.59 to 2). There was no difference in mean EPAP reduction in the group preferring Bi-CPAP compared with those preferring CPAP. An order effect emerged with 86% (6/7) patients receiving Bi-CPAP first showing a preference for this. Patients with OSAS show a slight preference for Bi-CPAP at out-patient initiation but this is not related to change in breathing pattern or reduction in mean EPAP level.

P242

Does overnight oximetry miss CPAP treatable obstructive sleep apnoea (OSA)?

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Introduction: In the UK many respiratory departments use overnight oximetry (OO) as a screening tool for the detection of OSA. However, studies have shown that this form of assessment has a significant false negative rate for detecting sleep disordered breathing compared to sleep studies which monitor airflow directly. In order to estimate the consequences of 'missing' patients with mild OSA, we examined the results and follow up of patients who we categorise as 'borderline' with oxygen desaturation indexes of 5–15 4% dips/hour. All patients had also undergone limited respiratory sleep studies (LSS). We were particularly interested in the influence of this further 'confirmatory' investigation on treatment decisions/outcomes.

Methods: Patients having undergone both OO and LSS were identified from our sleep and ventilation database. Patients with an ODI between 5 and 15 and baseline oxygen saturations above 92% were included in the analysis.

Results: Of the 42 patients who met the inclusion criteria, 9 (21%) were eventually established successfully on long term CPAP therapy resulting in significant improvements in ODI and sleepiness measured by the Epworth Sleepiness Score ($P = < 0.0001$ in both). All were male and presented with typical OSA symptoms. This group was compared to 33 patients who had either failed CPAP, had chosen to be referred for mandibular advancement splinting (MAS) or to pursue lifestyle changes. Comparing the CPAP and non-CPAP groups, the only difference in baseline characteristics was collar size (17.9in. versus 16.3in.; $P = 0.0026$) and gender ($P = 0.0449$). Of note, there was no difference in ODI, age, mean nocturnal or baseline saturations between the groups. Moreover, there was no difference in AHI indicating that the more comprehensive sleep study added little to eventual treatment decisions.

Conclusion: In our department we use a pragmatic approach to diagnosis and treatment of OSA by using a combination of overnight oximetry screening and patient treatment preferences. Even in patients with mildly deranged oximetry, limited sleep study results do not predict eventual long term treatment. Hence it is unlikely that oximetry is 'missing' significant CPAP treatable OSA.

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A motivational intervention to improve patient adherence to continuous positive airway pressure therapy: preliminary findings

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The treatment of choice for Obstructive Sleep Apnoea (OSA) is Continuous Positive Airway Pressure therapy (CPAP). However, the effectiveness of this treatment is limited by suboptimal adherence to the treatment. This study incorporated Health Beliefs constructs found to predict CPAP adherence before experience with CPAP into a theory driven Randomised Control Trial using a Motivational Interviewing (MI) intervention. Fifty-six consecutive patients (70% male, Mean age = 56.5, Mean RDI = 40.9) newly diagnosed with OSA who were naive to CPAP, were randomly assigned to a nurse-led MI+Standard Care intervention (26 participants, 54% male) or to Standard Care alone (30, 83% male). MI patients received 2, 45 min sessions of MI whilst commencing CPAP and a 30 min booster session after

1 month of CPAP experience. Objective CPAP adherence was assessed at 1, 2 and 3 months post-treatment initiation. Projected total recruitment at the conclusion of this randomised control trial is 120 patients. Preliminary findings are based on 17 MI patients and 17 standard care patients who had reached the 1 month post-treatment initiation time-point. Patients who received 3 sessions of Motivational Interviewing used CPAP 1.85 h more per night than patients who received standard care at 1 month post-treatment initiation (5.42 versus 3.57 h per night respectively, 95% CI = − 0.14 to 3.84). Patients who received MI also demonstrated more willingness to accept the treatment initially, with only 7% of patients declining to use the treatment at home as compared to 30% of patients in standard care who did not accept the treatment. Moreover, 59% of MI recipients used CPAP more than 6 h per night, while only 29% of standard care patients adhered to treatment at this level. Preliminary results indicate a positive trend towards more CPAP use after 3 brief sessions of nurse-led Motivational Interviewing as compared to standard care alone. The intervention can be delivered by nurses according to a manualized protocol, and the intervention is well accepted by the patients. Preliminary data supports an improvement in mean CPAP hours, consistent the Health Beliefs Model theory.

P244

A new method of measurement of respiratory movements in sleep apnea

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Considerable progress has been made over the last several decades in the correct diagnosis, treatment and follow-up of sleep disorders, especially sleep apnea. The gold standard for monitoring sleep disorders is polysomnography (PSG), however, because of technical difficulties and the cost of this method, new alternatives have become available. There has been a lot of interest recently in the detection of vital signals using non-contact radar technology that can be employed to measure respiratory movement. The aim of our study was to evaluate the analysis of the shape and amplitude of the signals from non-intrusive technology (non contact sensor) for monitoring respiratory movements compared to signals from the sum of thoracic and abdominal movements by means of piezoelectric sensor with the standard polysomnography (PSG) in the sleep laboratory carried out on 5 kinds of subjects. Two thousansd five hundred and ninety-one respiration events were analyzed from these subjects in all the different body positions. The non contact has been placed in a fixed place, in a distance of 125 cm from the floor and 60 cm from the subject. The signal from ''non contact sensor'' was concordant in 97.6% of the events. There are no differences when different non-contact positions are compared. The less satisfactory result was for the lateral decubitus position: when the subject's back was facing the non contact, concordance was 95,1%. The similarity of the signals from ''non contact sensor'' and from the sum was identical in 66.9% of the cases, 25.8% of the cases were similar and just in 7.3% of the cases was different. In conclusion, the ''non contact sensor'' measures the same information as the thoracic-abdominal bands do. The signal from ''non contact sensor'' is adequate in all the positions that have been measured and the quality of the signal is the same that the sum. Also, the non contact sensor offers several advantages: there is no contact with the subject, the sensor is very portable and the cost is very low. In future research, it is necessary to demonstrate if the ''non contact sensor'' can be used as an alternative to the thoracic-abdominal bands in the diagnosis of sleep apnea.

P245

Occurence of complex apneas in patients with OSAS during CPAP-titration

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Introduction: Complex apneas appear frequently in the initiation of CPAP therapy. Complex apneas are defined as each central apneic event occurring first during CPAP titration. Our aim was to investigate the prevalence of this respiratory event among apnea patients starting with CPAP therapy.

Materials and Methods: We investigated the data of patients being in our sleep lab in the first half of 2006, first diagnosed for OSAS and receiving CPAP-titration. We analyzed data from 50 patients, receiving three consecutive nights of PSG-one diagnostic and two nights of therapy (CPAP-titration). Parameters enrolled in analysis were: the number of the different kinds of apneic, hypopneic and complex apneic events, their duration, timing of the first complex apnea concerning sleep stage, body position and half of the night. Due to therapy we considered CPAP-pressure, sleep stage, body position and oxygen saturation in which the complex events occurred, especially the first one.

Results: Fourty-eight of the 50 enrolled patients (33 male, mean age 52 ± 7.1 years) got complex events during CPAP titration. More than 10 complex apneas per hour sleep (CAI) were seen in 10 of all (18%). The mean CAI was 15.6 ± 28.2 (1st night) and 8.2 ± 14.6 (2nd night). Within the first night, in 41.5% the first complex apnea was detected in N1 (51.3% 2nd night), 26.8% in N2 (17.9%), 14.6% in REM (23.1%) and 9.8% in SWS (2.6%). The mean duration of the first complex apnea was 15.1 ± 5.7 sec in the first night and 15.3 ± 4.8 sec in the 2nd night. The CPAP pressure at onset of the first complex apnea was 7 ± 2 mbar (1st night) and 7 ± 2 mbar (2nd night).

Conclusion: Complex apneas during CPAP titration seem to be very common. Mostly such events begin in N1. The onset may be linked to sleep stage, to applied CPAP pressure, to body position or other coexisting factors like sleep influencing diseases. Until now, the meaning and the effects of complex apneas are unknown. Our current practice is to try to eliminate these events by pressure modification, like change of CPAP-mode.

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Comparison between subjective and objective measurements in the evaluation of erectile dysfunction in patients with obstructive sleep apnea-hypopnea syndrome (OSAHS) (preliminary report)

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Background: Erectile dysfunction (ED) is associated with OSAHS with a reported incidence based on questionnaires of 30–45%. The aim of this study was to relate ED with OSAHS subjectively and objectively and also to evaluate the relationship between International Index of Erectile Function-5 (IIEF-5) and nocturnal penile tumescence (NPT).

Methods: Seventy male patients aged 26–64 years with a newly diagnosed OSAHS and treatment naïve were recruited from our Sleep Disorders Unit. Patients were asked to complete the IIEF-5. Exclusion criteria were: ED of duration less than six months, metabolic syndrome, neurological and cardiovascular diseases, psychic diseases, alcohol and drug abuse and patients under psychotropic drugs. Eligible patients underwent an overnight polysomnography (PSG) with simultaneous NPT, using the Rigiscan device.

Results: Thirty seven out of 70 OSAHS patients (52%) were found suffering from mild to severe ED according to IIEF-5 score.

Only 19 (51%) out of 37 patients with ED finally meet the inclusion criteria and were further evaluated with NPT. Fourteen of them (75%) had abnormal NPT, according Dacomed's criteria. Five of them didn't present any erection while nine presented only one erectile event and their case was classified as of organic etiology.

Conclusion: Our preliminary results showed that a large percentage of OSAHS patients suffers of ED of organic etiology. There is a good correlation between IIEF-5 and NPT measurements in the evaluation of ED in OSA patients. The study of the mechanisms involved in pathogenesis of ED in OSAHS as well as possible improvement after CPAP treatment is ongoing.

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Co-existence or residual sleepiness in treated patients with obstructive sleep apnea syndrome?

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The underlying mechanisms producing excessive daytime sleepiness (EDS) in patients with obstructive sleep apnea syndrome (OSA) are complex and poorly understood. A percentage of treated OSA patients remain sleepy during waking hours. The nature and causes of this continued sleepiness are variable and sometimes not fully clarified.

Aims: To evaluate the patients treated in the Sleep Laboratory of Hospital Pulido Valente, who have EDS after optimization of APAP (automatic positive airway pressure) treatment. To explore co-morbidities and determinant factors possibly related to this problem.

Methods: Data collection included all the 25 patients with EDS (Epworth scale) after APAP optimization refered to our laboratory for multiple sleep latency test (MSLT) in the last 4 years. Studied variables were: age, gender, body mass index, sleep habits, Epworth scale, co-morbidities, polysomnography (PSG) marks before and after/with APAP, APAP information and the MSLT results. A quantitative analysis was done, followed by the case study of each patient.

Results: Most patients (90%) were males with an average age of 56.1 years (SD = 9.3). 24 were obese or overweighted. All patients did APAP treatment for at least three months before MSLT, and had compliance >4 h 30 min. In spite of treatment optimization (according APAP information), 7 patients still have apnea/hypopnea index $>5\ h^{-1}$; 2 had periodic limb movement disorder; 6 had criteria for narcolepsy; 3 had idiopathic hypersomnia criteria; and 7 hadn't any abnormalities in MSLT, however 4 showed a reduced efficiency of sleep (PSG).

Discussion and Conclusion: Only 7 in 23 patients could be considered to have residual sleepiness linked to the OSA sub-optimal treatment. All the other patients may have "co-existent" EDS, explainable for other sleep disturbances, co-morbidities or idiopathic hypersomnia. The evaluation and management of the OSA patient suffering hypersomnolence after treatment is an opportunity for a case-management approach and to refine optimal OSA treatment, accepting that some situations will remain inexplicable or unsolved.

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Sleep disordered breathing and liver function

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Nonalcoholic fatty liver disease (NAFLD) is a common disorder of unknown aetiology typified by hepatosteatosis. Obstructive sleep apnoea-hypopnoea syndrome (OSAHS) is another common disorder with numerous systemic ramifications. Recent research suggests a possible link between the development of NAFLD and OSAHS. Based on the 2 hit hypothesis for NAFLD development, the intermittent, nocturnal hypoxaemia associated with OSAHS could represent the second hit. This study aimed to explore the prevalence of OSAHS in patients diagnosed with NAFLD and the prevalence of hepatic dysfunction in patients diagnosed with OSAHS.

Method: Fifty-one NAFLD patients and thirty OSAHS patients with no previous history of liver injury were surveyed. The NAFLD patients were given a questionnaire based on the Berlin and Epworth scoring systems. Their most recent blood tests were also obtained. The OSAHS patients completed a hepatic risk questionnaire. Their most recent sleep study was obtained and blood samples were taken.

Results: Based on updated normative values for alanine aminotransferase (ALT) [$M = \leq 30\ U\ L^{-1}$, $F = \leq 19\ U\ L^{-1}$], the proportion of abnormally high levels was raised in both NAFLD (74.5%) and OSAHS (53%). There was no significant difference between them ($P = 0.086$). Sixty-three percent of the NAFLD patients had a high risk for OSAHS on Berlin questionnaire. This subset of patients had a higher ALT than their low risk counterparts ($M = 71.39 \pm 37.8$, $P = 0.076$; $F = 49.00 \pm 31.7$, $P = 0.371$). Fifty percent of male and 78% of female OSAHS patients had elevated ALT (range = 13–89, mean = 33.85 ± 17.7, $P = 0.197$).

Conclusion: The results of this study suggest a high prevalence of sleep disordered breathing within NAFLD patients as well as a high rate of abnormal ALT within OSAHS patients. Further studies need to be undertaken to understand the precise mode of interaction.

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Effects on blood pressure after treatment of obstructive sleep apnea with an oral appliance with mandibular advancement, a 3 year follow-up

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Introduction: Obstructive sleep apnea (OSA) is a highly prevalent sleep disorder, 4% of males and 2% of females suffers from the disease even though they may not be aware of their condition.

Aim: The study purpose was to investigate if reduction of obstructive sleep apnea (OSA) with oral appliance (OA) treatment affects the patient blood pressure (BP) in a 3 months and 3 years perspective.

Methods: Twenty-nine consecutive patients with verified OSA; defined as AI >5 and/or AHI >10 h, received as a treatment an OA. The BP was measured at 3 study visits; before, after 3 months and after 3 years of treatment, respectively. The BP was measured twice with an electronic blood pressure monitor and the second value was registered as the BP of the visit. The treatment effect of OSA was measured after 3 months use by a repeated somnographic registration wearing the OA.

Results: A complete treatment response was defined as AHI <10 and this was achieved in 25 of 29 patients at the 3 months evaluation. At the 3 years follow-up there remained 22 patients in the study and they had a significant reduction of the systolic BP of -15.4 mm Hg and the diastolic BP of -10.3 mm Hg. This significance was received between baseline and the 3 months evaluation ($P < 0.001$), and, remained at the 3 years follow-up.

Conclusion: OA treatment reduced blood pressure in both 3 months and 3 years perspectives in patients with OSA.

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Patients with obstructive sleep apnea syndrome have different breathing route pattern in comparison with snorers

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Although nasal obstruction is associated with oral breathing and obstructive sleep apnoea syndrome (OSAS), it remains unknown whether increased oral breathing occurs in patients with OSAS free of nasal obstruction. This study evaluated the relationship between breathing route and OSAS in patients without nasal obstruction. We examined during an overnight polysomnography the breathing route of 41 patients (25 men; aged 26–77 years) with normal nasal resistance by using a nasal cannula/pressure transducer and an oral thermistor. The signal obtained classified each 30-sec epoch as either nasal,oral or oronasal.Thus, nasal breathing epochs were defined as epochs containing 3 consecutive phasic signals on the nasal channel only.Oral breathing epochs were defined as epochs containing 3 consecutive phasic signals on the oral channel only.Oronasal breathing epochs contained 3 consecutive phasic signals on both the nasal and oral channels.The occurence of nasal,oral and oronasal breathing was expressed as a percentage of the total sleep epochs analysed. Twenty-eight patients had OSAS [apnoea-hypopnoea index (AHI) >5) and 13 patients were simple snorers (AHI ≤ 5). Breathing route pattern in snorers (AHI ≤ 5) and apnoeics (AHI >5) AHI ≤ 5 AHI >5 p Nasal breathing (%) 87.9 62.4 <0.001 Oronasal breathing (%) 12.0 34.5 <0.001 Oral breathing (%) 0.1 3.1 0.007 Nasal breathing in snorers is significantly more frequent than in apnoeics who tend to spend significantly more epochs with oronasal and oral breathing.

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Sleepy severe OSA patients versus non sleepy severe OSA patients: demographic and polysomnographic characteristics based on ESS and MSLT data

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Study Objectives: To compare demographic and polysomnographic data of sleepy versus non sleepy severe obstructive sleep apnea (OSA) patients according to the Epworth Sleepiness Scale (ESS) and the Multiple Sleep Latency Test (MSLT).

Design: Comparative data collection.

Setting: Sleep Disorders Unit, Loewenstein Hospital-Rehabilitation Center, Raanana, Israel. Patients: 644 consecutive severe (Apnea Hypopnea Index (AHI) ≥ 30) adult OSA patients who underwent a polysomnographic evaluation in our Sleep Disorders Unit.

Measurements and Results: Sleepy severe OSA patients are slightly younger, more obese and surprisingly suffer less from hypertension than non-sleepy severe OSA patients. Sleepy severe OSA patients showed significant shorter sleep latency and lower percentage of SWS. They have higher Apnea Index (AI), higher AHI, both supine and lateral AHI; have a higher arousal index and a lower minimal SaO2 in REM and NREM sleep. After adjusting for confounders, logistic regression results indicated that higher AI is a significant risk factor for excessive daytime sleepiness based on both MSLT and ESS. In addition, lower percentages of SWS and minimal SaO_2 in NREM significantly differentiated sleepy from non sleepy severe OSA patients based on MSLT data. Shorter sleep latency differentiated sleepy from non sleepy severe OSA patients based on ESS data.

Conclusions: Sleepy severe OSA patients have more severe breathing abnormalities than non-sleepy severe OSA patients. Consequently, they have significantly lighter and more fragmented sleep, explaining the severe sleepiness during the day.

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Patient education in CPAP initiation – a problem based learning approach using small tutorial groups

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Purpose: To describe the theoretical framework and content of a nursing based educational program for CPAP initiation in patients with OSAS. Theoretical framework: Problem-based learning (PBL) has been used in a few patient education studies. Self studies and tutorial groups based on the problem-solving process are central. An integration of different areas of knowledge can be used. Motivation can be seen as an important factor for adherence. Drieschner et al. (2004) have described 6 internal determinants for treatment motivation; problem recognition, level of suffering, external pressure, perceived cost of treatment, perceived suitability of treatment, and outcome expectancy. Self-determination theory (Decci & Ryan 2000) describes different types of motivation and regulatory styles.

Results: The program is based on tutorial groups consisting of 4 patients and 4 spouses. Six 1 h sessions are included. As often in PBL, each session includes a brainstorming, followed by a discussion to formulate learning needs, a nurse led lecture related to the theme, as well as a second discussion and evaluation. The program integrates physiological, psychosocial and behavioral aspects such as follows; 1) What does obstructive sleep apnoea mean to you?, 2) What are the benefits of CPAP treatment?, 3) Practical training with CPAP device and mask, 4) How can you conquer problems and side effects and create a habit?, 5) What are the benefits of physical activity?, 6) What are the benefits of a wholesome diet?. Each session includes several video sequences where an experienced CPAP user describes the patient perspective. To increase self-determination and the motivation to engage in treatment each session focuses upon Drieschner et al. (2004) internal determinants, as well as relevant regulatory processes (Decci & Ryan 2000). Furthermore the patients receive a written educational material to be used for self-studies. The goal with the educational program is, besides to increase knowledge also to empower the patients, strengthen the internal locus of control and thereby increase adherence.

Conclusion: We describe a tutorial concept based on PBL. Patients are included in small tutorial groups in this educational program. Its efficiency will be tested in a large randomized trial.

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The side-effects to CPAP treatment inventory (SECI): testing regarding validity and reliability of a new self-assessment inventory of side-effects to CPAP treatment

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Purpose: To investigate the validity and reliability of the Side-Effects to CPAP-treatment Inventory (SECI).

Sample: A cross-sectional design was used. 350 OSAS patients (60% men) from 3 Swedish CPAP clinics with a mean use of CPAP treatment for 55.9 months (2 weeks-182 months) were included.

Instrument: SECI is a self-assesment psychometric instrument that includes 15 side-effects. Each side-effect includes 3 dimensions; frequency and magnitude of the side-effects and decrease of CPAP use, in total 45 items. Each item is to be answered on a five-point Likert type scale. The possible range for each scale can be 15–75. A higher score indicates a higher frequency and magnitude of side-effects, as well as a decreased self-rated CPAP use (i.e., adherence).

Statistical Processing and Analysis: To validate the SECI, item analyses were performed for the threes scales. These analyses included median and quartile score for separate items, item-total correlations corrected for overlaps and Cronbachs alpha if item deleted. A series of principal component analyses (PCA) were performed to investigate the dimensionality of the three scales of the SECI.

Results: Content validity was tested with good results by an expert group (4 MDs, 6 RNs, 1 BMA). The item analysis demonstrated good item-total correlations in the magnitude and adherence scales. Only one item demonstrated a correlation <0.3. The item-total correlations were generally weaker in the Frequency scale with three items <0.3. In the factor analysis two factors emerged. The first factor described symptoms, and the second described device related side-effects. The Cronbachs a of the three scales were adequate (0.75–0.83). The known group validity test showed that SECI was able to discriminate adherent and non-adherent CPAP users (i.e., patients using CPAP <4 h per night). The reliability was adequate for the subscales (0.72–0.86), except for the frequency subscales (0.62–0.67).

Conclusion: The high values of reliability and validity of this new instrument indicates that SECI can be used to measure side-effects to CPAP-treatment in OSAS-patients.

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Nasal surgery in obstructive sleep apnoea

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Although nasal surgery has limited efficacy in obstructive sleep apnoea treatment, some patients experience improvement. This study tested the hypothesis that post-surgery improvement is associated with increased nasal breathing epochs. Forty-nine OSA patients [mean apnoea-hypopnoea index (AHI) 30.1 ± 16.3 events h^{-1}] with symptomatic fixed nasal obstruction due to deviated septum were randomly assigned to either septoplasty (surgery group; 27 patients) or sham surgery (placebo group; 22 patients). Breathing route was examined during overnight polysomnography. Patients of the placebo group were non-responders, whereas in the surgery group, 4 patients were responders (14.8%) and exhibited considerable increase of nasal breathing epochs (epochs containing ≥ 3 consecutive phasic nasal signals), and 23 patients were non-responders presenting modest increase of nasal breathing epochs ($P<0.001$). The change in AHI was inversely related to the change in nasal breathing epochs ($R^2 = 0.775$; $P<0.001$); responders exhibited among the greatest increases in nasal breathing epochs. Baseline nasal breathing epochs were positively related to percent change in AHI ($R^2 = 0.610$; $P<0.001$). Responders had among the lowest baseline nasal breathing epochs; a cut-off value of 62.4% of total sleep epochs best separated (100% sensitivity, 82.6% specificity) responders/non-responders. Nasal surgery rarely effectively treats obstructive sleep apnoea. Baseline nasal breathing epochs can predict the surgery outcome.

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Low voltage electroencephalogram in patients with obstructive sleep apnea syndrome

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The purpose of this study was to verify the existence of a low voltage electroencephalogram (EEG) in patients with obstructive sleep apnea syndrome (OSAS), and relate this result with the sleep apnea index, or oxygen dessaturation. The hypothesis was that these patients had a low voltage EEG. The sample was made up of 45 men with OSAS, and 18 with periodic limb movements (PLM); 7 women with OSAS, and 22 with PLM, with ages between 30 and 60 years that were submitted to polysomnography. Spectral analysis of alpha, beta, theta and delta waves was performed in wakefulness, stage 1 and stage 2 of sleep, K complexes, and sleep spindles. Apnea-hypopnea index, periodic limb movements, oxygen dessaturation index, minimum oxygen and sleep efficiency were analysed. The results confirm our initial predictions that OSAS patients had low amplitudes in the EEG, in wakefulness, stage 1 and 2 of sleep. However, the lower amplitudes in OSAS do not correlate with the oxygen dessaturation index and minimum oxygen. These findings were observed only in the male population studied. A second phase of the study was performed in the frequencies that suggested the existence of two different populations of OSAS in the sample. We observed that the EEG had significant less amplitude in patients with higher body mass index (BMI) and poor sleep efficiency.

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CPAP compliance in UK group 2 driver licence holders with moderate to severe OSA

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It is known that CPAP therapy reduces accidents and improves alertness in drivers with obstructive sleep apnoea hypopnoea syndrome.

Aims of the study: 1. To look at CPAP compliance data in Group 2 driving license holders with moderate to severe sleep apnoea who were prescribed CPAP therapy.

Methods: Of all patients seen at the Sleep clinic of Birmingham Heartlands Hospital between August 2005 and June 2007, Group 2 license holders with an Oxygen desaturation Index (ODI) or Apnoea Hypopnoea Index (AHI) of 15 or more on diagnosis, who had completed at least 12 months since the start of CPAP therapy were analysed. Usage data was downloaded using the software provided by the different CPAP machine manufacturers. DVLA

reporting data was collected form the correspondence of DVLA to the Sleep consultant.

Results: There were 48 Type 2 license holders, of which 40 were Heavy Goods Vehicle (HGV) and 8 Passenger Carrying vehicle (PCV). All were male. There was wide variation in the hours of CPAP use with a range of 1.5 h month^{-1} to 308.8 h month^{-1} (0.05 h night^{-1} to 10.3 h night^{-1}). The median usage was 140.9 h month^{-1} (Corresponding to 4.7 h night^{-1}). 69% ($n = 33$) had evidence of having informed the DVLA, 31% did not ($n = 15$). There was no correlation between the hours of usage and evidence of having informed the DVLA. There was no correlation between hours of usage and BMI, Epworth Sleepiness score (ESS),and ODI/AHI.

Conclusion: 1. There was wide variation in CPAP usage in Group 2 driving license users. 2. 48% used it less than 4 h and 72% les than 6 h per night 3. Sleep physicians should closely monotor these patients regarding usage for road safety.

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Role of a second night limited channel sleep study in diagnosis of obstructive sleep apnoea in a district General Hospital

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It is known that OSA is not always picked up by a single nights study using oximetry or limited channel polysomnography.

Aim: To investigate whether a second additional limited channel sleep study identified further cases of OSA compared to a single set of measurements in patients referred to a sleep apnoea clinic in a district general hospital.

Methods: Sixty-four subjects with suspected OSA who underwent limited channel sleep study (Apnoescreen, Viasys) on 2 separate nights in close succession were analysed.

Results: 1st night 2nd night Number of patients 64 64 ODI >5 43 (67%) 43 (67%) AHI >5 26 (40%) 28 (43%) AHI >5 in current nights 5 (7.8%) 8 (12.5%) study but not the other ODI >5 in current nights 5 (7.8%) 6 (9.3%) study but not the other.

Conclusion: If using a cut off value of 5 for ODI and AHI, the total number of cases of OSA picked up on the two nights is similar and not statistically significant. However using a cut off of 5 for ODI and AHI, doing 2 sets of limited channel sleep studies increased the positive diagnosis by 31.2%.

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Sickle cell anaemia and sleep disordered breathing

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Sickle cell anaemia (SCA) is the most prevalent inherited disorder in inner cities in the UK and affects >10.000 patients of Afro-Caribbean origin in London alone. It is the most common cause of childhood stroke and is also associated with 'covert' infarction on MRI as well as poor growth and frequent pain. Sleep Disordered Breathing (SDB) and Obstructive Sleep Apnoea (OSA) are common in the general paediatric population and can have unique consequences such as failure to thrive and learning difficulties. Difficulties with attention and executive function and reduced IQ compared with siblings, which might be related to SDB, are common in SCA. However, although low oxyhaemoglobin saturation (SpO2) appears to predict CNS events and pain, there are few data on the prevalence of SDB in SCA. A retrospective study of 48 HbSS children (22 female), (half referred for overnight sleep studies, half selected from a clinic list) underwent overnight poligraphy. Median age was 12 (range 6 to 16) years. BMI's in all subjects were within the healthy or underweight range, median BMI z score -0.47 (range -2.13 to 0.96). For the whole group, the median AHI was 22.7 (range 7.7–54.3) events/hour and the median mean overnight SpO2 was 93 (range 81–98) %.There were no baseline differences between both groups in AHI. There was also no difference in AHI in children diagnosed with infarction ($n = 7$) compared with normal MRI ($n = 30$). AHI was not related to BMI but was higher in younger children ($R^2 = 0.16$, $P = 0.49$). No significant difference was seen in mean overnight SpO2 between the groups ($P = 0.8$) and no correlation between mean SpO2 and AHI ($P = 0.2$). All of the subjects presented with clinically significant sleep disordered breathing (SDB) on poligraphy. SDB may be more common than previously recognised in SCA. Defining OSA as an obstructive apnoea-hypopnoea index of five events or more per hour, all children in our study group showed some degree of OSA severity. However the origin of this sleep related breathing disorder appears to be different from that typically seen in non SCA children and warrants further investigation.

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Working memory ability during a 24-hour sleep deprivation paradigm in obstructive sleep apnea patients

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Very few studies examined the working memory ability (WM) especially the memory scanning process over sustained wakefulness in patients with obstructive sleep apnea syndrome (OSAS). The purpose of the present study was to assess whether the WM requiring the central executive in addition to the passive storage component, depend on the memory scanning level, using two versions of the Sternberg task, i.e. simple and complex, during the 24-hour period in OSAS patients compared to healthy controls. Thus we compared these data on both memory tasks requiring a similar memory load but differing in the level of memory scanning. After an 8-hour night sleep, the Sternberg tasks were administered during a 24-hour period in 12 OSAS patients and 6 matched controls. Before and after memory tasks, oxymetric parameters and visual analogue scales of arousal and alertness were performed to measure the effect of cognitive effort on these variables. The results show poorer performance in patients than controls only on the complex version ($T(548) = -2.43$, $P < 0.05$). The subjective ratings show a comparable complaint of increased sleepiness and fatigue throughout the 24h period in both groups while daytime oxygenation was significantly lower in OSAS patients. Subjective scores were also decreased by the memory tasks in both groups, as well as the daytime oxygenation. In OSAS patients, on the simple version, the percentage of correct responses was positively correlated with the nocturnal oxygenation ($rho = 0.59$, $P < 0.05$). On the complex version, the reaction time was negatively correlated with diurnal and nocturnal oxygenation ($rho = -0.60$, $P < 0.05$). No correlation was found with polysomnographic variables. Our data show impaired WM in OSAS patients when high level of memory scanning is required. This finding is more in favour of a deficit in the central executive (underlying attentional switching deficit) than storage component impairment. The strong association between oxygenation measures and performance on Sternberg tasks suggest that hypoxemia may be responsible for poorer WM in patients. Since frontal lobe involved in attentional processes and executive functions is sensitive to the hypoxic effects, the degree of hypoxemia appears to be a major factor in the pattern of WM dysfunction.

Sleep and Medical Disorders

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Are patients in peritoneal dialysis treatment just sleepy?

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Tiredness is insufficiently defined but often used and presented as a problem by dialysis patients, 12–97%, and it probably covers a number of conditions i.e. sleepiness, fatigue and depressive symptoms. Sleep problems is highly prevalent in peritoneal dialysis treatment, 49–73%. One simple question "Do you get too little sleep" discriminated patients with defined insomnia significantly in an earlier study. Other common problems in dialysis patients are symptoms of depression, 5–58% and anxiety, 12–52%. The aim of this study was to investigate correlations between sleepiness, fatigue, depression and anxiety in patients with peritoneal dialysis treatment at home. Fifty-five patients, 14 women and 41 men, mean 60.1 (SD14.4) years, with peritoneal dialysis treatment at home from six hospitals participated. Two psychometric tested questionnaires were used, The Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue scale and the Hospital Anxiety and Depression Scale (HADS). Finally the one simple dichotomous question "Do you get too little sleep?" was asked. Of 55 patients 50 reported fatigue. Patients with insomnia, according to definition, significantly answered that they got too little sleep ($n = 25$). Depression and anxiety symptoms were found in 12 patients. The correlation between fatigue and sleepiness was $r = 0{,}28$, $P < 0.05$, but the highest correlation was found between fatigue and depression, $r = 0{,}44$, $P < 0.01$. Correlation was also found between age and depressive symptom, $r = -0.28$, $P < 0.05$. Cronbachs alpha coefficient showed a reliability of 0.88 for FACIT-fatigue and 0.71 for HADS. In conclusion; sleepiness, fatigue, depression and anxiety seem to have a high extent of interference and the accumulation of the symptoms must be taken in account, when this probably increases the vulnerability and decrease performance status and health related quality of life. Further, strategies to identify patients at risk are essential in peritoneal dialysis home care. And the right treatment strategies and what to treat are further need to be explored.

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Abstract withdrawn

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Disturbances of normal sleep pattern as a possible reason of stress-induced visceral dysfunctions

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Sleep deprivation (SD), as other harmful stress conditions, may contribute to development of visceral disorders. It was shown (Pigareva, 2004) that SD (for 3 days, daily, 11:00–14:00) of Wistar rats during the 1st weak of pregnancy results in an increase of pup's mortality. The study was designed to clear whether the mortality was caused by the interruption of sleep rather than by manipulations producing SD. To answer this question, the same experiment was performed with the 2nd group of pregnant rats in the evening time (for 3 days, daily, 19:30–22:30), when sleep episodes are absent in rats, "nocturnal" animals. In this case the pup's mortality was even less than in control. The results support the idea that lack of sleep during the period of maximal sleep pressure, but not the stressful manipulations by itself, caused an increase in pup's mortality. We further hypothesized that disturbances of normal sleep pattern contribute to a development of stress-induced visceral disorders. To test this hypothesis we compared the severity of gastric erosion in rats stressed (3 h ulcerogenic stress: immobilization at low temperature +10 °C) in the morning (10:00–13:00) and in the evening (19:30–22:30). The severity of stress-induced gastric erosion was larger in the rats stressed in the morning. The results suggest that indeed disturbances of normal sleep pattern may aggravate stress-induced visceral disorders, at least, such as gastric ulceration. Activity of hypothalamic-pituitary-adrenocortical axis and circadian variation of corticosterone may be responsible for the circadian differences in the sensitivity of gastric mucosa to ulcerogenic action of stress in rats. On the other hand, hypothalamus is the important structure involved in sleep regulation. Also, cerebral cortex is involved in processing of visceral information during sleep (Pigarev, 1994). Results of this processing should be transmitted to the internal organs, probably via the hypothalamus engaging the hormonal systems. Thus, disturbances of the cortical processing of visceral information during SD may be an important mechanism of stress induced visceral disorders.

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Measure dim light melatonin onset before prescribing melatonin treatment!

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Background: Melatonin is a chronobiotic drug which advances sleep wake rhythm most if administered 5–6 h before Dim Light Melatonin Onset (DLMO). DLMO can be measured easily in saliva. DLMO is delayed in patients with chronic sleep onset insomnia associated with a delayed sleep phase syndrome. In our sleep clinic, specialized in the treatment of circadian sleep disorders, we see an increasing number of patients with melatonin treatment failures, due to inappropriately timed melatonin administration. In most patients DLMO was not measured before starting melatonin treatment. It takes probably a few months after stopping inappropriately described melatonin treatment, before the pre-treatment DLMO is reached, and consequently the appropriate time of melatonin administration can be determined. Therefore injudiciously prescribed melatonin can cause a considerable doctors delay. We reviewed the literature concerning relationship between DLMO and melatonin treatment results.

Methods: Pub Med and sleep and chronobiological societies abstracts (1990–2007) were searched using melatonin and dim light melatonine onset.

Results: In one study in adults with delayed sleep phase syndrome and in two studies in children with chronic idiopathic sleep onset insomnia the relationship between DLMO and the results of melatonin treatment on sleep onset was mentioned. All showed a significant correlation between DLMO and treatment effect, i.e. the later the DLMO, the more melatonin advanced sleep onset.

Furthermore we found two meta-analyses on melatonin in insomniac patients. One meta-analysis studied melatonin treatment effects in insomnia patients without measuring DLMO. This study did not demonstrate a significant treatment effect. The other studied the effects of of melatonin, administered before DLMO in patients with delayed sleep phase syndrome. This study, showed an evident treatment effect of melatonin.

Conclusion: Dim Light Melatonin Onset is not only important to diagnose circadian sleep disorders, but also to determine the optimal time at which melatonin has to be administered. To prevent unnecessary doctors delay in the treatment of insomnia with melatonine, DLMO should be measured before starting melatonin treatment.

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Sleep quality, hyperarousal, and sleeplessness behaviour in patients with a previous history of myocardial infarction

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Objectives: Stress and poor sleep are common in patients with coronary artery disease. This study was designed to identify possible variables of hyperarousal behaviour, sleep quality and sleeplessness behaviour that are related to myocardial infarction (MI) outcome.

Design: A logistic stepwise regression design.

Material and Methods: Self- administered questionnaires were answered by 186 patients with a previous history of myocardial infarction [mean (SD) age 66 yrs (9.7 yrs)]. The instruments used were the 26-item Hyperarousal Scale (H-scale), perceived sleep quality and the eight-item Vicious Cycle of Sleeplessness scale (VCS-8).

Results: The logistic model indicates that two variables of reactivity, introspectiveness and of environment factors on the H-scale and related to on the VCS-8, respectively were of important risk factors in patient with previous history of myocardial infarction ($O.R = 0.34$, $P < 0.0001$).

Conclusion: In patient with coronary artery disease with a previous history of myocardial infarction, hyperarousal and sleeplessness behaviour indicates to be important predictors for reinfarction and pre-mortality.

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Quantifying the differences in meaning between "sleepy", "tired", and "fatigued"

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Introduction: The terms sleepy, tired, and fatigued are often used interchangeably with potentially untoward effects. For example, a sleepy driver does not stop driving when a roadside billboard warns against being "fatigued". A common behavior therapy for insomnia instructs bedtime only when sleepy, but may be detrimentally interpreted as fatigue. Recently it has been suggested that questionnaires of daytime fatigue be used in the diagnosis and treatment of chronic insomnia since fatigue, rather than sleepiness, is a prominent daytime symptom. The aim of the present study was to quantify the meaning of the terms sleepy, tired, and fatigued using the Semantic Differential Technique (1) and to compare them in good and poor sleepers.

Method: From a principal components analysis a set of 13 polar opposite scales (e.g. pleasant-unpleasant, active-passive, light-heavy) was selected on the basis of their high loadings on the three most significant orthogonal components described as evaluative, activity, and potency. The concepts of "sleepy", "tired", and "fatigued" were then rated using these 13 scales by 125 young adult university students, half of whom were poor sleepers with a PSQI score >6.

Results: Fatigued was judged as more negative, active, and potent than sleepy with tired rated intermediately but closer to fatigued. There were no differences in these ratings between the good and poorer sleepers. The quantified meanings of these terms could also be visualized in 3-Dimensional space and the spatial distance between them calculated. There was a significant distance between sleepy and fatigued in this semantic space.

Conclusions: This semantic differential technique showed a considerable difference in the meanings of sleepy and fatigued with tired intermediate but closer to fatigued. In this study we found no difference between good and poor sleepers in these meanings, however, clinically diagnosed chronic insomniacs should also be studied. In any case these results highlight the need for sleep researchers and clinicians to recognize the distinctions between the terms sleepy, tired, and fatigued.

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Restless leg syndrome frequency in Turkish hemodialysis patients: depression and quality of life

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Background: The prevalence of restless legs syndrome (RLS) in hemodialysis patients ranging from 6.6 to 83% has been reported in different case series. The aim of this study was to assess the frequency of RLS in the hemodialysis patients, and to explore depression and associated with detrimental impact on quality of life.

Methods: The diagnosis of RLS was made using the criteria of The International Restless Legs Study Group. Each subject completed 3 questionnaires, which included the Beck depression inventory, Short Form-36 (SF-36) quality of life scale and The Epworth Sleepiness Scale (ESS). The following data were collected: age, gender, biochemical parameters including hemoglobin, serum ferritin, Kt/V index. All patients were interviewed and clinically examined by a qualified neurologist. The data on the patients with and without RLS or clinically polneuropathy (PNP) were compared.

Results: There were 41 male, 40 female, with a mean age of respectively 52 ± 15, 53 ± 17 years. RLS and PNP were found by 12% and 47%, respectively. ESS high score were only 7%. Beck depression inventory score were high with RLS compare without RLS patients (28.9 ± 9, P:0.007). General health in the RLS patients, physical functioning in the PNP patients were significantly lower score (GH: 20.7, P:0.036; PF:10.5, P:0.000). We did not observe any association between hemoglobin, serum ferritin and Kt/V index in the RLS patients. But, Kt/V index in the PNP patients were low.

Conclusion: The 12% frequency of RLS in hemodialysis patients was partly lower than that reported from similar studies in other countries. The presence of RLS and PNP in hemodialyzed patients negatively affects quality of life. RLS may be contribute to occurrence of depression in these patients. Diagnosis and effective treatment of sleep disorders will improve survival.

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Sleep features in a patient with dementia plus amyotrophic lateral sclerosis

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Amyotrophic lateral sclerosis (ALS) with frontotemporal dementia (FTD) is characterized clinically by frontal and neurological signs and symptoms, and pathologically by localized atrophy of frontotemporal lobes and neuronal ubiquitin-positive inclusion. There is a well-established link between ALS and FTD. Signs and neuropsychological features may precede or follow the onset of motor dysfunction. Sleep disturbances are found in the course of most dementing syndromes but these disorders have not systematically been investigated in ALS-FRD. We describe polysomnographic (PSG) findings observed in a patient with ALS -FTD. We carried out two consecutive video polysomnographic (vPSG) recordings according to standard methodology in a 56-year-old female that presented a progressive behavioural disorder that started four years ago. Neuropsychological studies showed a severe affectation of executive function with relatively preservation of episodic memory. Magnetic Resonance Imaging (MRI) of the brain showed cortical-subcortical atrophy and cerebral SPECT demonstrated prefrontal hypoperfusion. In two years patient showed progressive atrophy in extremities and fasciculations. Neurophysiological study showed findings compatibles with ALS. The biochemical and hormonal studies were normal. We observed an abnormal sleep architecture with REM sleep onset and an irregular distribution of REM sleep in both vPSGs. The number of awakenings was increased Typical images of NREM stages (spindles and K-complexes) was reduced. We observed slow wave sleep, REM sleep, total sleep time and efficiency index decreased too. vPSG recordings documented bursts of electromyographic activity in relation with oromandibular stereotypes. We report the following sleep alterations in ALS-FTD: Alterations in sleep architecture with REM sleep onset, and irregular distribution of REM sleep. Alterations in microstructure of sleep with reduced NREM sleep waveforms. Sleep Efficiency Index and sleep efficacy were reduced. vPSG allowed us to verify the persistence of oromandibular sterotypies during sleep.

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Spectral analysis of heart rate variability during sleep in patients with neuromuscular disorders and other extrapulmonary restrictive diseases

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Objective: Patients with chronic extrapulmonary restrictive disease (CERPD) are subject to various forms of sleep disordered breathing. We evaluated the capacity of the power spectrum analysis (PSA) of the heart rate variability to differentiate between obstructive apnoeas (OSA), prolonged desaturation events (PDE) of non-obstructive type denoting hypoventilation and periodic limb movements (PLMs).

Material and Methods: Ten control subjects, 20 patients with OSA, 10 patients with PLMs, 10 patients with CEPRD and PDE only, and 7 patients with CEPRD and mixed sleep pathology were evaluated. All participants underwent full night polysomnography. PSA were performed on ECG segments of 256 seconds length derived from a 20 min pre-sleep awake period, from periods of normal event-free sleep in different sleep stages, and from periods of interrupted sleep due to OSA, PDE and PLMs. The PSA of the HRV were quantified in two frequency bands: Low frequency (LF: 0.02–0.15 Hz) mainly sympathetic depended and high frequency (HF: 0.15–0.4 Hz band) parasympathetic depended. The ratio between LF and HF was subsequently calculated. The values of LH, HF and LF/HF observed during the pre-sleep awake period were used as the baseline reference values for the rest of the study.

Results: OSA and PLMs had a marked effect on all measures of PSA increasing LH, FH and LF/HF ratio. PDE significantly increased the LF and the LF/HF ratio but the HF spectral power remained the same.

Conclusion: HRV can differentiate between OSA/PLMs and PDE. Since polysomnography is an expensive and complex test the assessment of HRV may have an important role in the early diagnosis and follow up of sleep disordered breathing in patients with CEPRD.

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CSF hypocretin-1 in Parkinson's disease with and without dementia

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Background: Excessive daytime sleepiness (EDS) is frequent in Parkinson's disease (PD) and has been proposed as an associated clinical feature of PD with dementia (PDD). Neurophysiological studies have suggested that EDS in PD has narcoleptic features, but studies measuring hypocretin-1 cerebrospinal fluid (CSF) levels have shown inconsistent results. Recently, hypocretin cell loss has been reported in brain tissue from PD patients, correlating with advanced disease.

Objective: To assess CSF hypocretin-1 levels in both PD without (PDND) and with dementia (PDD).

Methods: Patients with PDND ($n = 21$), PDD ($n = 20$), and age-matched controls with no neurological disorder ($n = 22$) were studied. EDS was assessed using the Epworth Sleepiness Scale (ESS) with the assistance of the caregivers when needed. CSF levels of hypocretin-1 were determined using a direct radio-immunoassay (RIA) commercial kit.

Results: Patients with PDD, PDND and controls were similar in terms of age and gender. Patients with PDND and PDD had similar disease duration (10.2 ± 4.5 versus 10.15 ± 6.9 respectively) and higher ESS scores than controls (PDD = 13.25 ± 5.00, PDND = 10.34 ± 5.60, controls = 5.32 ± 2.73) ($P < 0.0005$). The PDD group had a trend towards higher ESS scores than PDND (t test; $P = 0.089$). No differences in CSF hypocretin-1 levels were observed among the three groups (in $\mathrm{pg\,mL^{-1}}$: controls = 321.15 ± 47.15; PDND = 300.99 ± 58.68; PDD = 309.94 ± 65.95). There was no correlation between CSF hypocretin-1 levels and both disease duration ($r = -0.03$; $P = 0.8$) or ESS scores ($r = -0.02$; $P = 0.8$).

Conclusions: PDD patients had slightly higher ESS scores than PDND but CSF hypocretin-1 levels were similar in both groups. We suggest that the hypocretin cell loss described in brains with advanced PD-a population of patients similar to those studied here-is not associated with a decrease in lumbar CSF hypocretin-1 levels.

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A case series of patients with catathrenia from a single UK sleep centre

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Introduction: Catathrenia (sleep related groaning) is a recently recognised parasomnia, now included in the International Classification of Sleep Disorders (1). It is benign, but can have a significant social impact. Knowledge is confined to a few case series, in which associations with sleep disordered breathing and variable responses to different treatments have been reported (2–3). Here we add to the existing literature by reporting our centre's experience of catathrenia.

Patients and Methods: Thirteen patients (5 male) diagnosed with Catathrenia between August 2004 and January 2008. Retrospective review of case notes and video-polysomnographic data.

Results: Mean age of symptom onset was 24.0 ± 11.46, age at PSG was 34 ± 9.7 years. The majority (11) presented with reports of groaning or unusual noises during sleep. Ten reported EDS and 8 disturbed and unrefreshing sleep, although only 5 had an ESS ≥11. Snoring and/or witnessed apnoeas were reported by 7 patients. Three patients had a family history of catathrenia and 1 of parasomnia. Mean TST was 437 ± 73.1 min and SE of TIB was 86% ± 12.2. Five patients were also diagnosed on PSG with OSA or UARS. Of those without OSA/UARS, the AHI was 10.5/hr ± 8.1 with 3 patients having an AHI ≥ 10/hr. Two patients had mild PLMS. Treatment: Six patients were given reassurance alone. One tried a mandibular advancement device, but discontinued as it was ineffective. Six started CPAP (4 with OSA/UARS, 2 for catathrenia alone). Three patients found CPAP ineffective; 1 is awaiting follow up; 2 continue successful treatment of severe OSA, but catathrenia persists.

Conclusion: Although the usefulness of CPAP has been reported in some cases of catathrenia (2,3), this has not been our experience. Less sophisticated respiratory sleep monitoring could result in some cases being misdiagnosed and treated as central sleep apnoea. Further work is required to establish the mechanisms of catathrenia and determine effective treatment.

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Objective and subjective parameters of depression, sleepiness and sleep quality in different sleep disorders

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Objective: Daytime sleepiness and disturbed sleep quality are core symptoms of sleep disorders. In addition, depressive symptoms are often reported. In the present study, we examined the possible interrelationships of daytime sleepiness, sleep quality and depressive symptoms in three major sleep disorders: obstructive sleep apnea (OSA; $n = 20$), restless legs syndrome (RLS; $n = 18$) and psychophysiological insomnia ($n = 11$).

Method: Otherwise healthy subjects without a history of psychiatric disorder or psychotropic medication use were included. All patients had a regular sleep wake cycle. The Epworth Sleepiness Scale (ESS) for daytime sleepiness assessment and the Pittsburg Sleep Quality Inventory (PSQI) for subjective sleep quality were administered. Participants filled in the Beck Depression Inventory (BDI) as indicator of subjective depression and underwent an standard psychiatric interview; observer ratings comprised the Hamilton Depression Scale (HAMD) and the Hamilton Anxiety Scale (HAMA).

Results: ESS scores were significantly higher in OSA compared to insomnia patients. PSQI and HAMA scores were highest in insomnia, whereas the BDI did not differ significantly among groups. HAMD scores were significantly higher in the insomnia compared to OSA. As assessed by linear correlations, measurements of sleepiness, disturbed sleep and depression were correlated differently in the three patient groups. HAMD and BDI scores correlated significantly in insomnia and RLS, but not in OSA patients. However, the BDI correlated with subjective sleep quality (PSQI) in this group. On the other hand, the HAMD and the HAMA correlated with the ESS in OSA.

Conclusion: As expected daytime sleepiness was highest in OSA, whereas insomnia patients showed the highest depression and anxiety scores and the worst subjective sleep assessment. The BDI, subjective assessment of depression, was unable to differentiate among groups, suggesting a limited sensitivity. Interestingly we found a relationship of the ESS and the HAMD/HAMA in OSA, suggesting a relationship between sleepiness and depression/anxiety in these patients, which was not present in insomnia and RLS.

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Polysomnographic findings in Cuban patients with hereditary spinocerebellar ataxia (SCA-2)

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Spinocerebellar Ataxia type 2 (SCA-2) is a molecularly well defined but rare neurodegenerative disorder. One of the main characteristics of SCA-2 disease progression is the early affection of sleep-relevant cerebral areas like the olivopontocerebellar region of brainstem, thalamus, substantia nigra, and anterior horn. Cortical involvement is only apparent in the terminal stage of the disease. A previous study of eight German SCA-2 patients with a medium-sized CAG expansion (38–49) and different disease duration (3–31 years) yielded REM sleep loss and an increase in SWS in advanced disease stages. Periodic leg movements, apnea or hypopnea were not prominent. We now present data on a larger sample of 28 Cuban SCA-2 patients (CAG expansion 34–44, disease duration 2–20 years) and age- and sex-matched healthy controls. Replicating earlier findings, disease progression in Cuban patients was accompanied by a decrease in REM sleep and an increase in SWS at the cost of light sleep. Unlike the German patients, however, clinically relevant leg movements and central apnoeic events were observed in several patients of the Cuban group. The current data strengthen the hypothesis that sleep may prove a valuable marker of disease progression.

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Identifying the concepts contained in health status measures in sleep medicine practice and research using the International Classification of Functioning, Disability and Health as a reference

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Objectives: To systematically identify and quantify the concepts contained in health status measures in sleep medicine practice and

research using the International Classification of Functioning, Disability and Health (ICF) as a reference.

Methods: We conducted a systematic literature review to identify and select generic and condition-specific measures/questionnaires hitherto applied in sleep medicine practice and research. We examined the contents of the selected measures by extracting the meaningful concepts contained in the items of the measures and through linking them to the ICF by two independent researchers using established linking rules. The frequencies of ICF categories representing the concepts contained in the instruments built the basis of the descriptive analysis and content comparison.

Results: We identified and linked eighty patient-administered instruments which could be extracted through the original articles. Of these, twenty-six were generic and fourteen were symptom-related (eight sleepiness/five fatigue/one tirednees). Among the condition-specific instruments we encountered twenty-five insomnia, eight Sleep Apnea, four Restless Legs Syndrome and four Narcolepsy questionnaires. Overall, the 2805 meaningful concepts contained in the items of all the sleep instruments were linked to 257 different ICF categories. Predominantly these were linked to the ICF component body function & structures (1865 concepts/117 categories), followed by 485 concepts linked to 102 categories of the component activities & participation, and 145 concepts linked to 25 categories of the component environmental factors. In addition 75 concepts were attributed to the last ICF component, personal factors. The individual instruments vary greatly with regard to the ICF categories covered.

Conclusion: The ICF provides a useful reference to identify and quantify the concepts contained in health status measures used in sleep medicine practice and research. This comparative study can aid researchers and clinicians to choose the most appropriate instrument for a specific comprehensive and/or differential purpose.

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Sleep disturbances as a predictor of long term sickness absence due to depression

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Objectives: Disturbed sleep has been suggested to increase the risk of long-term sickness absence, but most studies on this issue have been based on cross-sectional designs and self-reported sickness absence data. We prospectively examined disturbed sleep as a predictor of long-term sickness absence due to depression using national health records.

Methods: The sample included 53,706 employees (80% women) with no history of depression at study entry (the Finnish Public Sector study). They responded to a survey on sleep disturbances in 2000–2004 and the responses were linked to the records on subsequent overall long-term sickness absence and absences due to mental disorders (>90 days) obtained from the Finnish Social Insurance Institute register. Sleep disturbances were defined as reported problems with sleep in 5–7 nights a week using 4-item Jenkins Sleep Problems Scale. We used Cox proportional hazard models to estimate the association of sleep disorder with new long-term sickness absence. Adjustments were made for age, sex, socioeconomic position, health risk behaviour and psychological distress.

Results: 22 % of the study population experienced sleep disturbances. During a mean follow-up period of 3.4 years, 307 participants had a long-term sickness absence due to depression. Employees with sleep disturbances had 1.9 (95% CI 1.4 to 2.6) times greater risk of subsequent sickness absence than those sleeping well. The corresponding hazard ratio for overall long-term sickness absence was 1.8 (95% CI 1.6 to 1.9). However, there was no association between sleep disturbances and long sickness absence due to mental disorders other than depression.

Conclusion: These data provide prospective evidence on the status of sleep disturbances as an independent predictor of long-term sickness absence due to depression. Frequent sleep problems should be given more attention in the prevention of long-term work disability and depression.

Ageing

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High prevalence of circadian rhythm sleep disorder, irregular sleep-wake type in patients with senile dementia of Alzheimer's type

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Background: Disorganized sleep-wake patterns are often observed in elderly people with organic brain damages such as dementia or neurodegeneration. Some demented elderly show very severely fragmented sleep-waking, sleep period were divided into 3 or more segments due to chronic insomnia and daytime sleepiness. Irregular sleep-waking in these demented patients are usually classified as circadian rhythm sleep disorder, irregular sleep-wake type. Generally, irregular sleep-wake type is believed to be very rare sleep disorder, however, it may be more popular than we expected in persons with organic brain damages.

Study subjects and Methods: We measured rest-activity by wrist actigraph for 2–4 weeks and estimated behavioral and psychiatric symptoms in 137 patients with senile dementia of Alzheimer's type (average age, 77.3 years old) and age-matched 43 healthy elderly controls (78.1 years old).

Results & Discussion: Alzheimer patients showed constant decline in sleep efficiency determined with the progression of dementia scored by Functional Assessment Staging Test (FAST). Sleep efficiency in later dementia stage, especially after FAST6, was less than 60% on average. While total sleep bouts showed no significant change across the dementia stages, but showed very large interindividual variety. By contrast, daytime sleep bouts constantly increase with progression of dementia. We classified their disturbed sleep-waking into three types, insomniac, hypersomniac, and irregular sleep-wake type using average plus/minus 2SD values in the non-demented control group as cutoff points. As a result, prevalence rate of sleep disturbances, either of 3 types, steeply increased with progression of dementia. Among these disordered sleep types, insomniac type remained one third of them, and the prevalence of irregular sleep-wake type was constantly beyond that for hypersomniac or insomniac types.

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Scoring of leg movement according to the ASDA report 1993 and the WASM standards 2006: effects on age-related changes of periodic leg movement indices in 172 healthy subjects

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Introduction: In healthy subjects without sleep disturbance the incidence of periodic leg movements (PLMs) and PLM-related arousals increases with age. Here we report the effects on indices of PLMs and PLMs associated with cortical arousals dependent on the applied rules for scoring: ASDA Report 1993 (Bonnet et al. Sleep 16) versus WASM Standards 2006 (Zucconi et al. Sleep Medicine 7) in a large population of healthy controls of all adult age groups, collected within the European multi-center project SIESTA.

Methods: Sleep stages, leg movements (LMs), PLMs, as well as arousals according to ASDA and WASM rules were automatically identified by means of Somnolyzer (including a structured quality control procedure) in polysomnographic recordings of 172 healthy volunteers. Subsequently, the PLMI (index of PLMs/hr of sleep) and PLMAI (index of PLMs associated with an arousal/hr of sleep) are computed.

Results: Median and interquartile range for PLMI according to ASDA and WASM were: young adults (YA, 20–39 years, 25 m, 26 f): 0.0/0.7 and 1.8/2.8; middle aged (MA, 40–59 years, 24 m, 26 f): 0.5/3.4 and 3.0/10.2; elderly (ED, 60–95 years; 33 m and 38 f): 8.3/24.9 and 27.3/38.0. While changes in the definition of LMs increased PLMAI only slightly if the definition for the association between PLM and arousal is kept unchanged (YA: 0.0/0.0 and 0.0/0.3; MA: 0.0/0.2 and 0.2/1.0; ED: 0.7/2.8 and 3.5/8.3), PLMAI increased significantly due to the new definition that the arousal may start even before PLM onset, as long as it does not end more than 0.5 s prior to PLM onset (YA: 0.9/1.9; MA: 1.3/6.1; ED: 10.3/17.8). Increases in the PLMI and PLMAI were significant at $P < 0.001$ in all age groups.

Discussion: The choice of the classification rule for the scoring of LMs affects significantly the PLMI/hr of sleep. Due to the higher sensitivity of the WASM rules, the indices increase in all age groups (in the average by 2, 6 and 13 for YA, MA and ED, respectively). The significant increase in the PLMAI, however, is predominantly affected by the change in the definition of the association between PLMs and arousals.

Conclusion: New normative values are presented for PLMI and PLMAI according to the WASM and AASM criteria (Silber et al. 2007 American Academy of Sleep Medicine).

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Age-related changes in low frequency delta sleep and executive functioning in healthy elderly

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Age-related declines are found in sleep and in aspects of frontal lobe/executive functioning (e.g. non-verbal planning and verbal fluency). Recent studies have shown an interrelationship between these. In particular, Anderson and Horne (2003) demonstrated that aspects of executive functioning were associated with low frequency delta (< 1 Hz) during the first non-REMP, particularly in the left frontal area, in healthy individuals aged 61–75 years (mean age 67 y). Six years later, 11 of the Anderson and Horne (2003) original cohort of 24 were recruited for follow-up sleep EEG recordings and neuropsychological testing. Participants had remained healthy and were now aged 70–79 years (mean age 73 years). They continued to have similar sleeping habits and levels of daytime sleepiness as before. Non-significant declines were found in low frequency delta in the frontal regions, as well as in Verbal Fluency and Wisconsin Card Sorting Task (WCST) performance. Declines in the Tower of London (TOL) were found to be significant. The relationship between low frequency delta and all of the executive functioning tasks was no longer evident. It seems that the relationship between low frequency delta and executive functioning in older individuals may be vulnerable to convergence at the ages 70–79 years.

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Social cognition & prefrontal cortex impairment: sleep deprivation versus healthy ageing

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Sleep deprivation causes temporary and selective impairment in frontal lobe functioning in young adults. An earlier study (Harrison et al. 2000) from our laboratory has shown that these temporary changes are comparable to the changes in cognition associated with healthy ageing. The present study attempts to extend these findings into the area of social cognition (shown by other studies to be linked to frontal lobe function) in non-sleep deprived older participants, and compare these to changes in a young sleep deprived group. The older group was aged 65–79 years (mean 72 years; $n = 16$), the young control group aged 20–26 years (mean 22 years; $n = 16$) and the young sleep deprived group (36 h without sleep) was aged 20–25 years (mean 22 years; $n = 16$). All participants underwent neuropsychological testing at a similar time of day, including the Go/No-go, Emotional Prosody and Ekman 60 Faces. Each task had different levels of difficulty, to measure the effects of ageing on various aspects of social cognition. The older group performed significantly worse than both young groups on the more complex versions of the tasks but not on the more simple versions. Incidentally, these more complex versions of the tasks were those which the sleep deprived young group performed significantly worse on compared to the young control group. The results indicated that aspects of social cognition that are found to be affected by sleep deprivation are also affected by ageing. Moreover, the older group were not found to be comparable to a young sleep deprived group, as they performed significantly worse.

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Objectively measured daytime sleepiness in elderly primary insomnia patients

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Several studies indicate that non-elderly primary insomnia patients display normal or reduced objective sleepiness despite complaints of daytime sleepiness or fatigue. However, little research has examined daytime sleepiness in elderly individuals with primary insomnia. We examined multiple sleep latency test (MSLT) data in a large sample of elderly primary insomnia patients. After meeting DSM-IV criteria for primary insomnia, including a report of sleepiness, tiredness, or fatigue, 263 patients (173 f, 90 m; mean age 71.3 years, range 65–87) underwent polysomnography followed by an MSLT as part of the screening/baseline process for a randomized clinical trial. Data were collected at 21 sites and scored at a single site by technologists with established reliability. Mean MSLT latency for the entire group was 9.7 ± 4.7 min. Males had lower mean MSLT than females (8.7 ± 4.3 versus 10.2 ± 4.8 min, $P = 0.016$). Males and females did not differ in age nor was age associated with MSLT scores. Seventy one (27.0%) patients had MSLT scores < 6 min, a value that has been proposed as a criterion of excessive daytime sleepiness, and 169 (64.2%) patients had MSLT scores < 11 min, a value that has been proposed as a criterion of moderate daytime sleepiness. Mean MSLT for these elderly primary insomniacs was significantly lower than the pooled mean latency (12.6 ± 5.1 min; one-sample z-test, $P < 0.001$) for healthy older adults based on four published studies (total $n = 122$; aged 60–69). Mean MSLT in our sample was also significantly lower than the mean for a representative sample of the US general population (11.6 ± 5.2 min; one-sample z-test, $P < 0.001$). These data indicate that physiological sleepiness is common in elderly individuals with primary insomnia and suggest that ideal treatment would improve alertness as well as sleep in this population.

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Understanding quality of sleep in later life: the PSQI and subjective sleep quality

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Background: Good sleep in later life reduces risk of falls and depression, and is essential for maintaining activity and performance levels. Sleep is fundamental to health and well-being, with lack of sleep increasingly shown to impact on cardiovascular risk factors and diabetes. It is therefore surprising that sleep has been neglected by social gerontologists.

Aims and Methods: The paper examines the social patterning of sleep problems in later life, using the Pittsburg Sleep Quality Index (PSQI), which assesses sleep quality and disturbances over a one month time interval. Self-completion questionnaires were sent to 2,400 people aged 65+ (equal numbers of men and women, and age 65–74 and 75+) via 10 General Practices in South-east England1. A response rate of 50% was achieved. As well as the global PSQI score, the 7 components of the PSQI are analysed separately and related to socio-demographic characteristics.

Results: The conventional cut-off criterion for poor sleep quality is PSQI > 5. Using this criterion 48% of older people were 'poor sleepers', but in terms of 'subjective sleep quality' (PSQI component 1) only 16% of older people rated their sleep as 'fairly bad' or 'very bad'. The paper examines what factors account for this seeming anomaly between PSQI scores and 'subjective sleep quality'. Frequent wakenings during the night to go to the toilet or for other reasons resulted in an elevated PSQI score, but among older people these aspects were unlikely to result in self-rating sleep as 'bad'. Habitual sleep efficiency and taking sleeping medication were strongly related to poor subjective sleep quality for both men and women.

Conclusions: Greater attention needs to be paid to older people's subjective assessment of their sleep quality, since this has the greatest impact on their well-being, quality of life and whether they consume sleeping medication.

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The cardiovascular response to arousal from sleep is not influenced by the presence of flow limitation in older adults

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Introduction: Patients with sleep disordered breathing (SDB) have recurrent arousals that occur at the termination of respiratory events causing large blood pressure (BP) and heart rate (HR) surges; greater than those in healthy adults. This may contribute to sustained hypertension in these patients. The frequency of arousal from sleep increases in older adults, as does prevalence of SDB. However, relatively little is known about cardio-respiratory responses to arousal in older adults. This study tested the hypothesis that the presence of flow limitation on arousal augments cardio-respiratory responses in older adults.

Methods: Seven healthy mild snorers (60–75 years) were studied. Continuous positive airway pressure (CPAP) was applied and

arousals from stage-2 sleep were induced by auditory tones under 2 conditions: a non flow limited (nFL) condition with clinically effective CPAP levels applied (3.7 ± 0.4 cm H_2O) and a FL condition where mild resistance was produced by reducing CPAP pressure (2.9 ± 0.4 cm H_2O). The average number of arousals per subject was 15 ± 2 FL and 14 ± 2 nFL.

Results: Prior to arousal, FL compared to nFL conditions had lower minute ventilation (Vi, 5.5 ± 0.6 versus 7.8 ± 0.5 L min^{-1}), tidal volume (Vt, 420.6 ± 110.6 versus 602.5 ± 27.6 mL) and peak inspiratory flow (PIF, 17.3 ± 1.8 versus 24.1 ± 1.8 L min^{-1}) ($P<0.05$) but end tidal CO2, HR and BP were similar. Following arousal from FL compared to nFL conditions there were greater increases in Vi, Vt and PIF ($P<0.01$). This was mainly due to lower pre-arousal baselines although post-arousal peaks tended to exceed those achieved under nFL conditions (Vi, 13.0 ± 0.8 versus 11.8 ± 0.4 L min^{-1}; Vt, 1182.2 ± 72.9 versus 1065.8 ± 65.8 mL; PIF, 44.6 ± 3.5 versus 38.9 ± 1.9 L min^{-1}) but differences were not significant. HR and BP responses were similar between both conditions.

Conclusion: In agreement with previous observations in young healthy adults, cardiovascular responses on arousal from sleep in older adults are independent of respiratory conditions prior to arousal and the magnitude of respiratory responses on arousal. Hence larger cardiovascular surges associated with events during SDB may not be a consequence of flow limitation.

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Residual effects of zopiclone 7.5 mg and temazepam 20 mg on actual driving in healthy elderly volunteers

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Objective: A major problem of hypnotic drug use is residual sedation the morning after bedtime administration. This constitutes a particular safety hazard for patients who drive a car the next morning. Information on the severity of residual effects is mainly derived from young healthy volunteers' studies. However, the majority of users of hypnotics are elderly, i.e. 55 years or older, who may have an increased sensitivity to the residual effects of hypnotics. Still, no studies exist assessing the residual effects of hypnotics on driving performance in this population. The aim of this study was to investigate the residual effects of temazepam 20 mg and zopiclone 7.5 mg on driving performance in healthy elderly subjects. These drugs were selected because they are among the most frequently prescribed hypnotics in many countries and comparable studies have been conducted with zopiclone in young subjects.

Methods: Eighteen healthy elderly subjects (mean age $\pm$ SD: 64.3 ± 4.4 years) participated in a double-blind, three-way cross-over study. They received single oral doses of zopiclone 7.5 mg, temazepam 20 mg, and placebo at bedtime. Cognitive tests of tracking, divided attention, inhibitory control and memory were conducted the next morning, at 8:45 h and 11:45 h after administration. Between 10 to 11 h after administration a standardized driving test on a primary highway in normal traffic was performed.

Results: Driving was significantly impaired after administration of zopiclone 7.5 mg, but not after temazepam 20 mg. Delayed recall and recognition of verbal information, and inhibitory control were significantly worse after ingestion of zopiclone 7.5 mg. Temazepam 20 mg did not result in a significant impairment of cognition.

Conclusion: Bedtime administration of zopiclone 7.5 mg caused a significant deterioration of driving performance the next morning. In contrast, temazepam 20 mg was free from residual effects. The absence of residual effects of temazepam 20 mg and the severity of residual effects of zopiclone 7.5 mg on driving was similar to that found in previous studies with healthy young volunteers. This does not support the hypothesis that healthy elderly people are more sensitive to residual effects of hypnotics on driving than young volunteers.

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Analysis of slow-wave sleep EEG in demented subjects

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Aim: Dementia causes sleep disturbances and modifications in both macrostructure and microstructure of the sleep EEG. Here we investigate detailed EEG alterations in the slow-wave sleep (SWS) of demented subjects compared to elderly controls.

Methods: Five demented and 5 age- and sex- matched controls were studied. Each subject underwent two night polysomnographic recordings. The second recording was divided into NREM-REM cycles. For each of the first three NREM-REM cycles, 5 min of SWS were analyzed. We studied the range of delta activity (0.4 Hz–3.6 Hz), divided into eight sub-bands (0.4 Hz each), with period-amplitude analysis of visually well-defined delta waves.

Results: The demented subjects, compared to controls, showed a significant reduction, in both incidence and amplitude of delta waves, for waves <1.6 Hz, and a significant increase, in both incidence and amplitude again, for waves >2 Hz.

Conclusions: Period-amplitude analysis showed to be a discriminating tool between the two populations as far as SWS EEG patterns are concerned. Demented subjects had a reduction in slow delta activity (0.4–1.6 Hz), while they had an increase in fast delta activity (2–3.6 Hz). These results could support the hypothesis of a "pathological" delta activity in SWS. Furthermore, demented people may produce abnormal amounts of delta-frequency EEG during wakefulness. This slowing of the awake EEG may "intrude" during sleep, possibly contributing to this "pathological" delta activity in SWS.

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The influence of individual and institutional factors on care home residents' sleep

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There is a need to systematically assess the quality and pattern of sleep of older care home residents. Although it is widely held that sleep difficulties are common amongst care home residents, there is debate over the specific determinants of this poor sleep. Part of this complexity is because care home residents' sleep can be influenced by both individual and care home level factors. At the 'individual' level, these factors include age-related changes in sleep and the high prevalence of cognitive impairment within care home residents. At the 'care-home' level, sleep can be influenced by such things as inactivity, routines, lack of bright light and noise. This study seeks to explore the determinants of poor sleep in care homes. Data comes from one arm of a 4 year UK study entitled 'SomnIA: Optimising quality sleep among older people in the community and care homes'. Hundred residents in 7 care homes were asked to wear an actiwatch L for 14 days, whilst simultaneously keeping a written diary (with the assistance of a researcher). Actigraphy variables were created to examine aspects of sleep timing, sleep quality and circadian rhythmicity. Analysis was performed using Hierarchical

Linear Models. Unconditional HLM models were run to examine the proportion of the variance which exists at the night, individual and care home levels. Where a significant proportion of the variation exists at the care home level, it suggests that residents' sleep is largely influenced by the specific care home that they are in. Further models were run to explain the variance at each level. Results differed across the actigraphy variables. Residents' interdaily stability was determined both by individual differences and care home routines (with 33% of the variance at the care home level). Intradaily variability was largely determined by resident differences (with only 3% of the variance at the care home level). The sleep of care home residents is influenced by individual factors, care home differences and the intersection of the two. These findings have important implications for care home policy.

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Sleep wake/cycle patterns in systemic arterial hypertensive older adults

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Introduction: Sleep/wake cycle (SWC) patterns change with aging; older adults show fragmented sleep throughout the nighttime and fragmented waking throughout the daytime. Besides, the elderly are at-risk for systemic arterial hypertension and sleep appears to be the most important source of blood pressure (BP) modulation throughout the 24-h period. Objective: To evaluate SWC patterns in a group of hypertensive elderly subjects.

Methods: Subjects were 94 hypertensive older adults (22 men and 72 women) between 70 and 80 years of age. Motor activity was assessed for a whole week by mean of actigraphic recordings (Actiwatch-16/64) and the following SWC patterns were determined: sleep efficiency (SE) and nighttime awakenings (NA) during the nighttime, and waking efficiency (WE), naps (DN), daytime waking (DWED) and sleep episodes duration (DSED) during the daytime. In addition, sleep questionnaires were completed in a day-by-day-basis as were sleep logs.

Results: Through actigraphic recordings, mean values for the whole sample during the nighttime showed $90.5 \pm 5.3\%$ of SE with 2.0 ± 1.0 NA, and during the daytime WE was $91.3 \pm 6.5\%$ with 2.4 ± 1.2 DN, 344.3 ± 169.3 min. for DWED, and 27.9 ± 14.9 min. for DSED. When comparing subjects with controlled BP versus those with uncontrolled, either systolic (USBP) or diastolic (UDBP) BP, the USBP group showed smaller number of DN ($P<0.05$) and higher DWED ($P<0.04$), while the UDBP group presented smaller DWE ($P<0.05$) with higher DSED ($P<0.02$). Finally, through questionnaire information it was established that 56% refer having sleep problems, 23% were taking sleep pills, 92% awaken during the night with 63% having at least 2 awakenings every night, 41% present excessive daytime somnolence with 35% napping at least once/day. As a whole, 47% indicated having good sleep, 33% regular and only 20% as bad.

Conclusions: These results show different SWC patterns between hypertensive patients with and without controlled BP. In addition, differences were also apparent when the uncontrolled BP refers to systolic or diastolic measures. As a whole, these results suggest that SWC patterns could be relevant to help control BP in hypertensive older subjects.

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Relationships among sleep, the sleep EEG and visual texture discrimination task learning in middle-aged subjects

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Studies in carefully selected young adults suggest that visual texture discrimination task (TDT) learning depends on experience-dependent neuronal changes during subsequent sleep, in particular sleep containing slow wave sleep (SWS) and REM sleep. Here we used all-night EEG spectral analysis to investigate the relationships between sleep-related cortical activity and TDT learning in middle-aged subjects over a wide age-range. Twenty-one volunteers (13 females; age range: 28–57 years) participated in the study. SCID interview revealed major depression in 4 participants. Nocturnal sleep and the sleep EEG in 8 healthy subjects (4 females) were recorded in random order in a baseline night and a "learning" night following practice on the TDT. In all other subjects, one sleep recording always followed TDT training. All experimental nights were preceded by an adaptation night. TDT learning was quantified by comparing performance in morning and pre-sleep evening sessions. Whereas sleep variables did not differ, EEG power in the 14–20 Hz range in SWS ($P<0.04$, paired t-test) and REM sleep ($P<0.08$) was slightly enhanced following learning when compared to baseline ($n=8$). The increase in beta power in SWS was marginally related to improvement on the TDT ($r=0.67$, $P<0.06$, Pearson's product-moment correlation). While the mean TDT scores ($n=21$) were similar before and after sleep, individual changes in performance correlated positively with sleep latency, and EEG power <1 Hz in stage 2, SWS and REM sleep ($r=0.53$, $P<0.05$). Median split in younger and older age groups revealed the typical age-related changes in sleep and the sleep EEG, yet learning on the TDT did not differ between the groups. Finally, EEG spectra and changes in TDT performance over night were similar in the 4 depressed patients when compared to individually matched controls. We found no general improvement in TDT performance following sleep in a heterogenous group of middle-aged subjects. The positive correlation between sleep EEG low- and higher-frequency activity and individual changes on the TDT may suggest that sleep-related perceptual learning depends on cortical deactivation and activation patterns in nonREM and REM sleep rather than on the duration of distinct sleep states.

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Nitric oxide mediated recovery sleep is attenuated with age

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Inducible nitric oxide synthase (iNOS) mediated production of nitric oxide (NO) in the basal forebrain (BF)-an important structure for sleep/wake regulation-during sleep deprivation (SD) induces recovery sleep (Kalinchuk et al. 2006a, b). Aging is associated with changes in sleep homeostasis; one of the most frequently reported observations is the decrease in recovery NREMS intensity following prolonged wakefulness. However, the underlying molecular mechanisms responsible for this impairment are not well known. We hypothesized that aging can cause changes in the NO-mediated sleep induction. To test this hypothesis we implanted three different age groups of rats (young, 3 months; middle-aged, 12 months; old, 24 months) with EEG/EMG electrodes and a guide cannulae for microdialysis probes targeting the BF. The experimental schedule consisted of

continuous EEG recordings (sleep analysis), sample collection during baseline/SD for 3 h using in vivo microdialysis (NO analysis) or decapitation (iNOS analysis), and infusion of NO-donor (DETA/NO, 1 mM) to mimic the effects of SD. We found that 1) recovery sleep intensity (EEG NREM delta power, 0.7–4 Hz) attenuated with age, 2) neither iNOS nor NO increased in the BF of old animals during SD as compared to young and middle-aged, and 3) local infusion of DETA/NO into the BF failed to induce recovery sleep in aged animals. Thus, aging both attenuates the iNOS/NO response to SD, and reduces the sensitivity of the BF to the sleep promoting effects of NO. Together, these results support our hypothesis that aging impairs the mechanism by which NO induces sleep in the BF. The attenuation of NO-mediated sleep induction with aging may be one of the factors contributing to sleep impairments in the elderly.

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Exhaled nitric oxide in obstructive sleep apnea syndrome and healthy subjects: the influence of age and other clinical variables

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Background: Fractional exhaled nitric oxide (FENO) is a marker of airway inflammation. Obstructive Sleep Apnea (OSA) patients are expected to have morning elevated levels of FENO, due to sleep repetitive apneas.

Objectives: To evaluate diurnal variation in FENO in OSA patients and healthy subjects.

Methods: FENO was determined before (10:30 pm) and after overnight polysomnography (07:30 am) in 92 male, non smoking OSA patients with a mean age: 44.8 ± 7.7 years, a mean apnea/hypopnea index (AHI): 33.0 ± 26.8 h^{-1} and a mean body mass index (BMI): 31,1 ± 4,6 kg m^{-2} and also in 30 healthy male controls (mean age: 32.5 ± 6.8 years; mean AHI: 2.3 ± 1.5 h^{-1} and mean BMI: 25,3 kg m^{-2}). In a subgroup of OSA and healthy subjects ($n = 55$) FENO was also determined at 12:30 pm and 05:30 pm. All subjects performed the Epworth Sleepiness Scale (ESS) and a headache questionnaire.

Results: FENO was higher in the morning compared to the evening in OSA patients (morning: 25.4 ± 15.7/evening: 23.2 ± 14.0 ppb; $P = 0.005$), as well as, in healthy subjects (morning: 18.9 ± 7.7/evening: 16.9 ± 7.8 ppb; $P = 0.022$). FENO levels decreased during the day in both groups. OSA patients had higher FENO compared to healthy subjects: 7.30 am (OSA: 25.4 ± 15.7/Healthy: 18.3 ± 7.5 ppb; $P = 0.001$); 10:30 pm (OSA: 23.4 ± 13.9/Healthy: 16.3 ± 7.4 ppb; $P = 0.001$) and 12:30 pm (OSA: 25.7 ± 17.8/Healthy:16,1 ± 5.3 ppb; $P = 0.004$). There were a significant negative correlation with the minimal O2 saturation (cc = – 0,270, $P = 0.003$) and positive for the ESS scores (cc = 0,237; $P = 0.011$). There were no differences in FENO values concerning OSA severity, BMI and the presence of headache. AHI did not correlate with FENO. In a stepwise regression analysis model, age was the only variable ($r = 0,35$; $P < 0.01$) that explained the differences between OSA and healthy subjects.

Conclusion: Compared to healthy subjects OSA patients showed the same diurnal variation pattern with a decrease of FENO values across the day. Higher FENO values in OSA male patients seem to be explained by age and not by respiratory events. No other significant differences were detected, therefore the role of FENO as a inflammatory marker of OSA was not confirmed by our data.

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Correlates of insomnia among the elderly in Hungary – a nationally representative survey

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Background: It has been previously reported that the prevalence of insomnia is increasing with age. The mechanism of this association, however remains unclear. Our aim was to assess insomnia symptoms in a large cohort of elderly individuals (>65 years of age) and to find potential correlates of insomnia.

Subjects and Methods: Hungarostudy 2002 was a nationally representative door-to-door cross-sectional survey involving 12000 adult subjects in Hungary. Data of individuals more than 65 years old were analysed in the current study ($n = 2408$, mean age: 75 ± 6 years, males: 36%). In addition to questions about socio-demographic characteristics and health-related issues, the study questionnaire also included the Athens Insomnia Scale (AIS) and the Beck Depression Inventory (BDI). A cut off score of 10 was used to detect clinically significant insomnia on the AIS.

Results: The prevalence of insomnia in our population was 16%. Insomnia was twice as prevalent in women versus men (20 versus 10%, $P < 0.001$). Compared to good sleepers insomniacs were more likely to be widowed (43% versus 51%, $P = 0.005$) and less educated (elementary school or less: 60% versus 74%, $P < 0.001$). Age in this population was not meaningfully correlated with insomnia scores (rho = 0.07). Insomniacs versus non-insomniacs had more somatic illnesses (median 2 versus 1, $P < 0.001$) and more frequently complained about physical pain (90% versus 69%, $P < 0.001$). The AIS score strongly correlated with scores on BDI ($r = 0.52$, $P < 0.001$). Multivariate logistic regression model revealed that female sex (OR = 1.77, 95% CI 1.22–2.56, $P = 0.003$), number of comorbid somatic conditions (OR = 1.2, 95% CI 1.08–1.34, $P = 0.001$), chronic pain (OR = 2.53, 95% CI 1.52–4.22, $P < 0.001$) and scores on BDI (OR = 1.05, 95% CI 1.04–1.07, $P < 0.001$) were independently associated with the presence of insomnia.

Conclusion: Conditions commonly seen in the elderly like somatic diseases, pain and poor mental health are significantly associated with insomnia. Age per se was not correlated with poor sleep to any meaningful extent.

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The effects of sleep on procedural memory consolidation processes in young adults and the elderly

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Memory consolidation is conceptualized as time-dependent neural processes, triggered by a learning experience, that contribute to making a given learning experience less susceptible to interference. Post-training neuronal processes also result in robust, delayed performance gains that are expressed after sleep is afforded. The acquisition of motor skills is impaired in older adults, and sleep patterns undergo a significant alteration with age. Do sleep architecture changes have a role in the age-related decline in motor skill consolidation? Here we studied the effects of night' and day-time nap on memory consolidation in the elderly, and tested whether the beneficial effects of sleep recently observed in young adults (Korman et al. 2007) extend into old age. Healthy elderly

individuals were trained in a finger opposition sequence learning task (Karni et al. 1995). The effect of night and day sleep on the time-course of within-session and delayed practice-dependent gains was evaluated in terms of speed and accuracy of performance in two age-groups: young adults (18–35 years) and elderly (60–75 years). All participants were trained at noon and performance was re-tested immediately, at 12 and 24 h after training. Half the participants of each age-group were afforded a 90-min day-time nap immediately after training. PSG was obtained for the pre-training night, the post-training night and the nap. Within-session learning was similar in the young and elderly, although the baseline performance was significantly slower in the elderly. The afternoon nap in young adults had a significant impact on the time-course and magnitude of motor memory consolidation, as reflected in the shortening of the time interval for the expression of the delayed gains. In the elderly group, the nap and even the subsequent full night's sleep promoted delayed gains only in a sub-population of participants. Thus, the beneficial effects of sleep, in terms of motor skill consolidation, may be reduced in the elderly. We hypothesize that changes in sleep structure may contribute to these age-related deficits in motor learning. The interaction of memory and sleep may be age dependent; this may prove of importance in designing effective training & rehabilitation programs in older adults.

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Elevated daytime skin temperature in cognitively impaired elderly people

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With aging and even more so in neurodegenerative disease, the circadian rhythm of core temperature may show changes, such as a decreased amplitude. Changes occur as well in the regulation of skin temperature. Compared to younger adults, elderly people show attenuated skin blood flow responses to heat and cold and a lower maximal skin vasodilatation, regardless of gender and fitness. It has not been investigated previously how the diurnal profile in skin temperature changes with age and neurodegenerative disease. The aim of the present study was to elucidate this, as well as to investigate whether possible alterations in nocturnal and daytime skin temperature might be related to alterations in, respectively, sleep quality (Brain 2008; 131:500–513) and cognitive performance (Sleep 2007; 30:96–103). Using iButtons (Physiol Behav 2006; 88: 489–97), skin temperature (Ts) was monitored unobtrusively at home for 24 h in elderly people with different levels of cognitive decline; Subjective Memory Complaints (SMC, $n = 10$), Mild Cognitive Impairment (MCI, $n = 11$), Alzheimer Dementia (AD, $n = 25$) and healthy, age matched controls ($n = 11$)Activity was assessed with actigraphy. Lights out and get up time were measured with a pressure pad, put on the mattress, connected to a logger equipped with a light sensor (J Sleep Res 2006; 15:171). *T*-tests were used to evaluate group differences in the average daytime and night time proximal ($Ts_{proximal}$) and distal (Ts_{distal}) skin temperatures. The effects of activity and posture on Ts were analysed using mixed effect regression models. Preliminary analyses indicate that, only during daytime, all cognitively impaired groups maintained a higher Ts than controls. Group differences reached significance on Tsproximal for AD ($33.4 \pm 0.9\,^{\circ}C$, mean ± SD) versus controls ($32.6 \pm 0.7\,^{\circ}C$, $P = 0.01$) and on Tsdistal for SMC ($32.1 \pm 0.9\,^{\circ}C$) versus controls ($31.0 \pm 1.3\,^{\circ}C$, $P = 0.04$). Differences could not be explained by activity levels (all $P > 0.85$). The data suggest that the sympathetic vasoconstrictive response of the skin vasculature to an upright position is compromised in cognitively impaired elderly. An increased skin temperature may attenuate vigilance and contribute to cognitive complaints.

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Ghrelin promotes sleep in elderly men but not in elderly women

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We showed previously that pulsatile intravenous (iv) administration of the neuropeptide ghrelin increases slow-wave sleep (SWS) in young normal male subjects, whereas it does not modulate sleep EEG in young normal female subjects. In both gender the nocturnal secretion of growth hormone (GH) and cortisol is elevated after ghrelin. During ageing the influence of some peptides on sleep changes. For example the sleep promoting effect of GH-releasing hormone (GHRH) in male subjects is weaker in elderly subjects than in young men. On the other hand the sleep impairing effects of corticotropin-releasing hormone and somatostatin increase during ageing. It is unknown so far whether the effect of ghrelin on sleep changes during the life span. Furthermore it is unclear whether in young women estrogenes contribute to the gender difference in the effect of ghrelin on sleep EEG. To clarify these issues we examinded the effect of ghrelin on sleep-endocrine activity in 10 healthy women and 10 healthy men, 60 to 70 years old. In a randomized single-blind study sleep EEG (2300–0700) and the plasma concentrations of GH and cortisol (2200–0700) were examined simultaneously after four iv injections at 2200, 2300, 0000 and 0100 of placebo (PL) and of 4×50 µg ghrelin. In the males NonREM sleep increased from (mean ± S.E.M.) 238.7 ± 14.0 min after PL to 315.7 ± 8.5 after ghrelin ($P < 0.05$). Stage 2 sleep increased from 199.0 ± 19.1 to 230.6 ± 14.2 min ($P < 0.05$). Other sleep-EEG variables including wakefulness, SWS and stage REM remained unchanged. In women ghrelin did not affect sleep EEG significantly (NonREM sleep: 265.7 ± 9.5 after PL versus 272.7 ± 10.7 min after ghrelin). GH and cortisol were stimulated after ghrelin in women and men as well. The GH stimulating effect of ghrelin was more distinct than that of GHRH in elderly subjects in our previous study. Our data show that the sleep promoting effect of ghrelin in male subjects is preserved in the elderly. Similarly to our findings in young women sleep EEG remained unchanged after ghrelin in elderly women. Obviously the menopause does not modulate the effect of ghrelin on the sleep EEG. In both gender ghrelin stimualtes GH and cortisol in young and elderly subjects.

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Sleepiness is not always perceived before falling asleep in elderly, healthy, partially sleep deprived subjects

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Introduction: Many studies suggest, that it is nearly impossible to fall asleep without prior awareness of sleepiness, since certain physiological and cognitive indicators of sleepiness invariably precede sleep. However own results showed, that young, healthy, fully sleep deprived subjects did not always signal spontaneously perceived sleepiness (SPS) prior to microsleep (MS) or overt sleep (OS).

Objectives: To investigate whether healthy, elderly subjects after only partial sleep deprivation can fall asleep without prior signalling of SPS.

Methods: Eleven subjects (7 males, mean age 60.5 ± 10.0 years [SD]) underwent after a night with 5 h sleep 4 maintenance of wakefulness tests (MWT). Prior to each MWT they received the instruction: ''Indicate the earliest symptoms of sleepiness by pressing a button and try to stay awake as long as possible''. A financial reward was offered for optimal recognition of SPS and for

long sleep latencies. Subjective sleepiness was also rated retrospectively using the Karolinska sleepiness scale (KSS). OS was scored according to R&K. MS was defined as EEG activity compatible with sleep for $\geq$3s while the eyes were closed.

Results: Overall OS or MS occurred in 16 of 44 MWTs (5 of 11 subjects) but SPS was not signalled in advance in 12 (75%) of them. 4 of the 5 subjects did signal SPS too late or never in at least one of the 4 trials. In 10 MWTs with retrospective scoring of existing sleepiness (KSS $\geq$7) no SPS was signalled.

Conclusion: These findings confirm our earlier results and show that also elderly, only partially sleep deprived subjects frequently fall asleep before signalling SPS. It can be debated whether the MWT situation without performance feedback is representative for driving, certainly calling for further studies. However if such an inability to signal SPS could be reproduced in any driving situation, then this will have a major impact on both the prevention strategies and the punishment of the driver in a sleepiness induced motor vehicle accident. The discrepancy between SPS and retrospectively assessed sleepiness by KSS may be explained by the arousing effect of the interaction, and underlines the importance of choosing the adequate method to test sleepiness.

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Comparison of subjective and objective assessments of sleep in older subjects

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Introduction: Prior studies comparing subjective sleep assessments with objectively-recorded sleep have mainly been conducted in young subjects or in older subjects with medical, sleep, or psychiatric disorders. Healthy older adults have age-related changes in sleep quality, with less slow-wave sleep, more awakenings, and reduced total sleep time. The purpose of this study was to investigate how subjective reports of sleep relate to objectively recorded sleep in healthy older subjects.

Method: Subjects were 10 men (67 $\pm$ 7 years) and 13 women (62 $\pm$ 5 years), medically and psychologically healthy, without sleep complaints or disorders, and not on medications. They took part in a 32-day inpatient study that began with 3 baseline 8 h nights, scheduled at each subject's habitual bedtime. Baseline data (nights 2–3) are reported here. Objective sleep quality was determined from PSG scored visually in 30-s epochs. Subjective sleep quality was assessed after wake time using a post-sleep questionnaire (PSQ) based on the Karolinska Sleep Diary. Correlation between objective and subjective sleep measures was done using a Spearman correlation coefficient.

Results: Subjective sleep onset latency (SOL) was correlated with objective SOL ($r = 0.48$, $P = 0.001$), and wake after sleep onset was negatively correlated with reported number of awakenings ($r = -0.30$, $P = 0.045$). Scored wakefulness prior to scheduled wake time (min.) was associated with decreased subjective sleepiness ($r = -0.36$, $P = 0.02$) and increased refreshment after wake time ($r = 0.33$, $P = 0.03$). Stage 1 (min) was negatively correlated with subjective evaluation of sleep ($r = -0.5$, $P = 0.0005$) and soundness of sleep ($r = -0.34$, $P = 0.03$), while duration of Stage 2 was positively correlated with evaluation of sleep ($r = 0.32$, $P = 0.03$). Slow-wave sleep was correlated with total perceived sleep time ($r = 0.38$, $P = 0.01$).

Conclusion: These preliminary results are in agreement with previous sleep reports. We plan to examine additional nights scheduled at adverse circadian phases from these subjects to further explore the relationship between objective and subjective sleep.

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Linear dissipation of homeostatic sleep pressure across the night between the middle years of life

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Introduction: The decline in slow-wave activity (SWA) across the night is thought to reflect the dissipation of homeostatic sleep drive. Studies suggested age-related changes in the function (linear versus exponential) and in the slope underlying this decline. We evaluated if SWA in men and women dissipates differently with increasing age across topographical locations.

Methods: The sleep of 87 healthy volunteers (48 young, 20–30 years and 39 middle-aged, 40–60 years) was analyzed. Spectral analysis in SWA (1.00–5.00 Hz) was performed per N-REM periods for Fp1, F3, C3, P3, and O1 (expressed as % of the night). Linear and exponential decay functions were applied on individual datasets for each derivation. ANOVAs (2 age groups * 2 genders * 5 derivations) were performed on goodness of fit coefficient (R^2), slope, and intercept calculated individually for each derivation.

Results: For 77% young (18F-19M; 23.7 years $\pm$ 2.4) and 87% middle-aged subjects (20F-14M; 53.8 years $\pm$ 3.7; χ^2, n.s.), R2 of exponential fit was not significantly higher than of linear. Subsequent analyses were performed with this subsample of subjects using linear fit. Anterior derivations (FP1+F3) showed better fits than in posterior derivations (P3+O1). Slopes differed between age groups and across derivations: middle-aged subjects had a smaller SWA decay rate ($P<0.004$) and anterior regions showed a steeper SWA decay ($P<0.001$). SWA intercept was higher in young subjects ($P<0.001$), in anterior derivations ($P<0.000$) and tended to be higher in women ($P<0.07$).

Conclusion: For 80% of subjects between their twenties and sixties, linear function adequately explained SWA decline across the night with no significant impact of age on this proportion. In these subjects, anterior derivations better fitted linear model and had a steeper decline of SWA than posterior derivations. The dynamic of homeostatic dissipation was similar in men and women. Our results support the notion that age-related shallower dissipation of sleep homeostatic drive is similar across scalp topography and between genders.

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Insomnia

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Impact of psychological stress due to time constraint pressure on sleep architecture under the condition of repeated sleep restriction and subsequent recovery

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The purpose of this study was to examine the impact of psychological stress on sleep architecture under the condition of sleep restriction with time constraint pressure and subsequent restoration. Male participants ($n = 16$, Mean age;27.3 (SD;6.0) year) were required to attend a laboratory for sixteen consecutive nights for observation under the following conditions: Adaptation night (A; 2300–7:00), Baseline night (B; 2300–7:00), Sleep restriction night 1–10 (SR1-SR10; 0100–6:00) and Recovery night 1–4 (R1-R4; 2300–7:00). The data of four participants were, however, excluded from the analysis because of technical failures. During the period of sleep restriction, participants were required to complete an English transcription task by SR10. In addition, to expose the subjects to psychological stress due to time constraint pressure, we informed them we would not pay compensation (255,000 yen) at all if they could not complete it in time. However, we paid the compensation regardless of their achievement at the end of the experiment. Sleep architecture was evaluated by Sleep efficiency, %S2, %SWS, %REM and REM latency. We classified all variables into the Completed group (CG; $n = 6$), and the Non-completed group (NCG; $n = 6$), according to achievement of the task to reveal the impact of the psychological stress on sleep architecture. Two-way repeated ANOVA (Condition×Time-of-day) showed that significant differences between conditions were observed on %REM and REM latency ($F1,10 = 13.054$, $P = 0.005$, $F1,10 = 5.957$, $P = 0.035$, respectively), although no significant findings were observed on other indexes. For REM latency, the interaction of Condition and Time-of-day was significant ($F14,140 = 2.235$, $P = 0.035$). The results suggested that psychological stress have an impact on the expression of REM sleep. It should be noted that participants in NCG had not recovered by the fourth night of recovery sleep. Taken together, we considered that psychological stress might enhance the expression of REM sleep and suppress that of slow wave sleep, thereby deteriorating worker's health.

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Identifying insomnia using actigraphy: quantitative criteria

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Background: A lack of actigraphic quantitative criteria for identifying insomnia represents an important limit for the use of actigraphy in clinical practice. This study aimed to provide adequate quantitative criteria to diagnose insomnia using actigraphy.

Methods: Two databases (113 patients with insomnia, mean age 40.65 ± 13.15; 292 normal sleepers, mean age 37.91 ± 14.01) were compared in order to test the efficacy of a range of actigraphic parameters aimed at discriminating patients with insomnia from normal sleepers. Participants completed at least seven consecutive nights of actigraphic recording (Basic Mini-Motionlogger; Ambulatory Monitoring Inc., Ardsley, NY) to monitor their home sleep patterns. Sleep measures used for the current study were: sleep onset latency (SOL), wake after sleep onset (WASO), sleep efficiency percentage (SE%), number of awakenings longer than 5 min (EPW >5) and mean motor activity (MA).

Results: As expected, significant mean differences between the two groups were found for all sleep measures: SOL ($P < 0.0001$), WASO ($P < 0.0001$), SE ($P < 0.0001$), EPW >5 ($P < 0.0001$) and MA ($P < 0.001$). SE% (AUC value = 0.71) and EPW >5 (AUC value = 0.76) represented the most valid parameters for the identification of insomnia using the receiver operating characteristic (ROC) analysis.

Conclusions: We suggest the following preliminary quantitative criteria to discriminate patients with insomnia from normal sleepers: SOL of 12 min, WASO of 30 min, SE% of 90, EPW >5 of 1.8 and MA of 15. Unfortunately, one cannot apply these results in a general manner to other actigraph models and additional research is needed to compare results from different types of insomnia disorders.

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Low frequency domains of EEG segments in primary insomnia

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Introduction: This study compares signal processing in adults with primary insomnia. Morpheus® performs automated analysis of EEG using multidimensional mathematical analysis applying adaptive segmentation, fuzzy logic with Markov models. Morpheus® enables multiple spectral power EEG measurements. Modal frequency (FF) of EEG segments is one value analyzed. Primary insomnia patients often have normal sleep architecture using R&K EEG scoring. In research, patients selected for clinical trials have prolonged sleep latency and increased WASO. 75% of patients with insomnia do not meet these criteria. We compare insomnia screen fails (ISF) with normals (NL) and randomized insomnia (IN) patients.

Methods: Three groups of adults are examined based on R&K and automated analysis: 46 IN; 40 NL; and 39 ISF. A post-hoc analysis compared R&K to advanced analysis over two nights. Total sleep time (TST), latency to persistent sleep (LPS), and wake after sleep onset (WASO)are reported. FF is reported.

Results: ISF compared to IN and NL have minor differences in R&K sleep stages. Slow wave % was not different. The major change was LPS, WASO, and TST. Means/standard deviations in minutes for IN- TST 336 (67), LPS 43 (30), WASO 116 (62); NL-TST 419 (28), LPS 19 (14), WASO 48 (26); ISF- TST 375 (57), LPS 44 (38), WASO 72 (44). *T*-tests of R&K results at $P < 0.05$ were: (IN versus ISF) TST, WASO, and % stage 1 &2; (NL versus ISF) TST, LPS; (IN versus NL) TST, LPS, WASO. The spectral power of sleep is compared in all groups. Analysis of EEG segments measuring modal frequency (FF) below 6 Hz for IN is 67 min. (10), ISF 68 (11), and NL 75 (9). Comparison of ISF and IN groups to NL was different at $P < 0.001$. The ISF and IN group was not different $P = 0.96$. Other spectral parameters of the TST that showed significant differences included FF < 2 Hz and measures of high frequency states.

Conclusions: R&K measures of insomnia screen fail patients differed from normals primarily in LPS and WASO with little difference in sleep stage distribution. Adaptive segmentation demonstrated decreased sleep EEG synchrony (FF)in insomnia and screen fail insomnia patients compared to normals.

Morpheus® analysis of sleep EEG offers higher resolution in measuring states and processes of insomnia patients.

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High frequency spectral patterns in primary insomnia

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Introduction: This study compares signal processing in adults with primary insomnia. Morpheus® performs automated analysis of EEG using multidimensional mathematical analysis applying adaptive segmentation, fuzzy logic with Markov models enabling multiple spectral power EEG measurements. High frequency (HF) activity is analyzed. Primary insomnia patients often have normal sleep architecture using R&K EEG scoring. In research, patients selected for clinical trials have prolonged sleep latency and increased WASO. Seventy Five% of patients with insomnia do not meet these criteria. We compare insomnia screen fails (ISF) with normals (NL) and randomized insomnia (IN) patients.

Methods: Three groups of adults are examined based on R&K and automated analysis: 46 IN; 40 NL; and 39 ISF. A post-hoc analysis compared R&K to advanced analysis over two nights. Total sleep time (TST), latency to persistent sleep (LPS), and wake after sleep onset (WASO) are reported. HF spectral patterns are reported.

Results: ISF compared to IN and NL have minor differences in R&K sleep stages. The major change was LPS, WASO, and TST. Means/sd in minutes for IN-TST 336 (67), LPS 43 (30), WASO 116 (62); NL-TST 419 (28), LPS 19 (14), WASO 48 (26); ISF-TST 375 (57), LPS 44 (38), WASO 72 (44). *T*-tests of R&K results at $P<0.05$ were: (IN versus ISF) TST, WASO; (NL versus ISF) TST, LPS; (IN versus NL) TST, LPS, WASO. Analysis of EEG segments measuring HF states is reported. Means/sd of % HF TST for IN 20 (7); NL 15 (7); ISF 18 (7) with *t*-tests comparing groups significant $P<0.05$ comparing IN and NL with a trend ISF versus NL $P=0.05$ (one tail). Similar findings (ISF, IN versus NL) were noted for probability of state transition HF to HF $P<0.0004$ and % HF TST during hours 3–4 $P<0.006$. The probability of transition from HF to HF state in REM was significant $P<0.04$ (ISF, IN versus NL).

Conclusions: R&K measures of insomnia screen fail patients differed from normals primarily in LPS and WASO with little difference in sleep stage distribution. Adaptive segmentation demonstrated an increase in high frequency spectral pattern of the EEG in insomnia and screen fail insomnia patients compared to normals. Morpheus® analysis of sleep EEG offers higher resolution in measuring states and processes of insomnia patients.

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Cognitive behavior group therapy for chronic insomnia

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Introduction: Cognitive and behavioral therapies are effective in the treatment of insomnia. The aim of the study was to evaluate the effects of cognitive behavior group therapy on sleep parameters and daytime functioning of chronic insomniacs.

Material and Methods: Thirty-five patients meeting ICD-10 criteria of nonorganic insomnia (30F, 5M; mean age: 56.8; mean insomnia duration: 7.1 years) were assigned for cognitive behavior group therapy (six sessions, 6–10 patients). All participants completed the sleep diary, Athens Insomnia Scale (AIS), Beck Depression Inventory (BDI), State-Trait Anxiety Inventory (STAI) and the SF-36 questionnaire at baseline, post-treatment and the 3-months follow-up time points.

Results: At post-treatment, a substantial improvement of sleep onset latency (65.9 versus 40.5 min.; $P=0.001$), wake time after sleep onset (82.4 versus 34.3 min.; $P<0.001$) and sleep efficiency (69 versus 82%; $P<0.001$) was observed; 21/35 patients reported mean sleep latency below 30 min., and 20/35 patients had total wake time shorter than 30 min. These outcomes were accompanied by lower AIS scores (13.5 versus 8.6 pts.; $P<0.001$), lower BDI scores (13.1 versus 9.5 pts.; $P=0.001$) and lower trait anxiety (49.3 versus 44.9 pts.; $P=0.001$). Changes in sleep parameters were maintained during the 3-month follow-up ($n=27$), with additional improvement of total sleep time (5.4 versus 6 h; $P=0.03$). Follow-up data revealed also a significant increase in some quality of life demands: energy, emotional well-being, social functioning and reduction in state anxiety before sleep (41.8 versus 37.5 pts.; $P=0.003$).

Conclusions: The cognitive behavior group therapy was associated with sustained self-reported improvement of nocturnal sleep and daytime functioning.

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Long term follow up of melatonin treatment in children with ADHD and chronic sleep onset insomnia

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Introduction: Exogenous melatonin has proven to be effective in the treatment of chronic sleep onset insomnia in children with ADHD. However, no long term data concerning the required duration of the treatment and potential adverse effects are available. To obtain data about long term efficiency and possible adverse effects of melatonin we interviewed the parents of children with ADHD and sleep onset insomnia. These children participated in a previously published placebo-controlled study of melatonin treatment.

Methods: A structured questionnaire was sent to the parents of 100 children with ADHD and chronic sleep onset insomnia. Between november 2001 and june 2005 these children participated in a placebo controlled trial of melatonin treatment. The melatonin treatment was continued after this trial. The questionnaire evaluated issues regarding (dis) continuation of melatonin at follow up, current dosage and time of administration, the effect of discontinuation of melatonin on sleep and behaviour, adverse effects and satisfaction of the parents with melatonin as a treatment for sleep onset insomnia.

Results: Response rate was 93 percent and mean duration of follow up was 3.3 years. At the moment of follow up 80 percent of the participants still used melatonin. Seveny-five percent of all the participants temporary discontinued the melatonin treatment. After discontinuation 95 percent experienced a delay in sleep onset and 40 percent a delay in wake up time 25 percent of the participants reported adverse effects. Adverse effects were persistent in 7 percent of the cases. No serious adverse effects or other diseases were reported during treatment. Ninety percent of the parents stated that melatonin is an effective drug for the treatment of their children's chronic sleep onset insomnia.

Conclusion: Melatonin as a treatment for chronic sleep onset insomnia is usually required for a longer period of time (e.g. years) and discontinuation of the treatment often causes returning of the sleep onset insomnia. Long term use of melatonin seems to be save, no serious adverse effects or diseases occurred during treatment. Mild adverse effects were frequently reported. Most parents were

satisfied with melatonin as a treatment for their children's chronic sleep onset insomnia.

P302

A qualitative analysis of the impact of insomnia secondary to cancer

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Introduction: Sleep disturbance is one of the most frequently reported and distressing symptoms for cancer patients, both during and after completion of active treatment. Prevalence estimates suggest that approximately one quarter of these patients experience chronic insomnia which often fails to remit, even when the comorbid disorder is successfully treated. There are abundant data on the impact of sleep disturbance from primary insomniacs, but such data from the secondary insomnia population are scarce. Also, very few studies exploring 'impact' have utilised qualitative methodologies which access the patient experience in a more direct way. Therefore, the purpose of this study was to conduct a qualitative exploration of the impact of sleep disturbance in a group of patients with insomnia secondary to cancer.

Methods: A qualitative research study was undertaken with a reference group of 12 cancer patients with secondary insomnia (8F, mean age = 57 years). 3 focus groups were set-up to consider the following: (i) when did your sleep first become disturbed? (ii) what caused this disruption? (iii) what was the impact of poor sleep? (iv) when did you become concerned about your sleep? Transcripts were independently analysed by 3 readers in order to identify participants' responses to the questions and the subsequent themes and sub-themes that emerged.

Results: All participants reported that their sleep first became disturbed around the time of cancer diagnosis/treatment and cited the stress of being diagnosed, the side effects of cancer treatment and the lack of a daily routine as responsible for causing this disruption. The impact of poor sleep on the individual was far-reaching with main themes being relationships with others, cognitive consequences, affective responses, physical symptoms and behavioural modifications (each of these themes contained several sub-themes). Participants became particularly concerned about their sleep disruption once they had moved into 'follow-up' cancer care due to their belief that sleep should have normalised.

Conclusion: These findings indicate that secondary insomnia is a prevalent, invasive and persistent disorder which has far-reaching consequences for numerous aspects of psychological wellbeing.

P303

A modified Posner paradigm experiment investigating the components of attention driving the attention bias to sleep-related stimuli in psychophysiologic insomnia

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Psychophysiologic insomnia (PI) is a disorder of somatized tension and learned sleep-preventing associations (ICSD-R). Numerous authors contend that PI is the result of numerous psychological factors. Accumulated evidence supports the notion that PI are preoccupied with sleep, and the impact of not sleeping, and that this drives various behaviours, e.g. selective attention (SA) and monitoring, that result in worrisome thoughts and excessive anxiousness. Indeed, the concept of SA is incorporated into many of the proposed models of insomnia. SA, more commonly termed Attention Bias (AB), can be measured objectively using computerised cognitive probe tasks where information processing speed is taken as a proxy for biases in attention. These tasks use salient and neutral word or picture stimuli within an experimental test paradigm, and most identified AB effects have been attributed to perceived threat. Direct assessment of AB in PI is limited, however a surge in recent experimentation have reveiled that the existence of AB in Pi is a robust and testable phenomenon (Marchetti et al. 2005). This current experiment attempts to underpin the components of attention, i.e. engagement or disengagement processes, which are responsible for the AB data of PI, through the use of a Modified Posner Paradigm. The data suggest that delayed disengagement away from salient stimuli are responsible for the AB effects captured. All findings are discussed in relation the existing research on PI and attention bias.

P304

Impact of insomnia on occupational functioning: a 'crystallisation' of qualitative methods

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Introduction: Impaired occupational functioning is listed as a daytime consequence of insomnia in both the ICSD-2 and DSM-IV-TR. The small body of published literature in this area focuses mainly on absenteeism; only recently has the field attempted to look at aspects of performance/productivity. Much of this recent work has relied on nomothetic methodologies (e.g. asking participants to rate the extent to which an aspect of work performance is affected), thus failing to capture the insomniac's experience of the workplace. We report here focus group and prospective audio-diary data on the perceived impact of insomnia on vocational functioning.

Method: Eleven volunteers (9f; age range 20–64, $M = 38$) with persistent primary insomnia (DSM-IV criteria) took part in one of three focus group discussions. Groups explored the impact of insomnia on aspects of Quality of Life and daytime functioning. A sub-sample ($n = 8$) was also asked to keep an audio-diary for seven days (two entries per day), assessing the relationship between sleep quality and next day functioning. This particular analysis represents a focused, comprehensive look at how insomnia was perceived to affect work/university functioning.

Results: Several interesting themes emerged. Cognitive, affective, and physical functioning decrements, as a result of poor sleep, contributed to reduced work performance/output. The workday was thus commonly viewed as 'a struggle' or 'an effort'. Participants described well-developed 'compensatory mechanisms' to try and mask/attenuate the impact of sleep disruption (e.g. scheduling of daily tasks, forced physical activity). The students within the sample described how insomnia obstructs learning and overall university performance. Interestingly, this inability to retain and learn information prevented some from re-training for a preferred occupation. 'Good sleep', as gauged by audio-diary entries, had a profound impact on increasing work enjoyment and productivity.

Conclusions: Insomnia can affect occupational functioning in several ways. More prospective studies are required to assess the relationship between sleep parameters and next day vocational performance (subjectively and objectively).

P305

Cognitive event-related potentials (ERPS) in psychophysiological insomnia sufferers and personality as measured with the NEO-FFI: preliminary results

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Introduction: Some insomnia models suggest that personality traits like introversion and neuroticism are more marked in insomnia

individuals than in good sleepers. The link between personality traits and arousal levels in insomnia sufferers is poorly understood. The aim of this study is to relate personality factors to N1, P2 and N350 (ERP indexes of arousal and inhibition) in psychophysiological insomnia sufferers (Psy-I) and good sleepers (GS).

Methods: Twelve Psy-I (mean age = 45.2 years) and 12 GS (mean age = 37.8 years) were enrolled. Participants completed the NEO Five Factors Inventory (NEO-FFI) and underwent four consecutive nights of PSG (N1 to N4). ERPs N1 and P2 were recorded in the evening and awakening on N3 and N4, and N350 at sleep-onset on N4. Auditory stimuli elicited ERPs.

Results: Independent sample *T*-Tests revealed that scores on the five factors (Openness, Conscientiousness, Extraversion, Agreeableness, Neuroticism) did not differ between groups ($P<0.05$). Pearson correlations revealed that 1) as Openness score increased, both Psy-I and GS showed larger N350; 2) as Psy-I displayed higher Conscientiousness score, the less aroused they were (smaller N1) while the opposite was observed in GS; 3) as Extraversion scores increased, N1 amplitude decreased in Psy-I, whilst more inhibition at sleep-onset (larger N350) was observed in GS ($P<0.05$). Neither scores on Agreeableness or Neuroticism were related to ERP amplitudes in Psy-I. However, as Neuroticism and Agreeableness scores respectively increased, GS displayed more signs of arousal (larger N1) and inhibition (larger P2).

Conclusion: These preliminary results suggest that as both groups score higher on Openness, and as good sleepers are more extraverts, the less they have difficulties initiating normal sleep processes. Surprisingly, while greater neuroticism was not related to greater arousal in psychophysiological insomnia sufferers, it was in good sleepers. On the other hand, as psychophysiological insomnia sufferers displayed more introversion, the more aroused they also were.

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P306

Differences in higher cognitive processing between acute and chronic insomniacs

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Introduction: To date, little is known about the characterological make-up of acute insomniacs and in what ways they differ from chronic insomniacs. This lack of direction negates the possibility of understanding the key processes involved in the transition from acute to chronic insomnia and limits efforts to develop and refine preventative strategies. The aim of the present study was to compare acute and chronic insomniacs with an aim to determine differences in perceptions of stress and coping as well as higher-order cognitive processing strategies.

Method: In a cross-sectional survey, 524 participants were recruited from the general population, using a convenience sampling technique (74 chronic insomniacs; 146 acute insomniacs; and 304 normal sleepers). Participants completed a demographic and screening questionnaire to determine their sleep status as either (normal sleeper, acute insomniac, or chronic insomniac). Additionally, participants completed the Perceived Modes of Processing Inventory (PMPI), which measures the type of processing used when faced with threatening information, and the Positive and Negative Affect Scale-State Version (PANAS), which measures stress-related coping resources.

Results: A multinomial logistic regression showed that the introduction of the independent variables significantly increased prediction accuracy (from 52.2% to 61.8%). However, demographic variables did not significantly increase prediction accuracy. Type of processing and negative affective state significantly differentiated group membership for both the acute and chronic insomniacs.

Discussion and Conclusion: The results suggest that there are significant differences between the groups, with acute insomniacs predominately employing automatic processing and chronic insomniacs employing emotional processing. However, we could not ascertain whether these results were indicative of the transition or the condition. A longitudinal study, examining the transition between acute and chronic insomnia is needed to fully explore the relationship between stress, coping and insomnia status.

P307

Facial EMG responses to emotional stimuli related and non-related to sleep in people with primary insomnia and in good sleepers

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The role of emotional arousal in insomnia is theoretically considered as a predisposing and a perpetuating factor (e.g. Morin, 1993) but, so far, no study has evaluated it directly. The aim of this study was to compare physiological and subjective responses of a group of young people with chronic primary insomnia and of a control group to emotional stimuli related or not related to sleep. Twenty-one people with insomnia and eighteen good sleepers took part to the study. Participants were invited to watch and rate a set of neutral, positive and negative pictures taken from the International Affective Picture System (IAPS, Lang, Bradley, Cuthbert, 2001) and a set of previously validated pictures related to 'good sleep' and 'poor sleep'. Physiological measures included the recording of facial activity over the corrugator and the zygomatic muscles. Subjective ratings were measured through the Self-Assessment Manikin (SAM, Bradley, Lang, 1994). Preliminary results on 25 participants (12 people with insomnia and 13 good sleepers) indicated that people with insomnia present higher activity in the zygomatic muscle in response to all stimuli. Positive and sleep-positive stimuli elicited a higher response in both the groups in the zygomatic muscle compared to the negative and the sleep-negative stimuli. No significant effect was found respect to the corrugator muscle. Respect to the subjective ratings, people with insomnia rated all stimuli as more arousing compared to good sleepers. Moreover, only people with insomnia rated as emotionally activating the stimuli associated with poor sleep, but not those related to good sleep. Results are consistent with Lundh and Broman's theory of insomnia (2000), which suggests that primary insomnia is characterised by a predisposition in responding with high levels of arousal to new, sudden or emotional stimuli (hyper-arousability).

P308

Insomnia prevalence in patients that attended to their general practitioner in primary health care system in Figueiró dos Vinhos and the consequences in life quality

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To determine the prevalence of insomnia complaints in patients that often go to their general Practitioner in primary health care system in Figueiró dos Vinhos, and the consequences in the life quality, we applied a questionnaire witch included the Pittsburg Sleep Questionnaire Index, the Insomnia severity index, the

Epworth sleepiness scale and the Life quality associated with health state questionnaire SF-36. The sample was made up of 292 participants, aged between 20 and 60 years, with a higher percentage of women (71,2%). The purpose of this study was to characterize the prevalence of the insomnia complaints, in these patients and related these with their life quality. The hypotheses were that the insomnia was more prevalent and that there would be changes in the life quality. The subjects had in general, better life quality when compared with general population. However, the existence of highs prevalence of insomnia complaints (57,9%), moderate to severe (11,6%) and excessive daytime sleepiness (20,2%). Female presented higher results. We found that life quality his highly sensitive to insomnia complaints and worsen with severity of insomnia and daily consequences. These findings suggest that even thou the sample may not be representative of the Portuguese population, the dimension of the problem in Portugal could be under estimated or became worse over the years.

P309

Short-term cognitive behavioral therapy for chronic insomnia

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Background and Objectives: Insomnia is a very common complaint with which physicians frequently meet and a social problem which costs a great deal. Recognition that cognitive and behavioral factors play an important role in insomnia has led to increased interest in therapies targeting these factors. Nowadays Cognitive Behavioral Therapy (CBT), in some cases coupled with drug therapy, is considered as the most effective treatment of chronic insomnia. We plan to investigate the efficacy of cognitive behavioral therapy for chronic insomnia.

Methods: We examined all of 22 chronic insomnia patients from May of 2007 to August. They voluntarily participated in CBT because they couldn't be satisfied with their sleep. Four sessions of CBT for insomnia included sleep hygiene education, stimulus control instruction, sleep restriction therapy, relaxation training, and cognitive therapy. All the patients completed the questionnaires including sleep diaries, visual analogue scale of subjective satisfactions with one's own sleep, the Pre-Sleep Arousal Scale, and the Dysfunctional Beliefs and Attitudes about Sleep Scale at the beginning and ending of CBT.

Results: Sleep logs showed that CBT-treated patients achieved a 40.5% reduction in their sleep latency and 19.6% increase in their total sleep time by study completion. Their nocturnal wake time after sleep-onset and number of awakenings were decreased 41.1% and 21.2% respectively and their sleep efficiency was increased 13.3%. The degree of cognitive arousal and physical arousal decreased 53.9% and 23.2% respectively. In addition, the degree of dysfunctional belief and thought associated with sleep diminished 29.2% after completion of CBT.

P310

The association between polysomnography indexes with Athens Insomnia Scale and Epworth Scale in sleep apnea patients in a Greek hospital

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Objective: The aim of this study was to test whether polysomnography indexes are accordant with daytime sleepiness and insomnia to patients with obstructive sleep apnea syndrome (OSAS).

Method: Epworth Scale and Athens Insomnia Scale (AIS) were administrated to 58 patients (46 males and 12 females) mean age equal to 52.8 (SD = 11.6). All patients underwent a polysomnography (PSG) test and RDI, TST, NREM, REM, MTV, Wakefulness Saturation (%), Lowest Saturation (%), Saturation < 90% (min) and Arousal index were recorded.

Results: Epworth scale was normally distributed according to Kolmogorov-Smirnov test. The mean value for the total sample was 10.82 (SD = 5.19) with range from 2 to 23. Epworth scale had acceptable internal consistency (Cronbach's $\alpha = 0.87$). Convergent validity analysis showed a significant correlation between Epworth and AIS scale ($r = 0.47$, $P = 0.001$). Furthermore, the mean score on Epworth scale was significant greater for patients who were characterized as having insomnia according to AIS score ≥ 6 (12.16 ± 4.9 versus 8.7 ± 4.6, $P = 0.018$). Additionally, score on Epworth scale was significantly correlated with PSG parameters with correlation coefficient ranging from -0.36 (Lowest Saturation) to 0.45 (Arousal Index). No significant association of AIS score with PSG parameters was found. Within the patients, insomnia was diagnosed in 54.2% of the cases according to AIS score. AIS scale hasn't been administrated to OSAS patients before in Greece.

Conclusion: PSG indexes are discordant with insomnia in patients with sleep apnea. Further studies are needed to carefully explore the association between the characteristics of the AIS and the burden of the OSAS disease.

P311

Eszopiclone co-administered with fluoxetine for insomnia co-existing with major depressive disorder (MDD): a subgroup analysis

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Introduction: In a study of eszopiclone+fluoxetine in comorbid insomnia and depression, co-therapy produced greater improvements in sleep, including sleep maintenance (a common complaint in depression), and in a measure of depression (Hamilton Depression Rating Scale; HAM-D17) versus fluoxetine monotherapy. This analysis evaluated whether baseline sleep severity impacts the treatment response.

Methods: Patients met DSM-IV criteria for MDD and insomnia, with screening HAM-D17 (excluding sleep items) > 14. All patients received fluoxetine QAM, and were randomized to eszopiclone 3 mg ($n = 270$) or placebo ($n = 275$) QHS for 8 weeks. Changes in wake time after sleep onset (WASO) and HAM-D17 total score were analyzed in subgroups based on total sleep time (TST) > 6 h ($n = 62$) or TST $\leq$ 6 h ($n = 467$). Data were analyzed using ANCOVA.

Results: At baseline, WASO was worse in patients with TST $\leq$ 6 h versus TST > 6 h (~80 min versus ~40 min, respectively), but HAM-D17 total scores were similar (mean ~22). At the end of treatment, larger improvements with eszopiclone+fluoxetine versus placebo+fluoxetine were generally observed across endpoints. For the TST $\leq$ 6 h group, there were significant differences between eszopiclone+fluoxetine and placebo+fluoxetine for WASO (average over 8 weeks: medians of 27 min versus 43 min, respectively, $P < 0.0001$) and HAM-D17 (mean reductions at Week 8: 13.7 versus 11.5, respectively, $P = 0.004$). Similar findings were noted for the TST > 6 h group (WASO: 15 min for co-therapy versus 35 min for monotherapy; HAM-D17 reductions: 13.0 versus 11.3, respectively), although the treatment differences were not significant due perhaps to the small sample sizes in this subgroup.

Conclusions: In this analysis, regardless of TST severity, eszopiclone+fluoxetine co-therapy provided significant improvements in sleep maintenance and HAM-D17 relative to fluoxetine monotherapy.

P312

Psychological vulnerability to insomnia: a study among good sleepers

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Introduction: The aim of this study was to verify the existence of a psychological profile related to vulnerability to stress-related sleep disturbances among good sleepers.

Methods: One hundred ninety-six young adults (147 females, 49 males; mean age 20.17 ± 0.996, range 19–28 years) participated in an in-class survey to third year medical students (response rate 89.5%). Participants were classified in one of two groups: (a) good sleepers (PSQI total score < 5; $n = 86$); and (b) poor sleepers (PSQI total score > 5; $n = 110$). The independent variable measured vulnerability to stress-related sleep disturbance (FIRST; Drake et al. 2004). Using a median split on FIRST scores, good sleepers were separated into two subgroups: those scoring low (≤ 19) on the FIRST scale ($n = 49$) and those scoring high (> 19) on this measure ($n = 36$). Dependent variables were measures of insomnia severity (ISI), mood (POMS-48), rumination and emotion regulation (ECQ-R and ERQ), arousability (APS), pre-sleep arousal (PSAS), coping stress strategies (CISS), and personality factors (NEO-FFI). The psychometric properties of all questionnaires have been very well documented. First, the association between all dependent variables and FIRST groups was analyzed with univariate logistic regressions. Second, a logistic stepwise regression model was carried out to study the independent contribution of all variables to FIRST groups.

Results: The final multivariate stepwise regression model showed that being female (OR = 4.53; $P = 0.046$), high pre-sleep cognitive arousal (OR = 1.32; $P = 0.001$), high arousability predisposition (OR = 1.15; $P = 0.006$), and using emotion-oriented coping stress strategies (OR = 1.05; $P = 0.049$) were the variables most related to high vulnerability to stress-related sleep disturbance, after controlling for other confounding factors.

Conclusions: These data suggest that female gender, high cognitive arousal, high arousability and emotion-oriented coping stress strategies predispose to stress-related sleep disturbance among good sleepers. It appears that physiological and emotional hyperarousal are predisposing factors to chronic insomnia and should be the target of our preventative strategies for this disorder.

P313

Differential sleep effects of eszopiclone treatment and discontinuation in patients with primary insomnia and insomnia co-existing with major depressive disorder (MDD) or generalized anxiety disorder (GAD)

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Introduction: Insomnia comorbid with psychiatric disorders remains poorly understood compared with primary insomnia (PI). In PI, sleep improves rapidly with eszopiclone therapy, is sustained with treatment, and diminishes with treatment discontinuation. We sought to determine whether this pattern also characterizes the treatment response of insomnia occurring with MDD and GAD.

Methods: We compared subjective sleep data from 3 randomized, double-blind, placebo-controlled studies of eszopiclone: 1) PI patients received eszopiclone 3 mg or placebo for 6 months ($n = 830$); 2) MDD patients were treated with fluoxetine along with either eszopiclone 3 mg or placebo for 8 weeks ($n = 545$); 3) GAD patients were treated with escitalopram oxalate along with either eszopiclone 3 mg or placebo for 8 weeks ($n = 595$). All studies included a 14-day, single-blind, placebo run-out period (MDD subjects continued fluoxetine and GAD subjects continued escitalopram).

Results: Eszopiclone significantly improved all sleep measures versus placebo in all 3 studies during double-blind treatment ($P < 0.0001$). Sleep latency (SL) and wake time after sleep onset (WASO) continued to improve to a greater degree after the first week of therapy in comorbid MDD compared with comorbid GAD and PI ($P < 0.05$) patients. Sleep improvements observed versus placebo during the double-blind period were consistently maintained following eszopiclone discontinuation only in comorbid MDD ($P < 0.05$).

Conclusion: The pattern of improvement in insomnia occurring with MDD differed from GAD and PI. Improvement in insomnia with eszopiclone was more gradual and better sustained after hypnotic discontinuation in comorbid MDD than in comorbid GAD or PI.

P314

ERPS and spontaneus fluctuations in the quality of sleep in insomniacs and good sleepers

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Previous results [1,2] show that in primary insomniacs P300 amplitude is significantly higher compared to good sleepers only with the occurrence of a bad night. These results suggest a relationship between cortical arousal and spontaneus fluctuations of the quality of sleep in insomniacs. Aim of the present study was to deeply investigate this relationship considering also earlier ERPs components related to basic level of arousal [3]. 11 primary insomniacs and 11 healty matched controls were actigraphically monitored for 1 week. At their homes, each day, before and after sleep, subjects filled in a diary and their N1, P2 and P300 ERPs (oddball paradigm) were recorded through portable equipment. For each subject diary and actigraphic data were used for identifying the worse (N−) and the best (N+) sleep quality night in the week. The mean amplitudes of the N1 and the P300 from FZ, CZ and PZ of both groups were submitted to separate ANOVAs considering NIGHT (N− versus N+), GROUP (insomniacs versus controls), TIME of day (presleep versus postsleep) and LEAD (Fz versus CZ versus Pz.) as factors. ANOVA on N1 amplitude showed a significant GROUP X TIME X LEAD interaction ($F(2,40) = 3{,}61$; $P < 0.04$). Post Hoc Test indicates that N1 amplitude recorded from FZ is significantly higher in insomniacs compared to controls both in the evenings before the N− and in the evening before the N+. ANOVA on P300 amplitude shows a significant GROUP X NIGHTX LEAD interaction ($F(2,40) = 3{,}16$; $P < 0.05$). Post hoc Test indicates that in insomniacs P300 amplitude recorded from FZ is significantly higher compared to controls, only with the occurrence of the N−. The relationship between ERPs amplitude and spontaneous fluctuations in sleep quality of primary insomniacs occurs for late but not for early ERPs components.

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P315

Morning cortisol response in patients with parasomnia and insomnia

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Primary insomnia is associated with a disturbance of the HPA axis as demonstrated by the awakening salivary cortisol response. Cortisol immediately after awakening has been reported to be significantly decreased in primary insomnia and correlated negatively with the subjective estimation of sleep quality. Patients with parasomnias experience a high level of distress from their sleep disturbance, however cortisol regulation has never been studied in these patients. The purpose of this study was to compare awakening cortisol responses in patients with parasomnias with those in insomnia and normal controls and relate this to sleep disturbance that night.

Methods: Seven patients with primary insomnia, 9 patients with parasomnias (2 sleepwalkers, 6 night terrors, 1 RBD), and 15 age and sex matched controls took part. Subjects completed baseline questionnaires concerning sleep disturbance, anxiety, depression and general health and gave 2 saliva samples, the first immediately on waking and the second 30 min later, together with subjective ratings of the night's sleep including description of dreams. Parasomnia patients followed this procedure on 2 mornings, one after a 'bad' night with episodes, the other on a relatively good night. Salivary cortisol was measured by radioimmunoassay.

Results: Absolute levels of cortisol were higher in both sleep disordered groups than in controls but there was no significant difference. Insomnia patients and parasomnia patients on 'good' nights had similar ACR slopes to controls, but there was a variable response on parasomnia 'bad' nights with some patients having a fall rather than a rise after waking. Initial cortisol levels were significantly positively correlated with decreased subjective measures of sleep quality ($P = 0.02$). Early waking was significantly correlated with a decreased ACR ($P = 0.011$). Cortisol levels on awakening showed higher variability in those subjects reporting anxiety dreams or episodes of night terrors during the night.

Conclusions: We demonstrated a significant relationship between cortisol levels and subjective measures of poor sleep quality and early awakening. Occurrence of episodes of parasomnia was associated with cortisol response unlike that of controls.

P316

Workplace performance, but not punctuality, is consistently impaired among people with insomnia

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Background: While impaired occupational functioning is a diagnostic criterion for primary insomnia in DSM-IV and ICSD-2, relationships between insomnia and work performance have tended to focus on absenteeism, with relatively less attention paid to the quality of performance in the workplace.

Aim: To compare longitudinally the work performance of people with insomnia (PWI) and controls using the Occupational Impact of Sleep Questionnaire (OISQ).

Design: Eighty-six participants aged 25–50 yrs: 43 meeting DSM IV criteria for primary insomnia; and 43 controls completed a 9 month prospective study with assessments at baseline, 4 and 8 months.

Results: Mean baseline OISQ scores were significantly elevated among PWI (19.6 ± 13.2 versus 10 ± 7.74; $F = 16.83$, $P < 0.001$). Repeated measures analyses showed that OISQ differences between the groups remained stable and significant across the nine months of the study (main group effect $F = 19.10$; $P < 0.001$). Expressed in terms of comparative percentage decrement, PWI showed a consistent 10% decrement in subjective occupational performance when compared with controls. Daily sleep diaries were completed for 9 months and averaged for each month.OISQ scores negatively correlated with mean TST ($r = -0.47$, $P < 0.001$) and mean SE ($r = -0.56$, $P < 0.001$), and positively with mean WASO ($r = 0.66$, $P < 0.001$). Work limitations also positively correlated with PSQI (mean $r = 0.59$, $P < 0.001$) and fatigue (mean $r = 0.65$, $P < 0.001$) at each time point. Thus, in each case, as the sleep parameters indicate worsening sleep quality, the work assessment scores indicate worsening occupational performance. Exploring individual items within the OISQ revealed significant stable group differences over 3 time points. At baseline all items significantly differentiate between groups, with the exception of "start your job as soon as you arrive" and "handle the workload", these items, were, however found to significantly differentiate groups at subsequent data collection.The only item failing to discriminate between groups for the duration of the study, was that related to "arriving at work on time". Absenteeism and punctuality may not capture the full impact of insomnia on workplace performance, with the present data showing significant and stable decrements among PWI.

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Perception of drug treatment in patients with chronic insomnia

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NICE guidance on the treatment of insomnia (NICE 2004) called for research on the best ways to provide information to sufferers. The main aim of this study was to evaluate patients' perceptions of the information they had received about insomnia and about the treatment they had been given, using a questionnaire. We sent the questionnaire to 157 patients with chronic insomnia who had been referred to a specialist sleep clinic (a psychiatric clinic specialising in anxiety, mood disorders and sleep problems such as insomnia and parasomnias). Group T comprised 91 patients who had completed an insomnia group treatment programme, which included education about sleep science and medication, sleep hygiene and strategies to improve sleep, and cognitive-behavioural treatment (CBT). Group C was 66 patients who had attended the sleep clinic in a similar period and were eligible for the psychological treatment but had been unable to attend. We report here only answers to questions about medications and attitudes toward treatment. Fifty-one completed questionnaires were returned by course participants (T) (56%) and 17 by attenders at clinic (C) (26%), an overall response rate of 43%. Eightyeight percent of patients were currently taking regular sleep medication or had tried it in the past. Of these 87% (T 90%, C 80%) said their medication helped them sleep, 80% (T 86%, C 63%) said it helped them feel better in the daytime and 73% (T 79%, C 53%) said it helped them to do more in the day. When asked if they were nervous about taking medication for a long time, 30% said they were, with a lower incidence of nervousness in the group who had received psychological treatment (T 22%, C 53%). Overall, 41% said they were satisfied with treatment, 31% neither satisfied nor dissatisfied and 27% dissatisfied. Free text (qualitative) data will also be presented. When asked about alternative and complementary

therapies, 88% said they had tried them and of these 8% reported that they helped a great deal, 39% said they helped a little or for a short time and 52% said they did not help at all. This small study provides data about the perceptions of patients with chronic insomnia in the UK. Patients reported marked beneficial effects of medication on daytime function, although there may be a responder bias.

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Insomnia CBT: symptoms of insomnia and Glasgow Contents of Thoughts inventory

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In cognitive-behavioural treatment of insomnia, the therapist frequently encounters patients' dysfunctional beliefs about sleeplessness and its consequences. Unrealistic expectations towards amount of sleep, fear of fatigue after a night of poor sleep or sleep of less than expected hours and related sleep effort are part of insomnia hyperarousal structure. It has been shown that insomnia prevalence in studies depends on whether insomnia and it's consequences being a problem or simply sleep difficulties have been questioned. We studied correlations of reported number of hours of sleep, daytime fatigue, insomnia consequences being a problem and Glasgow Contents of Thoughts inventory results in the process of validation of the Estonian scale. Subjects, measures and procedure. One hundred and seven six female and 122 male subjects, mean age 28,18 years SD 12,54 randomly selected from inhabitants of Tartu, filled in a four-point response scale self report questionnaire, consisting of subjective report of sleep related symptoms, lifestyle data and comorbidities, Glasgow Contents of Thoughts Inventory, Emotional State Questionnaire (EST-Q) (Aluoja, Shlik). Data was tested for normality.Pearson correlations were drawn. Results 22% of subjects reported unability to sleep despite adequate opportunity as a problem often or always. Glasgow Contents of Thoughts Inventory score had normal distribution. Glasgow Content of Thoughts inventory overall score was significantly positively correlated with daytime fatigue ($P<0.00$) and daytime consequences of insomnia seen as a problem ($P<0.00$) but not with number of hours of self-reported sleep time. Sleep length was negatively correlated with daytime fatigue ($P<0.00$). The overall score was also positively correlated with EST-Q depression generalized anxiety, panic disorder, fatigue and insomnia subscale scores ($P<0.00$).

Discussion: High insomnia symptoms prevalence similar to other studies was found in this relatively young sample. Sleep effort related and general arousal reflecting thoughts at bedtime are more related to daytime fatigue than actual perceived sleep length. Glasgow Content of Thoughts Scale results should be studied respectively in psychiatric diagnosis groups.

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The influence of contextual cues on wakefulness measured by the EEG in insomnia patients: a preliminary study

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Introduction: The behavioural perspective of chronic primary insomnia posits that contextual cues related to sleep (such as the bedroom) may lead to a conditioned arousal response, resulting in a difficulty of falling asleep and/or staying asleep. Recent research has shown that hyperarousal is also present on the level of the cortex (as measured by EEG), so one might assume that these sleep related cues may also have an influence on specific EEG components.

Method: Wake EEG (eyes closed) and PSG (F3, C4 and O1) were obtained in 11 primary insomnia patients, diagnosed according to the DSM-IV criteria. EOG and EMG were recorded in both measurements and used for artefact rejection. Impedances were kept below 10 kOhm. For the wake EEG, a minimum of 90 seconds of artefact-free wake-EEG data per patient was used for further analysis. For the sleep EEG, the first 5 min of wakefulness during the sleep onset period were selected. FFT analyses of both conditions were performed using Neuroguide software (Thatcher, 1997). Relative theta (4–8 Hz), alpha (8–12 Hz) and beta (20–30 Hz) EEG power in F3, C4 and 01 were evaluated. Bonferroni correction for location was performed.

Results: The results indicate a significant increase in theta power at C4 ($t\ (10) = 2.877,\ P<0.05$)* and O1 ($t\ (10) = 2.681,\ P<0.05$)* when lying awake in bed with eyes closed compared to the wake EEG measurement performed in an experimental room of our lab. No differences were observed for alpha or beta power.

Conclusion: The heightened theta power when trying to fall asleep suggests that the context of lying in bed serves as a cue that might initiate sleep onset processes. The lack of decrease in beta power might be an indication of interference of these processes. However, an age-matched control group of healthy sleepers is necessary to validate this hypothesis.

*Bonferroni correction already applied.

P320

Has acupuncture an impact on insomnia – a randomized controlled trial

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Introduction: Acupuncture has been suggested to be an effective treatment for insomnia. Acupuncture as treatment for musculoskeletal pain yields to improvement of sleep quality. The aim of the study is to evaluate the effect of acupuncture on patients with insomnia.

Methods: Twenty five patients (21 women and 4 men-age range 18–64) with insomnia were recruited for the trial. All subjects had sleep latency of >30 min, frequent awakenings and difficulties falling asleep again at least 3 times a week for >3 months. Subjective assessments were done using the Hospital Anxiety and Depression (HAD) scale, Karolinska Sleep Diary (KSD), Karolinska Sleep Questionnaire (KSQ), Epworth Sleepiness Scale (ESS) and Fatigue Sleepiness Scale (FSS). Blood pressure and heart rate were measured pre- and post treatment with an ambulatory system during 24 h. Motor activity and sleep/wake cycles were investigated using an Actigraph one week pre and post treatment. Levels of saliva cortisol was measured 5 time during one day pre and post treatment. The treatment group received 10–12 acupuncture sessions, 2 times a week for 4 weeks and then once a week another 2–4 weeks. The choice of acupuncture points was based on experience in previous studies i.e. principle points. The number of needles were 8–12. The stimulation was manual with twirling the needles to evoke the sensation of de Qi 3 times during the 30 min treatment. The control group was given individual instructions in Progressive Muscle Relaxation (PMR). The instructions were given by a physiotherapist and further instructions by a practising PMR at home with help from a Compact Disk. The home training was followed up after 4 weeks in the physiotherapy clinic.

Results: Subjective self ratings indicate improvement trends for the whole group in several factors. The FSS ratings showed a significant difference for the whole group pre and post treatment as did some of the factors in SF-36. No significant difference has been found between the treatment group and the control group. If any there were only minor changes in the results of the actigraph, blood pressure and heart rate.

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"Late-life insomnia" is not a distinct aetiological category

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Introduction: The widely held assumption that insomnia in old age is causally related to the circumstances of old age, implies that "late life insomnia" is a distinct aetiological category. However, since any chronic non-fatal condition will accumulate in older populations (irrespective of the age of onset), it is likely that "late life insomnia" includes a sub-group whose insomnia originated in younger adulthood. These analyses estimate the size and significance of that sub-group.

Method: Data were provided by the Medical Research Council Cognitive Function and Ageing Study (MRC CFAS), a population-based cohort comprising 13,004 individuals aged 65 and above, from five sites across England and Wales. At screening 2496 respondents (unweighted prevalence = 19.2%) reported sleep problems "often or all the time", and were judged free of cognitive impairment. All of these respondents were asked to identify the age of onset of their insomnia symptoms. Those whose symptoms arose before the age of 65 were categorised as "earlier life onset", while those whose symptoms arose after the age of 65 were categorised "late life onset" people with insomnia.

Results: Of 2496 respondents reporting chronic insomnia symptoms in later life, 1189 (47.6%) reported "earlier life onset" while 52.4% reported "late life onset". The distribution of ages indicating earlier onset extended to teenage years, with 10% reporting symptoms since the age of <25. Age of onset (earlier v later) was not significantly related to sex (chi-square = 0.21; $P = 0.34$) or occupational class (chi-square 3.82; $P = 0.71$). However, those reporting "late life onset" symptoms showed significantly higher levels of physical disability, assessed by the Townsend disability index ($t = 10.45$; $P < 0.001$), and greater levels of impairment on Instrumental Activities of Daily Living ($t = 9.14$; $P < 0.001$).

Conclusion: "Late life insomnia" is a heterogeneous category representing, at the very least, clinically distinct earlier and later life onset types. These groups differ in history and health status and, as suggested by earlier longitudinal analyses (Morgan and Clarke, 1997), may also show differential clinical outcomes.

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What is the best case definition of insomnia?

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Prevalence of complaints of insomnia varies greatly in epidemiological studies due to the different questions used to assess insomnia. These sleep disturbances do not always indicate major impairment for the affected individuals, but there is a sizeable portion of subjects for whom these complaints pose a serious concern. As such, they prompt the individuals to consult health care professionals and use medication and thus clearly have an economic impact. We aimed to compare the frequency with which different indicators of sleep disturbance, used commonly in epidemiological studies about insomnia, were reported in a sample and to determine which of these indicators can predict more accurately a clinically significant insomnia.

Methods: A randomly selected sample of adults ($n = 755$; 60.3% women: mean age (SD) 44.7 (13.9) completed a postal survey on sleep. Questions that were particularly salient were: sleep satisfaction, sleep quality, the weekly frequency of sleep difficulties, the presence of insomnia symptoms, sleep duration (total nocturnal sleep time and sleep efficacy) and distress associated with the sleep difficulties. Subjects were classified as "suffering from a clinically significant insomnia" if they had initiated actions to alleviate their sleep complaint: using sleep-enhancing drugs and/or having attended a consultation with a specialist for sleep.

Results: Frequency of sleep disturbance ranges from 6.8% to 44.9%, depending on the definition being used. Total nocturnal sleep time <6 h set the lowest frequency, while the frequency of reported insomnia symptoms, using severity quantifiers, raised to 44.9%. 108 respondents (14.2%) were included in the group of subjects with a clinically significant insomnia. ROC curves plotted for each indicator showed that their predictive power to discriminate subjects were modest (AUC between 0.54 and 0.70). The question "how worried/distressed are you about your sleep problem"?, from the Insomnia Severity Index, showed the highest accuracy.

Conclussions: In large epidemiological surveys, where self-report is the only option available, chosing questions that maximize the amount information obtained from them provide an accurate picture of insomnia in a parsimonious way.

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Treatment of behavioural sleep disorders without 'distress'

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Background: Behavioural sleep problems (bedtime resistance and sleep association disorder) are common in children. Treatment regimes include components of graduated extinction frequently leaving a child to cry in distress for long and specific periods of time. This paper presents evidence of the Sensible Sleep Solution (SSS) for behavioural sleep problems that do not involve distressed crying.

Methods: Eleven mothers (mean age 34.6 years, average education 13.75 years) of 6 boys and 5 girls presented (aged 12–65 months, mean (SD) age = 34.1 (18.8) months) at the Paediatric Sleep Clinic for behavioural sleep problems averaging 27 months duration. Parents completed a range of sleep and behaviour questionnaires pre and post questionnaires. All children had sleep association disorders and bedtime resistance, four were co-sleeping. A psychologically based behavioural program individually tailored to each child, avoiding "distressed" crying was implemented over 4–6 weeks. Changes in total sleep time (TST), sleep onset latency, family functioning and bedtime behaviours were evaluated.

Results: Nine pre and post diaries were available to date. Mean weekly TST increased from 27.5 h (one showing no change and one showing a slight decrease) and a mean (SD) reduction of sleep onset latency from 23.43 (14.7) mins to 13.6 (5.12) mins. Bedtime resistance was eliminated for all participants and all co-sleeping in the four patients ceased. Treatment was achieved without typical distressed crying and treatment outcomes have been sustained 4–8 weeks after the last visit. Qualitative analyses showed 100% of respondents reported this to be a relatively stress free method with significant improvement in family function and well being.

Conclusions: Preliminary data suggests that the SSS is a socially acceptable, effective treatment for bedtime resistance and sleep association disorder. It retains the powerful effects of extinction-based procedures minimising the "extinction burst." Findings extend the literature on the treatment of paediatric bedtime resistance to clinical psychology and paediatric care.

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Attentional bias in people with primary insomnia and good sleepers in the detection of subliminally presented sleep-related stimuli – a comparative study using the Posner paradigm

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Insomnia is a common psycho-physiological disorder which is notoriously difficult to treat. It's aetiology has been explored in the

formulation of cognitive models (Espie et al. 2006; Harvey 2002) which emphasise the importance of cognitive processes in the possible maintenance of the disorder.The models support the role of attentional bias for sleep-related stimuli as a maintaining factor for the disorder (Marchetti et al. 2006; Jones et al. 2005).Anxiety literature has found attentional bias at the subliminal level of attentional processing (Koster et al. 2006; Cooper and Langton, 2006) but no such work has been carried out in insomnia.

Methods: The Posner Paradigm demonstrated the orientation of spatial attention towards positive and negative sleep-related and neutral words at 100 ms, to 25 people with Primary Insomnia (PI) and 25 Good Sleepers (GS).The distribution of visual attention was measured by latency to detect dot probes which followed presentation of word cue.Group allocation was retrospective using Pittsburgh Sleep Quality Index (PSQI) and Insomnia Severity Index (ISI).

Results: $2\times2\times3$ factor ANOVA reveals a significant main effect for validity overall ($P<0.001$) and a significant main effect of word valence ($P<0.05$). Post-hoc analyses showed a significant difference only for normal sleepers,between positive and negative words. Clinical re-evaluation using ISI for group assignment showed no significant main effect for sleep quality or word valence,even thought state anxiety in PI group was significantly higher ($P<0.01$).

Discussion: As anxiety literature is showing delayed disengagement at earlier processing,and we believe anxiety to be a central feature of insomnia maintenance,we had expected to see an attentional bias for sleep words in PI group.This was not observed. As the methodology was similar to a previous study conducted in our Sleep Lab (Marchetti, 2006) which found attentional bias at 500 ms,we can reasonably attribute the differences observed due to presentation times.Thus we conclude that anxiety may not be the sole determining factor in insomnia-related attentional biases. Future studies using EMG or eye-tracking are required to fully appreciate the attentional processes in poor sleep and the true role of anxiety in insomnia-related biases.

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Cognitive behavior therapy for insomnia comorbid with chronic pain: an uncontrolled pilot study of effects on pressure pain threshold assessed with algometer

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Objective: Insomnia is a common comorbid problem in patients with chronic illness. It has been proposed that the sleep disturbance could serve as a maintaining factor in some conditions, e.g. chronic pain. This study investigates the effect on pressure pain threshold (i.e. the minimal pressure that induces pain) when treating insomnia in patients with chronic pain.

Method: An uncontrolled pilot study at an outpatient pain clinic. Five adults with chronic benign musculoskeletal pain and comorbid insomnia received 5 sessions of cognitive behavior therapy for insomnia, delivered in a group setting. Assessment was completed at baseline, after treatment and at 2- and 4-month follow-up visit.

Results: The patients improved from "clinical insomnia of moderate severity" to "sub threshold insomnia" on a brief self-report screening form. Sleep diaries showed a significant decrease in sleep onset latency, number of wakenings, and wake time after sleep onset while total sleep time increased. Assessment with algometer showed a significantly higher pressure pain threshold after treatment, although no longer significant at 4-month follow-up. There were no changes in perceived sleep quality, daily pain level, fatigue or quality of life.

Conclusion: The results from this small and uncontrolled study indicate that pressure pain threshold could be affected by treatment of comorbid insomnia in patients with chronic benign musculoskeletal pain. The study does not allow any conclusions on causality but calls for further investigation on the topic.

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Does REM sleep contribute to subjective wake time in primary insomnia? A comparison of polysomnographic and subjective sleep in 100 patients and matched controls

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Primary insomnia (PI) is characterized by low subjective sleep quality which can not always be verified using polysomnography (PSG). To shed light on this discrepancy, subjective estimates of sleep and PSG variables were compared in patients with PI and good sleeper controls (GSC). One hundred patients with PI (age: 42.57 ± 12.50 years, medication free for at least 14 days) and 100 GSC (41.12 ± 13.99 years) with a sex distribution of 46 men and 54 women in each group were included. While PSG data was available for all included subjects, sleep questionnaire data (SF-A, Schlaffragebogen A) was available for 81 PI patients and 56 GSC subjects. For direct comparison of subjective data, a matched PI subgroup was used. Both PSG and questionnaire variables showed clear impairments of sleep quality in PI compared to GSC. The arousal index within total sleep time was increased, which was mainly due to a strong increase within REM sleep. When comparing PSG and subjective sleep data, both groups unexpectedly tended to overestimate their sleep time. This overestimation (retrospective "misperception" of sleep time in the positive direction) was more pronounced in GSC subjects and appears to be a typical property of sleep perception. However, more PI than GSC subjects estimated wake times longer than obtained from PSG. Linear modeling analysis of subjective wake time in terms of PSG parameters revealed that in addition to PSG defined wake time, REM sleep time contributed significantly to subjective wake time. This REM sleep contribution was larger for PI than for GSC subjects. Our findings suggest that REM sleep quality is distinctively modified in PI patients. Although PI patients had less REM sleep overall, the stronger dependence of subjective wake time on REM time was sufficient to cause a worse estimation of subjective sleep in the PI group. We see the increased arousal index in REM sleep as an additional indicator of this different REM sleep quality.

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Frequency of insomnia symptoms in PCPS patients: results of the EQUINOX international survey

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Introduction: To determine the frequency of various insomnia symptoms in patients complaining of these symptom (s) according

to DSM-IV and ICSD criteria, a cross-sectional survey, EQUINOX (Evaluation of daytime QUality Impairment by Nocturnal awakenings in Outpatient's eXperience), of patients visiting Primary Care Physicians' (PCPs) offices was conducted in 10 countries from different regions of the world.

Methods: The survey included Finland, Greece, Jordan, Lebanon, Mexico, Morocco, the Philippines, Portugal, Sweden and Switzerland. A questionnaire including the assessment of eligibility criteria, socio-demographic characteristics, sleep habits, sleep disturbances and their consequences was designed by sleep specialists and then locally translated. Patients >18 years old having insomnia symptoms who were not on hypnotics in the previous four weeks were enrolled by PCPs over a 2-day period.

Results: In total 5293 subjects complaining of insomnia symptoms (63.9% females; mean age 47.9 ± 15.3 years) were included in the analysis. Percentages of subjects presenting with at least one insomnia symptom were 78.0% for Difficulty Initiating Sleep (min Finland 54.5%-max Philippines 88.7%), 80.2% for Difficulty Maintaining Sleep characterized by night-time awakenings (Finland 78.5%–Philippines 86.7%), 66.9% for Early Morning Awakenings (Finland 55.2%–Philippines 78.0%) and 78.6% for Non-Restorative Sleep (Sweden 66.5%–Jordan 92.6%).

Conclusions: Insomnia characterized by difficulty maintaining sleep with night-time awakenings is reported as frequently as difficulty initiating sleep, and sometimes more frequently in specific countries. This should be taken into account by primary care physicians in the diagnosis and management of insomnia.

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Insomnia in patients with chronic kidney disease

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Background: The prevalence of sleep disorders including insomnia is high among patients with end stage renal disease. Very little is known, however, about sleep problems in patients with less severe renal impairment. In those patients insomnia is likely closely related to renal function. In this analysis we wanted to compare the prevalence of insomnia in kidney transplanted patients (Tx) versus chronic kidney disease patients (CKD) not yet requiring renal replacement therapy with comparable range of renal function.

Methods: Cross sectional data from 738 Tx and 160 CKD patients are analyzed. We used Athens Insomnia Scale to assess insomnia symptoms, the Centre for Epidemiologic Studies-Depression (CESD) scale to measure depressive symptoms, the Restless Legs Syndrome Questionnaire and the Berlin questionnaire to assess high risk of prevalent sleep disorders. Socio-demographic and clinical data were collected from the patients and from the charts.

Results: CKD patients were significantly older (60 ± 17 versus 48 ± 13 years), there were significantly more women (59% versus 40%), more depressed patients and more patients with high risk for sleep apnea in that group (31% versus 22% and 41% versus 27%, respectively). The AIS score was significantly correlated with renal function ($r = -0.147$, $P < 0.001$). The prevalence of insomnia was higher in the CKD population versus the Tx group (15% versus 8%, $P < 0.01$), In multivariate analysis, however, the treatment modality (Tx versus CKD) was not associated significantly with insomnia, when corrected to age, sex, estimated GFR, serum albumin and education, comorbidity, depression and other sleep disorders.

Conclusion: Insomnia, when corrected for differences of the socio-demographic and clinical characteristics of the two populations, is not different between chronic kidney disease and kidney transplanted patients.

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Bristol Insomnia Group: has it made a difference after 10 years?

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For nearly ten years the Bristol Insomnia Group has offered cognitive behavioural management and support for people with chronic insomnia. This report brings together outcomes from these outpatient courses held at a neuropsychiatry centre for people with primary or secondary insomnia (most often due to depression or anxiety). The group sessions, with up to 10 participants, are led by up to four members of a team consisting of a doctor (sleep specialist), two occupational therapists and a research sleep scientist. Components of the group intervention are education about sleep science and medication, sleep hygiene and strategies to improve sleep, together with cognitive-behavioural treatment (CBT). Participants who were in the group on prescribed medication continued to take it. In order to assess efficacy we asked participants to complete sleep diaries, quality of life scale (SF36) and the dysfunctional beliefs and attitudes scale (DBAS) at the beginning and end of the course. Sleep diaries were completed at three-month follow up and SF36 was repeated in a single postal survey. Sleep diaries completed before and at the end of the course show modest improvements in sleep onset latency and total sleep time although these are not statistically significant. SF36 scores show statistically improved scores in mental health ($P = 0.022$), energy and vitality ($P = 0.006$) and health perception ($P = 0.001$) by the end of the group programme. DBAS scores show statistically significant decreased scores ($P = 0.0002$) post-group. Feedback indicated that participants worried less about sleep after the course. Improvements and modification to the group programme will be discussed but these results demonstrate promising sleep parameter improvements after attendance at the group. Measured quality of life changes, and therefore better daytime functioning, in people with long-term insomnia are becoming more evident as further data is collected.

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Using combined heart rate and fMRI recordings for studying the neurobiology of hyperarousal in primary insomnia

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Background: Neurobiological correlates of hyperarousal in primary insomnia have been seldom studied. In the current study, we investigated the association between heart rate fluctuations and brain activity using combined electrocardiography (ECG) and functional magnetic resonance imaging (fMRI) recordings. We hypothesize that heart rate might be a valid indicator for autonomic arousal in primary insomnia.

Methods: Eight patients with primary insomnia and eight age- and gender-matched healthy controls were investigated using surface ECG during fMRI scanning. The investigations were performed in the afternoon. Participants were lying supine in the scanner for approximately 40 min and were instructed not to move voluntarily. In the first half of the experiment, participants were instructed via headphones to open and close their eyes for periods of 52.5 s. A heart rate regressor for the fMRI data has been calculated by subtracting artefacts of the fMRI data acquisition from the ECG traces and using an automatic heart beat detection after eliminating extrasystoles. Head movement effects as well as pulse-by-pulse cardiac effects have been taken into account in the fMRI analysis.

Results: Between-group differences in the strength of association between heart rate and brain activity clusters were found in cerebral areas, that are linked to emotional arousal, and were suggested to play a role in the neurobiological pathway of hyperarousal in primary insomnia. The methodology seem to be suitable for measuring heart rate related brain activity.

Conclusion: Combined measurement of ECG and fMRI is methodologically challenging but might help to understand the neurobiological correlates of arousal fluctuations in patients with primary insomnia.

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Sleep symptom changes while using an internet intervention for insomnia

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Insomnia is the most common sleep complaint in adulthood, with more adults reporting sleep problems each year. For roughly 10% of the adult population, insomnia becomes chronic and can impair daytime functioning. Although cognitive-behavioral therapy for insomnia (CBT-I) has been shown to be an efficacious treatment for insomnia, several barriers prevent wide-spread access to CBT-I, including a lack of professionals trained to deliver the treatment. Given that the Internet has become an important source of healthcare and medical information, we evaluated whether an Internet intervention designed to provide CBT-I in five core components could help fill this treatment gap. The five treatment cores were Behavior Cores 1 and 2 (Sleep Restriction and Stimulus Control), Sleep Hygiene, Cognitive Restructuring, and Relapse Prevention. Forty-five participants were randomized to either receive the Internet intervention (Sleep Healthy Using The Internet: SHUTi) or serve as wait-list controls, and all subjects completed insomnia severity ratings (Insomnia Severity Index, ISI) at pre-treatment and post-treatment. For treated adults, insomnia severity scores decreased significantly over the 6-week intervention (15.75 to 6.00), whereas control participants showed no change (16.27 to 15.50), $P<0.001$. Of the 22 participants randomized to receive SHUTi, 20 completed weekly insomnia severity ratings after each of the five core treatment components. The largest changes in insomnia severity scores occurred after completing the two behavior cores (ES = 0.32) and the final core stressing relapse prevention (ES = 0.27). The proposed presentation will provide detailed descriptions of each treatment core, as well as corresponding data from several measures of insomnia severity collected following usage of each core (e.g., sleep efficiency, wake after sleep onset, number of awakenings, sleep soundness, and sleep medication usage). Determining when symptoms change following particular aspects of treatment can help inform clinicians and researchers about the essential components of effective interventions and improve overall treatment.

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Preliminary investigations of the use of aromatherapy for treating mild to moderate insomnia

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Background: A local survey indicated CAM treatments for insomnia were more popular than prescription hypnotics, leading to a series of 4 pilot studies investigating aromatherapy essential oils.

Methods: Studies employed single-blind crossover designs, with balanced treatment order and washout periods (up to 1 week), with self-declared insomniacs (estimated sleep latency of more than 30 mins. or less than 6.5 h sleep with Pittsburgh Sleep Quality index: PSQI or similar). Treatments were 3 drops (0.15 ml) of essential oil self-administered to bedclothes at home for 2 nights, with actigraphy (CNT) and subjective scales assessing mood and sleep (e.g. Leeds Sleep Evaluation Questionnaire: LSEQ, PSQI, VAS). The first study compared lavender to jasmine-a stimulant and almond oil as placebo in 12 females, 50–59 years, the others employed mixed sex groups of 10 or 12 participants, 19–53 years, comparing geranium and bergamot respectively to almond oil together with a no treatment control to investigate possible placebo effects, including extended treatment of 2 weeks geranium or almond in the fourth study.

Results: Some placebo effects (almond oil) were seen contrasting with the no treatment control, generally reflecting trends for longer sleep, less waking and reduced fragmentation with actigraphy and improved subjective sleep. Some further improvements were seen with active treatments producing significant contrasts with placebo (and/or jasmine for lavender) including greater sleep time (actigraphy) with lavender, improved perceived sleep onset, quality and ease of awakening. Improved sleep onset (geranium), actual sleep time (bergamot and geranium) and reduced fragmentation (bergamot, extended geranium) recorded with actigraphy, supported by improved perceived sleep onset (bergamot and geranium) though no morning hangover and improved alertness/arousal after bergamot and geranium.

Conclusions: Placebo effects were seen with both subjective and objective measures reflecting expectancy. However, increased sleep time seen with acute administration for all 3 essential oils against placebo and supported by subjective measures, suggests aromatherapy may be a useful treatment in mild to moderate insomnia and provide an alternative to prescription hypnotics.

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Pain outcomes among chronic hypnotic drug users following effective CBT-I

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Introduction: While evidence suggests a reciprocal relationship between pain and sleep (e.g. Smith & Haythornthwaite, 2004), clinical trials outcomes continue to deliver equivocal results, with results showing that successfully treated insomnia can have no effect on pain experience (DeNucci et al. 1998), while successfully treated pain can have no effect on sleep quality (Ashworth et al. 2007). Vitiello et al's (2007) recent findings that CBT-I for older patients can have 'analgesic' effects introduces the possibility that results may be both age and severity sensitive. We address this possibility in a secondary analysis of pain outcomes in patients successfully treated using a standardised CBT-I package.

Method: Of 209 patients randomly assigned to the CBT-I (5×50 min sessions) or 'treatment as usual' (TAU) arms of a pragmatic trial, 137 (69 CBT-I & 68 TAU) completed baseline and 3 month follow-ups (which included the PSQI & SF-36 assessments). All participants had been using hypnotic drugs for at least 1 month, and met DSM-IV severity criteria for insomnia. Those scoring above or below the median SF-36 pain dimension score at baseline were categorised as "lower pain" or "higher pain" respectively. Pain scores were then analysed in a repeated measures ANOVA with time (baseline; follow-up) as within subject, and pain severity (higher; lower) and group (CBT-I; TAU) as between subject factors.

Results: Mean baseline pain scores did not differ significantly between the groups (CBT-I = 53.8; TAU = 54.4). At 3 month follow-up CBT-I treated patients showed a significant improvement in global PSQI scores (mean difference −3.8, 95% confidence interval −4.8 to −2.8, $P = 0.002$). Follow-up changes in pain

scores significantly interacted with severity, with the greater change shown for the "higher pain" groups (time×severity $F = 13.02$; $P < 0.001$). While these mean reductions in "higher pain" were greater for the CBT-I group (9.1% versus 6.3%), the trend did not reach significance (group×severity $F = 2.82$; $P = 0.095$).

Conclusion: Among a wide age-range of patients with insomnia, improvements in SF-36 pain scores are more likely among those experiencing higher pain. Despite evidence of trend, such change was not significantly affected by CBT-I.

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Interpretive bias in chronic insomnia

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Introduction: Models of insomnia describe the role of cognitive processes in the maintenance of chronic insomnia and various studies have shown the importance of attentional bias. Several psychological disorders are also characterized by disorder-congruent interpretations of ambiguous stimuli. Despite that, only very few studies have investigated the role of interpretive bias in insomnia. Hence, the present study was designed to investigate the presence of an interpretive bias in insomniacs, using a lexical decision task.

Method: Participants (13 insomniacs and 17 normal sleepers) were required to read ambiguous sleep-related and anxiety-related sentences and make a lexical decision about the subsequently presented target words. We hypothesized that insomniacs would respond faster (are primed) to insomnia-consistent targets following insomnia-related ambiguous sentences than to insomnia-inconsistent targets. In addition they were asked to complete various questionnaires and to keep a sleeplog for two weeks.

Results: Significant differences were obtained between the insomniacs and the normal sleepers in age, sleep parameters and in all questionnaires. A 2×2×2 ANOVA-analysis (group×sentence type-target type) of the task showed an interaction between group and sentence type ($F = 3.68$; $P = 0.065$). Both groups showed speeding effects on insomnia-related sentences, but only insomniacs responded faster to anxiety-related sentences. These results may indicate that there is an attentional bias in insomniacs for both sentence types. Control subjects surprisingly show a speeding effect, but only to insomnia-related sentences. Possibly the context of the sleeping centre, including keeping a sleeplog, may have had a priming effect on the control subjects. In this sample, no evidence was found for a disorder-congruent interpretive bias. The attentional bias of insomniacs on the anxiety-related sentences might indicate that more general, so-called transdiagnostic, cognitive processes have an influence upon the interpretation of both insomnia- and (co-morbid) anxiety-related information. Mindfulness-Based Cognitive Therapy is based on these processes. It would be interesting to further investigate these processes in insomnia.

Molecular Biology-Endocrinology-Biochemistry

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Restricted and disrupted sleep: changes in HPA axis regulation and stress reactivity

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Frequently disrupted and restricted sleep is a common problem for many people in our modern around the clock society. In the long run, insufficient sleep may have repercussions for health and can perhaps sensitize individuals to psychiatric diseases. In this context, we applied an animal model for chronic sleep restriction to study effects of sleep loss on neurobiolgical and neuroendocrine systems that have been implied in the pathophysiology of depression, particularly, the serotonergic system and the hypothalamic-pituitary-adrenal (HPA) axis. Adult rats were exposed to a schedule of chronic partial sleep deprivation allowing them only 4 h of sleep per day. Sleep restriction was achieved by placing the animals in slowly rotating drums. To examine the regulation and reactivity of the HPA axis, blood samples were collected to measure adrenocorticotropin (ACTH) and corticosterone (CORT) responses. While 1 day of sleep restriction had no effect on HPA axis stress reactivity, sleep restriction for a week caused a blunted pituitary ACTH response in a conditioned fear paradigm. Despite this lower ACTH response, the adrenal CORT release was normal. The blunted pituitary response may in part be related to a reduced sensitivity of serotonin 1-A receptors and/or receptors for corticotropin-releasing hormone (CRH) since sleep restricted rats showed a similar reduction in ACTH release to direct pharmacological stimulation with a serotonin-1A agonist or CRH. Together, these data show that chronic sleep restriction may gradually lead to changes in neurotransmitter receptor systems and neuroendocrine reactivity in a manner that is similar to what is seen in depression. This experimental study thus provides strong support for the hypothesis that disrupted and restricted sleep may contribute to the symptomathology of psychiatric disease.

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Daily expression of clock genes hPer2 and hBmal1 in human peripheral blood mononuclear cells during 40-h sleep deprivation

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Introduction: The prevalence of sleep deprivation appears to be on the rise. Subjects undergoing acute sleep deprivation often Report a transient circadian rhythm disturbance. Recent studies suggest that monitoring clock genes in peripheral blood mononuclear cells (PBMCs) is useful for assessing circadian rhythms in humans. The aim of the study was to evaluate whether 40-h acute sleep deprivation affects the daily expression of two key clock genes, hPer2 and hBmal1, in human PBMCs.

Subjects and Methods: Nine healthy males, mean age 29.1 years, were enrolled in the study. The investigation took place 56 h, including a baseline night, 40-h of total sleep deprivation and a recovery night. An indwelling catheter was placed in the antecubital vein for the 56-h period and blood samples were taken at 4 hourly intervals for three consecutive nights. Total cellular RNA was isolated from PBMC samples using the PAXgene Blood RNA Kit. The levels of expression of two clock genes, Per2 and Bmal1, as well as the in-house gene 36B4, were determined using quantitative one-step RT-PCR on a Light Cycler 2.0 Instrument.

Results: Analysis of variance revealed a significant diurnal variation in expression levels of hPer2 and hBmal1 during baseline conditions (first 24-h cycle) ($P<0.001$, $F=8.20$ for hPer2; $P<0.001$, $F=8.19$ for hBmal1) as well as during the sleep deprivation period (second 24-h cycle) ($P<0.001$, $F=5.8$ for hPer2; $P<0.001$, $F=8.0$ for hBmal1). The mRNA levels of both genes were significantly elevated during daytime activity and low during the night. Statistical analysis with single cosinor method revealed a significant circadian variation in the expression of hPer2 ($P=0.029$) and hBmal1 ($P=0.023$) in baseline conditions but found no significant circadian variation in sleep-deprived conditions (hPer2 $P=0.395$, hBmal1 $P=0.29$).

Conclusion: Our results suggest that 40-h acute sleep deprivation in light conditions blunts the expression of hPer2 and hBmal1.

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Heterogeneous distribution of the 5-HT1A receptor mRNA in chemically identified neurons of the mouse rostral brainstem

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Serotonin (5-HT) is involved in the regulation of sleep and wakefulness, but the mechanisms underlying its role are still largely unknown. Because of the growing use of mice in the study of sleep, we found important to investigate the anatomic/cellular organization of the serotonergic system in areas controlling rapid eye movement sleep that have been poorly studied in this species. Serotonergic neurons of the raphe nuclei have widespread projections throughout the CNS where they impact through specific receptors. Among these, the 5-HT1A receptor type (5-HT1AR) participates in the inhibitory effects of 5-HT at "pre-synaptic" level, where it acts as somato-dendritic autoreceptor on 5-HT neurons, and at post-synaptic targets of serotonergic projections. Our aim was to identify the neuronal phenotypes expressing 5-HT1AR mRNA in the mouse rostral brainstem, using double in situ hybridization histochemistry (ISHH) and immunohistochemistry combined with ISHH. 5-HT1AR mRNA was found to be especially abundant within 5-HT neurons in all anterior raphe nuclei, but notable differences were observed regarding other neuronal phenotypes expressing this transcript in the dorsal (DR) versus the median (MnR) raphe nuclei. Within the DR, only an individualized group of GABAergic neurons in its rostral part was found to express high levels of 5-HT1AR mRNA. In contrast, numerous intermingled non-serotonergic neurons were endowed with 5-HT1AR mRNA throughout the MnR. Outside raphe nuclei, high levels of 5-HT1AR mRNA were visualized within GABAergic neurons of the Gudden's dorsal tegmental nucleus and the interpeduncular complex. Glutamatergic neurons in the pontine reticular formation and the internal part of the lateral parabrachial nucleus also expressed relatively high levels of 5-HT1AR mRNA. In contrast, only few cholinergic and catecholaminergic neurons were labeled by 5-HT1AR mRNA probe. These results suggest that 5-HT1A receptors mediate 5-HT action on serotonergic, GABAergic and glutamatergic, but not cholinergic, neurons within the mouse brainstem. They thus provide a neuroanatomical basis for revisiting 5-HT-mediated control of sleep and wakefulness.

Pharmacology-Animal

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What does paroxetine do with sleep? Its effects in mdr 1a/1b (−/−) and fvb wild-type mice

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It is not unusual to suffer from sleep disturbances while experiencing a depressive episode or other psychiatric diseases like obsessive compulsive disorder, panic disorder or schizophrenia. So far, the direct effects of antidepressive medication on sleep have not been clearly described neither in humans nor in animals. In clinical approaches, selective serotonin reuptake inhibitors (SSRIs, i.e. paroxetine) are reported to suppress sleep and induce wakefulness. In our approach to verify the potential effects of SSRIs on sleep, a multidrug-resistance gene 1-type P-glycoproteins (mdr 1-type P-gps) deficient mouse model [mdr 1a/1b (−/−)] has been used. P-glycoprotein (P-gp) is a major component of the blood brain barrier (BBB) and an ATP-binding cassette transport protein responsible for the efflux of many drugs from the brain back into the periphery. Transported substrates for P-gp include anticancer drugs, the immunosuppressive drug cyclosporin, the glucocorticoid dexamethasone as well as various antidepressive drugs like amitriptyline, mirtazapine and paroxetine. Due to P-gp deficiency in knockout mice, paroxetine is able to remain longer in the brain, thus, hopefully allowing for a better understanding of the function of SSRIs on sleep regulation. According to our data, paroxetine appears to suppress nonREM and REM sleep in mice with no significant difference between genotypes. Furthermore, it seems to cause more fragmentation of nonREM sleep again in both genotypes compared to vehicle or saccharine treatment.

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Sleep-inducing effects mediated by a selective orexin-2 receptor antagonist during the light phase in the rat

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Orexin peptides produced by neurons within the lateral hypothalamus are known to promote wake. A recent study using the OX1/OX2 receptor antagonist ACT-078573 has provided evidence of its hypnotic activity during the active period in animals and humans. Using selective orexin receptor antagonists, the present study investigated the specific role of selective blockade of OX1 and OX2 receptors in sleep modulation. Pharmacological treatments were performed in male Sprague-Dawley rats implanted with telemetric devices for recording of EEG/EMG sleep, locomotor activity and body temperature. Separate groups of animals received selective antagonists at OX1 (SB-408124, 30 mg kg^{-1} sc) or OX2 (JNJ-10397049, 0.3–30 mg kg^{-1} sc and 50–100 mg kg^{-1} po) receptors, or the dual OX1/OX2 receptor antagonist ACT-078573 (100–300 mg kg^{-1} po) and their corresponding vehicles either at two hours into the light phase or at dark onset. As expected, ACT-078573 (100 mg kg^{-1} po) given at dark onset was effective in promoting NREM and REM sleep. SB-408124 did not demonstrate sleep-promoting effects after treatment. When administered either during the light or the dark phase, JNJ-10397049 showed efficacy at 3 mg kg^{-1} sc and 100 mg kg^{-1} po in both sleep induction and promotion. Power spectral densities in NREM and REM sleep were not altered. These effects lasted for 2 h following the treatment in the light phase and were associated with a decrease in locomotor activity and body temperature, and about 6 h in rats treated at dark onset. These data indicate that the sleep-inducing and promoting effects of orexin receptor antagonists can be revealed during the sleep period and are mediated through the OX2 receptor. These promising candidates for the treatment of insomnia might be a novel non-scheduled class of hypnotics as opposed to classical GABA modulating agents.

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Effects of moclobemide administration on REM sleep regulation in the rat

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Introduction: The administration of monoamine oxidase inhibitors has been shown to depress REM sleep (REMS) occurrence in different species. Such a REMS deprivation is followed by a REMS rebound during the withdrawal period [1], but the quantitative aspects of the relationship between the REMS loss and the REMS rebound are unknown. The aim of the present experiment is to clarify these aspects.

Methods: Thirty male Sprague-Dawley rats (Charles River), adapted to normal laboratory conditions (ambient temperature, Ta: 25 ± 1 °C; Light-Dark cycle 12 h:12 h; Light: 09:00 h-21:00 h) were implanted, under general anaesthesia, with electrodes for EEG and with a thermistor for hypothalamic temperature recording. Sixteen animals were injected intraperitoneally (IP) at 09:00 h with a single dose of either moclobemide (100 mg Kg^{-1}; courtesy of "F. Hoffman-La Roche Ldt"; $n = 8$) or vehicle (20% Tween80 in 0,9% NaCl; $n = 8$). Fourteen animals were injected IP with three subsequent doses of either moclobemide (33 mg Kg^{-1}, $n = 7$) or vehicle ($n = 7$) at 09:00 h, 14:00 h, and 19:00 h. EEG was recorded during the two days that preceded (baseline, BL) and the six days that followed (recovery, R) the treatment (T).

Results: Data from the two experiments have been pooled. The changes in REMS amount are expressed as the cumulative percentual difference with respect to BL: a) vehicle: T, 1.0 ± 2.6; R1, 3.1 ± 3.8; R2, 1.6 ± 5.8; R3, 3.6 ± 6.6; R4, 4.0 ± 9.0; R5, 6.4 ± 11,5; R6, 5.9 ± 13.8; b) moclobemide: T, −57.8 ± 5.5; R1, −24.3 ± 3.5; R2, −17.1 ± 5,7; R3, −9.3 ± 8.9; R4, −4.2 ± 12.0; R5, 1.4 ± 15.4; R6, 5.8 ± 17.9.

Conclusions: The results of the present study suggest that, in the rat, as previously observed following exposure to low Ta [2], the REMS debt induced by moclobemide administration is fully recovered during the days that follow the treatment. These results confirm that, in the rat, REMS occurrence is under a precise homeostatic control.

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CRH-R2 evidently is not involved in effects of CRH on sleep suppression

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Corticotropin-releasing hormone (CRH) is generally considered as a wake-promoting, thus sleep suppressing neuropeptide. In our previous study, the importance of central CRH-R1 regarding sleep-

wake regulation was demonstrated with conditional CRH-R1 KO mice, in which intracerebroventricular (icv) injected CRH did not promote wake, or inhibit non-rapid-eye-movement sleep (NREMS). However, it is still unknown of whether or not CRH-R2 plays a role in the processes of vigilance state regulation exerted by CRH. We therefore compared effects of CRH on sleep in conventional CRH-R2 deficient mice (CRH-R2 KO) with those in wildtype littermates (WT). Under isoflurane anaesthesia, four EEG-electrodes, two EMG-electrodes, and an icv cannula were implanted. Three doses of CRH (0.3, 1.0, and 3.0 μg) were administered icv 30 min prior to the light onset. Each vigilance state (wake, rapid-eye-movement sleep (REMS) and NREMS) was visually classified from EEG and EMG recordings. CRH dose-dependently increased wake and suppressed sleep in WT and in CRH-R2 KO animals immediately after injections compared to vehicle control. Elevated waking levels declined between two and eight hours after injection returning to baseline levels in a dose-dependent fashion. Changes in NREMS were contrarious to wake responses after CRH injection. REMS levels dose-dependently decreased and were almost completely suppressed after 3.0 μg of CRH for up to four hours after injection in both genotypes. During the dark period, all animals showed more or less pronounced rebound effects which in most cases were dose-dependent. The present study demonstrated no distinct differences in the effects of CRH on sleep between WT and CRH-R2 KO animals, indicating that CRH could exert its action on promoting wake per se without the presence of CRH-R2. As suggested in our previous experiment, CRH-R1 rather than CRH-R2 would be important for CRH-mediated sleep-wake regulation.

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Comparison of D-amphetamine, caffeine and modafinil on sleep/wake profile and behavioural activity in the rat

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This study compared the effects of D-amphetamine, caffeine and modafinil on sleep/wake profile and behavioural activity in rats. These arousal promoting agents of different mechanism of action have been utilised clinically to treat hypersomnia/narcolepsy and provide useful agents for pharmacological validation of preclinical models. Telemetric recording of electroencephalogram (EEG) and electromyogram (EMG) was used to derive the following sleep parameters in rats; time spent in awake (awake), NREM sleep time & latency, REM sleep time & latency and Total Sleep Time (TST). D-amphetamine (0.3, 1, 3 mg kg^{-1} i.p.), caffeine (3, 10, 30 mg kg^{-1} i.p.) and modafinil (10, 30, 100 mg kg^{-1} i.p.) were administered at CT 0 (“lights-on”). Behavioural activity (immobility time, locomotor activity, rearing and grooming) of the three compounds was assessed separately in rats at the same doses using the LABORAS system. The results obtained confirmed a pro-arousal profile in terms of dose related increases in general activity, time spent awake and NREM & REM latencies for all three compounds. This was accompanied by decreases in time spent in NREM and REM sleep. Interestingly, modafinil induced a more prolonged REM sleep reduction with respect to TST during the wake-promoting effect compared with an equipotent dose of D-amphetamine. Furthermore D-amphetamine and caffeine but not modafinil induced a rebound hypersomnolence after their wake-promoting effects. The analysis of behavioural activities showed that D-amphetamine and caffeine induced a greater increase of self-grooming when compared to other activities. This increase may be due to drug induced stereotypy and/or anxiogenic-like activity for D-amphetamine and caffeine. This study suggests that use of the rat CT 0 sleep model combined with behavioural assessment using LABORAS may provide a useful preclinical strategy for assessing novel potential therapies treating sleep disorders such as hypersomnolence and narcolepsy.

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Basal forebrain adenosine receptors and REM sleep recovery in rats

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Sleep deprivation (SD) leads, in the basal forebrain (BF), to increased extracellular concentrations of adenosine, which is one of the key factors in NREM sleep homeostasis. However, the role of adenosine in the regulation of REM sleep recovery is less well understood. We hypothesize that adenosine can act through A1 (A1R) or A2A receptors (A2AR) on the BF waking-active cells to regulate REM recovery. To test this hypothesis we infused, using in vivo microdialysis, A1R antagonist, 8-cyclopentyl-1,3-dimethylxanthine (CPT), A2AR antagonist, 3,7-dimethyl-propagylxanthine (DMPX), and the combination of both antagonists into the BF of rats during SD. Under general anaesthesia, male Wistar (300–400 g) rats were implanted with electrodes for EEG and EMG recording, and with a unilateral guide cannula for microdialysis probes targeting the BF. The experimental schedule consisted of recording of natural sleep-waking cycle for 24 h, SD for 3 h with microdialysis infusion of artificial cerebrospinal fluid, or SD accompanied by infusion of CPT at 3 different doses (1, 5 and 100 uM), DMPX (5, 10 and 50 uM) and the combination of both (10 uMDMPX+5 uMCPT, 10 uMDMPX+100 uMCPT, 50 uMDMPX+5 uMCPT). The EEG recordings were scored for REM sleep, nonREM (NREM) sleep, and delta power during NREM sleep was calculated. We found that CPT at 1uM ($n = 4$) induced a significant decrease in REM sleep recovery during 12 h after SD as compared with the effect of sole SD. REM sleep recovery had a tendency to decrease in rats infused with DMPX at doses 5 and 10 uM, but the effect was not statistically significant. These results suggest that adenosine acting through A1R in the BF could exert an indirect effect on promotion of REM sleep recovery after SD.

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Depression and sleep: a comparative study on EEG activity after different antidepressant treatments in mice

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Depressed patients frequently experience sleep disturbances, e.g., a longer sleep latency and a shorter sleep continuity. However, more evident changes in their sleep patterns can be detected in their EEG traces such as shorten REM sleep latencies and lowered power in their slow-wave activities. Meanwhile, effects of antidepressants are described often to suppress REM sleep, but their effects on nonREM sleep are rather obscure and the way of action are not fully investigated. In this study, different classes of antidepressants were tested in normal C57BL/6J mice to understand whether antidepressants elicit significant modulation in specific EEG frequencies. Male mice were implanted with EEG and EMG recording electrodes under ketamin-xylazine anesthesia. After the baseline recording, 2 tricyclic drugs: clomipramine or trimipramine, and a selective noradrenaline reuptake inhibitor: riboxetine (0 and

10 or 30 mg kg^{-1} bw each) were injected ip at ZT6. Polygraphic data were processed by the LabVIEW-based acquisition program, in which an FFT algorithm served for the analysis of the particular EEG frequency contents. Vigilance states were visually defined, and the power array of each EEG frequency band was compared in a three dimensional manner with or without antidepressants. Clomipramine and reboxetine suppressed REM sleep but increased nonREM sleep in a dose-dependent fashion. Within 15 min after injection, sharp increases in delta power and broad reduction of theta power were evident especially after the high dose, compared with those after saline injection. The magnitude of altered EEG was larger and the drug effects remained longer upon REM sleep than nonREM sleep. Trimipramine did not clearly affects sleep EEG at the low dose, but the high dose totally suppressed the whole power of all bands. The results demonstrated common features in EEG changes affected by antidepressants. Although the suppression of REM sleep could be induced by monoaminergic drugs, a shifted peak of increased delta power was first shown in a rodent model. Screening EEG traces might be useful to detect potential antidepressant agents.

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Inhibitory effect of state independent ponto-geniculo-occipital waves on seizure ocurrence induced by local application of penicillin into the temporal lobe amygdala

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It has been shown the induction of state independent ponto-geniculo-occipital waves (PGO) during 20 to 24 h, by microinjecting carbachol into the parabrachial region (Pb). This experimental approach allows to further explore the probable inhibitory effect of PGO wave on epileptic seizures. In order to explore the possible inhibitory role of the phasic phenomena of REM sleep (PGO) over epilepsy, we have analyzed the epilepsy evolution produced by local administration of Na-penicillin (PCN), during sustained PGO activity and irrespective of current state.

Methods: The development of experimental epilepsy was compared among nine chronically implanted, adult, male cats, by means of polygraphic 23 h recordings. Our protocol consisted of sets of 4 trials: carbachol; PCN; carbachol followed by PCN and finally PCN followed by carbachol. Each cat received one single set and all trials were carried out with a seven days interval, in order to compare the epileptic activity both in the presence of PGOs and without them. Cats were prepared for sleep and PGO wave recordings. Cannulae were implanted in the amygdala and Pb for PCN and carbachol application respectively. PCN (100 i.u. 1.0 μL^{-1}) was applied alone, and also preceded (one hour) or followed (one hour) by carbachol (4 μg 0.25 μL^{-1}) microinjection into the Pb for inducing PGOs. Two consecutive 23-h sleep recordings during each experimental trial were performed.

Results: PGO waves exert an inhibitory influence over: 1) Generalized convulsive seizures (GCSs) number and duration; 2) spike frequency; 3) increase the latency onset of GCSs and reduce the motor component of seizures and; 4) restores sleep alterations produced by experimental epilepsy. Our results support an inhibitory influence of PGOs over PCN epilepsy development. These data support the hypothesis that the phasic phenomena of REM sleep have a depressor effect on epilepsy development, inhibit seizures and normalize sleep architecture changes induced by epilepsy. We suggest that one possible function of PGO activity is to protect the brain from intense changes in neuronal excitability; namely convulsive activity.

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Effect of vagus nerve electrical stimulation and topic naloxone in the nucleus of the solitary tract on sleep and electroencephalographic activity in cats

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Our laboratory previously reported that vagus nerve electrical stimulation (VNS) induced changes on sleep and behavior in cats. We described an increase in total time of REM sleep and slow wave sleep (SWS). An increase of the ponto-geniculo-occipital (PGO) wave density during REM sleep and a spectral power increase in the bands corresponding to sleep spindles (8–14 Hz) and delta waves (1–4 Hz) were also reported. The nucleus of the solitary tract (NTS), receiving vagus nerve afferents, plays a role in the control of sleep mechanisms. This nucleus contains enkephalinergic neurons and opioid peptide receptors, which are thought to play a functionally important role. To study the role of NTS opioids on sleep changes induced by VNS, we examined the effects of topic NTS microinjection of an opioid antagonist (naloxone, Nx) in freely moving cats. Six male cats were stereotaxically implanted for conventional sleep recordings and an electrode with cannula was placed in the NTS for Nx administration (1 μg 1^{-1} μL during one min.). An electrode for VNS was also implanted. All cats were submitted to 11 rounds of 23 h continuous sleep recordings in five categories: base line (BL), saline solution in NTS (SS 1 ml), Nx in NTS, SS+VNS (1 min, 5 times, 1 h interval, 30 Hz, 0.5 ms, 2–3.5 mA), VNS, and Nx+VNS. The EEG power spectrum of SWS, total time and number of sleep stages were analyzed. The VNS induced an increase in SWS and REM sleep total time. The Nx alone, increased the Intermediate stage (SWS-REM sleep transition) total time. VNS+Nx increased the SWS and the Intermediate stage total time. A power increase in the bands corresponding to sleep spindles (8–14 Hz) and delta waves (1–4 Hz) with VNS were observed. VNS+Nx only, increased the power in the sleep spindles band, and Nx diminished the delta waves band power. The present results suggest that NTS opioids could modulate the slow EEG activity during sleep, and that the enkephalinergic inhibition dissociates the REM sleep and SWS EEG activity by increasing the intermediate stage duration. We concluded that the opioids participate in the modulation of the VNS effects on sleep.

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A role for GABAA α4-subunit-containing receptors in sleep regulation?

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GABAA receptors containing the α4-subunit are highly expressed in the thalamic relay nuclei which play a key-role in generating patterns of electrical activity occurring in the brain during sleep and waking. Notably, the α4-subunit is preferentially associated with the δ-subunit and these α4βδ-GABAA receptors show a predominant extrasynaptic localization and specific electrophysiological properties. We performed in α4-GABAA knockout (α4-KO) mice and their wild-type (WT) control littermates, continuous, long-term infra-red activity recordings ($n = 23$ α4-KO versus $n = 17$ WT), as well as 24-h baseline EEG recordings ($n = 8$ α4-KO versus $n = 9$ WT). Mice were also submitted to 6 h sleep deprivation (SD) by gentle procedures, a well-established method to enhance sleep pressure thereby uncovering potential differences in sleep homeostasis. The two genotypes showed remarkably similar daily amounts of rest under baseline conditions (12 h : 12 h LD) with the exception of the last 3-h interval of the dark period, where α4-KO mice rested

significantly more than the WT mice. In addition, α4-KO mice had significantly more long-lasting rest episodes (of duration 33–128 min), suggesting that their sleep may be more consolidated. Preliminary analyses of EEG recordings showed no difference between the genotypes in time spent in the different vigilance states. Spectral analysis of the baseline EEG showed that EEG power in non-rapid eye movement (NREM) sleep was significantly lower in α4-KO mice, specifically in the frontal derivation, in frequencies between 9.00–15.00 Hz (12-h light periode) and 8.00–17.00 Hz (12-h dark period). Further analyses of EEG recordings are ongoing to evaluate the effects of the genetic deletion of these receptors on the response to sleep deprivation. The decreased EEG power density in NREM sleep observed in the α4-KO mice suggest a role of α4-GABAA receptors in generating brain rhythms associated with NREM sleep.

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Endotoxin-induced alterations of sleep in corticotropin-releasing hormone type 2 receptor knockout mice

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In animal studies, bacteria, viruses, or their products such as endotoxin (lipopolysaccharide, LPS) have been shown to enhance non rapid-eye-movement sleep (NREMS) and EEG-delta activity. The promotion of NREMS after infection is due, in part, to the release of the somnogenic cytokines such as interleukin-1β, and tumor necrosis factor-alpha and their interactions with the neuropeptides growth hormone-releasing hormone and corticotropin-releasing hormone (CRH). Moreover, by quantitative trait loci analyses it was shown that CRH type 2 receptor (CRH-R2) is one of the candidate genes responsible for enhancing NREMS in response to infectious challenge in mice (Toth and Williams, 1999). In line with this evidence, we investigated sleep-wake behaviour of the CRH-R2 knockout mice during acute infection induced by the peripheral administration of components of the bacterial cell LPS. The mice were implanted with EEG/EMG electrodes and entrained into 12:12-h light-dark cycles. Following baseline recordings they were intraperitoneally injected with 1 ug kg^{-1} LPS or pyrogen free saline at the beginning of dark period of the light-dark cycle, and sleep patterns were compared between CRH-R2 KO mice and wild-type littermates. In response to peripheral LPS administration the amount of NREMS in wild-type mice was apparently increased during the first 5 postinjection hours. Interestingly, in CRH-R2 knockout mice LPS elicited only slight NREMS enhancement in the same portion of the dark period. Moreover, this effect was evident only for 2 h with subsequent boost of wakefulness thereafter. Collectively, these preliminary data, in agreement with previous evidence, support the involvement of CRH-R2 in mediating NREMS enhancement induced by peripheral immune challenge.

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The A1 adenosine agonist R-PIA increases sleep in immature rats

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The total sleep time observed in immature precocial species is greatly increased when compared with sleep quotas recorded in adults. On the other hand, adenosine is a neuromodulador particularly important in embryonic development and in the control of sleep. Previous studies showed that adenosine and the selective adenosine A1 agonist R-PIA caused significant reductions in the spontaneous activity of immature rats. The present report aims at recognizing whether the reduction in activity reflects a change in EGG sleep parameters. Male Sprague Dawley rats were individually housed and maintained under 12/12 L/D schedule immediately after weaning (21 days old, 60 g b.w.). The animals were chronically implanted for conventional polysomnography. The EEG was digitized at 256 samples/s and computer stored for off line analysis. The recordings were scored in 30s epochs according to standard criteria and the relative spectral power was divided in delta (0.1–4 Hz), theta (4–8 Hz), alpha 2 (12–20 Hz), beta 1 (20–30 Hz) and beta 2 (30–40 Hz) ranges which were compared after intraperitoneal injection of saline and R-PIA (0.1 mg kg^{-1}, 30 min before lights on). The administration of R-PIA increased the total EEG power (81%, $P<0.001$) as well as the power in theta (15%, $P<0.05$) and delta (12%, $P<0.001$) bands but decreased alpha 1 (75%, $P<0.001$) and beta 2 (40%, $P<0.01$), showing that the previously observed reductions in motor activity were in fact increases in both NREM (delta) and REM (theta) sleep. The results confirm earlier observations made in adult rats and in fetal precocial species (sheep) and extend them to immature altricial animals in which the need of sleep is greatly increased, confirming the importance of adenosine in the function and development of the embryonic brain.

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Effects of pilocarpine on the hippocampal-neocortical dialogue during waking in rats

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Hippocampal rhythmic slow activity in the theta range (6–10 Hz) occurs during exploratory behavior and REM sleep in rodents, carnivores and primates. Theta activity has been implicated in various theories of hippocampal function, from sensory processing to control of voluntary movement. Acetylcholine has important functions in the control of cortical arousal during waking and REM. Pilocarpine, a cholinergic agonist with moderate affinity for M1 and M2 muscarinic receptors and higher for M5, increases the theta activity in the cortex of rats. The aim of this study was to analyse the effects of pilocarpine on the interaction between hippocampus and neocortex and focused in the coherence function during wakefulness Five Wistar rats (350–375 g) were implanted with electrodes for EEG recording in frontal cortex (AP+2.0, ML+2.5) and hippocampus (AP -4.0, ML+2.0, DV-3.0) relative to Bregma, with reference in the cerebellum. One cannula was placed in the lateral ventricle. EMG recording was obtained over the dorsal neck muscles. After recovery and habituation, monopolar EEG, EMG and behavioural states were recorded along 2 h in freely moving animals during the dark period. Recordings were made after injection of saline and pilocarpine (120 and 360 mg in 1 microlitter, i.c.v.). Histological studies were made to confirm cannula and electrodes placement. EEG and behavioral visual scoring was used to distinguished vigilance states. Four periods of 15 min following the i.c.v. injection were used to calculate power spectrum and coherence function to study the interaction between hippocampus and cortex. After a short lag, the i.c.v. injection of pilocarpine caused an increase in the coherence between neocortical and hippocampal EEG during active and passive waking in theta (4.1–8 Hz) band, but no changes were observed in delta band. The coherence returned to control values after 45 min. In conclusion, pilocarpine caused an increase in cortical theta activity which can be interpreted as changing the transference rate of information from hippocampus -as generator- to frontal cortex during waking states.

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Paradoxical sleep deprivation enhances the rewarding effects of cocaine in mice

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We have recently verified that paradoxical sleep deprivation (PSD) facilitated amphetamine-induced behavioural sensitization by increasing its conditioned component. The aim of the present study was to investigate the effects of PSD on another animal model of addiction (which measures the rewarding properties of drugs: the conditioned place preference-CPP-paradigm) using another widely abused psychostimulant (cocaine). Of note, important differences between behavioural sensitization and CPP have been reported in the literature. Thirty-nine male Swiss mice (40–45 g) were randomly allocated to 3 groups ($n = 13$): NSD-COC, SD-COC and SD-COC-SD. The animals were maintained in their home-cages (NSD) or submitted to PSD for 72 h (SD). The multiple platform method of PSD was employed. Immediately after PSD or home-cage maintenance, mice received an ip injection of $10\,mg\,kg^{-1}$ cocaine (COC) and, 5 min later, were confined for 10 min in one compartment of the CPP apparatus (half of the animals of each group was confined in the compartment A and the other half in the compartment B-unbiased design). The NSD-COC and SD-COC groups returned to their home-cages whereas the SD-COC-SD group continued in PSD. Six hours later, all the animals received an ip injection of saline and, 5 min later, were confined for 10 min in the other compartment (different from the one where they had received COC). All mice were then returned to their home-cages. After 72 h, mice were placed in the CPP apparatus and the time spent, the number of entrances and the locomotion frequency in the compartments A and B were recorded for 5 min. Only SD-COC and SD-COC-SD groups presented a significant increase in time spent in the COC-paired compartment compared to the saline-paired compartment. In addition, locomotion of SD groups in the COC-paired compartment was significantly augmented without concurrent modifications in the number of entrances in this compartment compared to the saline-compartment. We conclude that PSD facilitates COC-induced CPP as well as conditioned locomotion to this drug. From a translational standpoint, we suggest that PSD may enhance drug-craving and drug-seeking behaviour in humans.

Pharmacology-Human

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Effects of a single dose of modafinil on EEG during the MWT during acute sleep deprivation

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Introduction: Modafinil is a wake-promoting compound currently used for the treatment of excessive sleepiness in sleep disorders such as narcolepsy, obstructive sleep apnea and shift work sleep disorder. Sleepiness can be reliably induced in healthy volunteers by sleep deprivation and is associated with characteristic changes in the spectral composition of the EEG, in particular in the delta and theta band frequencies. We investigated the effects of a single dose of modafinil, compared to placebo, on waking EEG spectra from 0 to 25 Hz during a 38 h sleep deprivation period.

Methods: Quantitative EEG analyses were performed on 2 mins of EEG data obtained at the beginning of Maintenance of Wakefulness Tests (MWT) performed at 2 h intervals for the last 20 h of a 38 h period of sleep deprivation in 23 healthy young male individuals. Participants were woken at 0700 h on day 1 and kept awake until 2100 h on day 2. Administration of a single dose of either modafinil (200 mg) or placebo occurred at 0200 h on day 2. Each participant completed both conditions in a 4-period randomized cross-over design trial. 4 h time bins were created to assess time course effects of modafinil compared to placebo.

Results: In the placebo condition, sleep deprivation led to an increase in low EEG band frequencies and spindle activity (1–7 and 14 Hz $P<0.05$) and a reduction in high alpha and beta band activity (10, 11 and 18–21 Hz $P<0.05$). Sleep deprivation-induced changes in low, alpha and beta band activity were attentuated by modafinil. Compared to placebo, modafinil suppressed delta and theta band activity (1–6 Hz, $P<0.05$) and increased power in high alpha and beta band frequencies (11, 12 and 18–25 Hz, $P<0.05$) between 2 and 6 h post-dose and 8–12 h post-dose (1–6, 10, 11 and 19–25 Hz, $P<0.05$). From 14–18 h post-dose, modafinil suppressed delta and theta band activity and increased beta band activity but no longer affected high frequency alpha (1–5, 19 and 21–23 Hz, $P<0.05$).

Conclusion: A single 200 mg dose of modafinil attenuates the increase in low frequency activity and the reduction in high alpha and beta activity associated with sleep deprivation for 12 h after drug administration.

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Novel therapies in REM sleep behaviour disorder

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Background: Rapid Eye Movement (REM) sleep behaviour disorder (RBD) is characterised by the loss of the normal REM sleep atonia leading to the acting out of dreams, often with associated injury. Schenck first identified clonazepam as an effective treatment for RBD and for many years it has been the first line treatment with subsequent data confirming its long term efficacy. Melatonin has been reported as effective in 3 case series but few other therapies have been identified to date. Within the Respiratory Sleep and Support Centre at Papworth, numerous patients commenced on clonazepam developed unacceptable daytime somnolence. This led to a number of patients using shorter acting hypnotics often with good effect. A retrospective case notes review was therefore performed to examine all the treatments we have used for RBD.

Methods: A large database of patients was reviewed to find all patients with treated RBD. This included patients with idiopathic and secondary RBD. One of the authors (KA) contacted all patients and used a standardised questionnaire to review medication, dose range, efficacy and side effects as well as overall patient satisfaction.

Results: Thirty-eight patients were treated (mean follow up 2 years). Clonazepam was used as the first line therapy for 35/38 patients with 21/35 complaining of side effects (early morning/day time sleepiness, low mood or confusion) that usually occurred at doses >1 mg. Temazepam, Melatonin and in particular Zopiclone were subsequently used successfully and had a lower reported incidence of side effects.

Discussion: Despite its efficacy, Clonazepam may not be well tolerated. Zopiclone has not been reported as an effective treatment for RBD before. In our cohort it was better tolerated than clonazepam. This highlights the need for awareness of the potential side effects of clonazepam and the need for novel therapies for those who fail to tolerate it.

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Comparative placebo-controlled polysomnographic and psychometric studies on the acute effects of gabapentinversus ropinirole in restless legs syndrome (RLS)

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Objective: Dopamine agonists are currently considered the first-line therapy in RLS. Comparative studies on different treatment strategies are scarce. Thus, the aim of the present investigation was to compare the acute effects of gabapentin (GPT) and ropinirole (ROP) in placebo-controlled sleep laboratory studies in RLS patients.

Methods: Forty patients (28 females, 12 males, aged 56.0+17.9 years) with the diagnosis of primary RLS (ICD-10: G25.8) were included in a single-blind, placebo-controlled cross-over study with 300 mg GPT. Another forty RLS patients (19 females, 21 males, aged 58.0+12.8 years) received 0.5 mg ROP in the same design. Polysomnographic and psychometric measures were obtained in three sleep laboratory nights (adaptation, placebo and drug night). Descriptive data analysis included the Wilcoxon test for differences between the active drugs and placebo and a Mann-Whitney U-test for inter-group differences.

Results: Sleep initiation and maintenance was significantly improved after GPT, while it remained unchanged after ROP, with the inter-drug differences reaching the level of statistical significance. Sleep architecture showed differential changes after the two drugs: While GPT decreased S1, increased S3+S4 and SREM and shortened REM latency, ROP increased S2, decreased S3+S4 and SREM and increased REM latency. Periodic leg movements (PLM) were more pronouncedly decreased after ROP (−64%) than after GPT (−41%). Snoring improved after ROP only (−43%). The arousal index decreased significantly after GPT (−34%) and increased after ROP (+12%). Subjective sleep quality was significantly improved after GPT only. Concerning awakening quality, thymopsychic and noopsychic variables no differences between the two treatment strategies were observed.

Conclusion: While the dopamine agonist ROP showed acute therapeutic efficacy in regard to PLM measures, but not in regard to objective and subjective sleep and awakening quality of RLS patients, GPT showed acute therapeutic efficacy in both PLM measures and objective and subjective sleep and awakening quality, which seems of importance for the acceptance of a drug, patients' compliance and prognosis.

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Effect of repeated doses of the novel sleep compound eplivanserin on cardiac ventricular repolarisation in healthy subjects

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Introduction: Eplivanserin, an Antagonist of Serotonin Two A Receptors (ASTAR), is being developed at the 5-mg dose for chronic insomnia characterised by night-time awakenings. An electrocardiogram (ECG) study was performed to assess the potential effect of eplivanserin on cardiac ventricular repolarisation at an effective dose (5 mg) and at a supra-therapeutic dose (10 mg) mimicking the worst case exposure (interaction, population).

Methods: In this Phase 1, single-centre, double-dummy, parallel-group study, healthy males and females ($n = 90$) were randomly assigned to receive eplivanserin, moxifloxacin 400 mg (positive control) or placebo (PBO) PO once daily (eplivanserin or PBO Days 1–21; moxifloxacin Day 21 only). The primary endpoint was change from baseline in QTcF (Fridericia correction); secondary endpoints included change from baseline in heart rate (HR), QT, QTcB (Bazett's correction) and QTcN (study population specific QT correction). Standard tolerability and safety measures were also assessed.

Results: As expected, moxifloxacin 400 mg produced a consistent statistically significant increase in corrected QT interval (mean effects: QTcF:+8.13 ms) versus PBO, thus, validating the study. There were no significant differences between eplivanserin 5 or 10 mg versus PBO in QTcF from 3-h to 7-h post-dose on Day 21 (mean effects around -0.44 and -0.56 ms, respectively). The upper bound (UB) of the 2-sided 90% CI of QTcF was 3.01 ms and 2.88 ms for eplivanserin 5 and 10 mg, respectively, and 11.04 ms for moxifloxacin 400 mg. The largest QTcF time-matched mean difference for eplivanserin 5 and 10 mg versus PBO showed an estimate (UB 95% CI) of 0.66 ms (5.02 ms) and 2.18 ms (6.53 ms), respectively, and 11.28 ms (15.66 ms) for moxifloxacin 400 mg. Eplivanserin had no effect on HR. Eplivanserin did not prolong QTcF (>450 ms for males, >470 ms for females), or increase QTcF over 60 ms from baseline. No clinically significant changes were seen in laboratory parameters, vital signs or other ECG parameters.

Conclusion: In this ECG study, eplivanserin 5 mg day^{-1} and the supra-therapeutic dose of 10 mg day^{-1} had no significant effect on cardiac ventricular repolarisation, as assessed by QTc intervals, or impact on HR.

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Quetiapine improves sleep in demented patients

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The specific receptor binding profile of this compound suggests a favourable effect on sleep which could be demonstrated in healthy subjects and, recently, in patients with primary insomnia. The present open-labeled pilot study which was approved by the local ethical committee was designed to observe the effects of quetiapine 12.5–50 mg daily on sleep and nocturnal behaviour in patients with dementia. Twenty-one patients suffering from Alzheimer's disease or frontotemporal dementia were included (mean age 71.8 ± 7.7 years; 17 male, 4 female). For quantitative analysis, a sample of 11 patients resulted. After inclusion, patients underwent two weeks of inpatient treatment; they were accomodated together with their caregivers who thus could observe and judge the patients' nocturnal behaviour. Patients received 12.5 mg quetiapine initially; in some of them, the dose was increased later. After discharge, patients continued as outpatients with a continuous quetiapine medication over four weeks. Subjective estimates of sleep quality improved continously during treatment. Actigraphy resulted in a decreasing nocturnal activity score per minute, and a longer period of complete inactivity between midnight and 6:00 am. Polysomnography data from 4 patients were compared between time points, exhibiting an increase in total sleep time, and a continuously increasing sleep efficiency. Observer ratings of general psychopathology and depressive symptomatology showed significant improvement. 8 patients and 9 caregivers rated the global efficacy of treatment as ''good'', the rest rating ''neutral'', none ''bad''. Tolerability of medication was rated ''good'' by all patients and caregivers. The data thus indicate an overall favourable effect. To summarize, quetiapine appears a promising candidate for the treatment of dementia-related sleep problems.

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Evaluation of the interaction of pantoprazole on the pharmacokinetic profile of the novel sleep compound eplivanserin in healthy male subjects

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Introduction: Eplivanserin, an Antagonist of Serotonin Two A Receptors (ASTAR), does not bind to GABA receptors (unlike benzodiazepines) and increases slow wave sleep (SWS). It is being developed at the 5-mg dose for chronic insomnia characterized by night-time awakenings. The solubility of eplivanserin is dependent on pH. This study evaluated the effect of pantoprazole (an agent that reduces gastric acid with minimal interaction with the cytochrome P450 system) on the pharmacokinetic profile of eplivanserin.

Methods: Single-centre, open-label, non-randomized, 2-period, uncontrolled, single-group study, in which 12 healthy male subjects received 1 oral dose of 5 mg eplivanserin alone (Period 1, Day 1) followed after at least 13 days of wash-out period by 8 once-daily oral doses of 40 mg pantoprazole (Period 2, Days 1–8), with 5 mg eplivanserin coadministered on Day 8 of Period 2. Blood samples for the assay of eplivanserin and its active N-demethyl metabolite, SR141342, were collected over a 4-day period after each eplivanserin administration. Blood sample collection for pantoprazole assay occurred over a 24-h period after the last dose of pantoprazole. Eplivanserin, SR141342 and pantoprazole plasma concentrations were determined by validated LC-MS/MS methods. Pharmacokinetic parameters were calculated using a non-compartmental analysis.

Results: The pharmacokinetic profile of eplivanserin or SR141342 was not altered by pantoprazole. Estimated ratios (co-administration/alone) for C_{max} and AUCs ranged from 0.91 to 0.97 and 90% CIs were within the [0.8–1.25] bioequivalence interval. No serious adverse events were reported.

Conclusion: The 8-day repeated dosing of pantoprazole did not meaningfully alter the pharmacokinetics of eplivanserin or

SR141342. As a result, dose adjustment is not required when eplivanserin is coadministered with a drug that increases gastric pH. Eplivanserin was well tolerated both alone and in combination with pantoprazole.

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The pharmacokinetics of an oral contraceptive were not affected by repeated doses of the novel sleep compound eplivanserin in healthy women

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Introduction: Eplivanserin is an Antagonist of Serotonin Two A Receptors (ASTAR) that is being developed at the 5-mg dose for chronic insomnia characterized by night-time awakenings. It increases slow wave sleep (SWS), and unlike benzodiazepines does not bind to GABA receptors. In-vitro studies have shown that eplivanserin has no potential to induce CYP1A, 2A and 3A. To evaluate any effect in vivo, the pharmacokinetic profile of oral contraceptive steroids was evaluated after repeated supra-therapeutic doses of eplivanserin.

Methods: Single-centre, open-label, non-randomized, uncontrolled, single-group study, in which 18 healthy young female subjects received 21 daily oral doses of Minidril® (ethinyloestradiol and levonorgestrel), coadministered with 60 mg eplivanserin from Day 15 to Day 21. On Days 10, 13 and 21, blood samples were collected over a 24-h period after dosing for analysis of ethinyloestradiol and levonorgestrel, and on Day 21 for analysis of eplivanserin and SR141342, its active N-demethyl metabolite. Ethinyloestradiol and levonorgestrel were assayed by a validated GC/MS method after liquid-liquid extraction, and eplivanserin and SR141342 by a validated LC-MS/MS method. Pharmacokinetic parameters were calculated using a non-compartmental analysis.

Results: The pharmacokinetic profiles of ethinyloestradiol or levonorgestrel were not altered by repeated oral administration of 60 mg eplivanserin. 90% confidence intervals of estimated ratios (co-administration/alone) for C_{max}, C_{min} and AUC_{0-24} were within the [0.8–1.25] bioequivalence interval, for both ethinyloestradiol and levonorgestrel. No serious adverse events were reported.

Conclusion: Repeated daily supra-therapeutic doses of eplivanserin did not alter the pharmacokinetics of a coadministered oral contraceptive containing ethinyloestradiol and levonorgestrel. The combination of eplivanserin and Minidril® was well tolerated.

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Sleep and psychomotor performance in healthy subjects after morning or evening administration of eplivanserin, a novel sleep compound

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Introduction: Eplivanserin, an Antagonist of Serotonin Two A Receptors (ASTAR) that increases slow wave sleep (SWS) and (unlike benzodiazepines) does not bind to GABA receptors, is being developed at the 5-mg dose for chronic insomnia characterized by night-time awakenings. Sleep, motor activity, attention, short-term memory, alertness and mood were assessed in healthy subjects after morning or evening administration of 3 doses of eplivanserin or placebo.

Methods: Double-blind, double-randomized, placebo-controlled, 4-period, cross-over study, in which 16 young healthy male subjects were randomized to receive treatment in the morning (8 subjects) or evening, (8 subjects) and then randomized to a treatment sequence of 4 periods with an oral single dose of eplivanserin (1, 10 and 40 mg) and placebo, with a 1–2 week washout between each of the 4 periods. Measurements included EEG parameters, psychomotor tests [Critical Flicker Fusion (CFF), Choice Reaction Time (CRT), Compensatory Tracking Test (CTT) and Sternberg Memory Scanning Task (STM)] and subjective ratings of sleep.

Results: Morning or evening administration of all 3 doses of eplivanserin doubled the time spent in SWS, in correlation with a decrease in Stage 2 sleep. Sleep efficiency improved, and episodes of wake after sleep onset (WASO) $\geq$120 seconds decreased, after all 3 doses. There was no dose-dependant effect. Sleep latency and sleep duration were unaffected. Time of eplivanserin administration did not affect performance on attentional or psychomotor tasks (CRT, CTT) or short-term memory (STM). A slight decrease in CFF threshold detection was observed at all doses (most likely related to a direct effect on pupillary response, myosis as observed with other $5HT_2$ antagonists). Subjective CNS impairments were not reported. No serious adverse events were reported.

Conclusion: Time spent in SWS was doubled after single oral doses of eplivanserin 1, 10 and 40 mg in healthy subjects, with no dose-dependent effects. Regardless of time of administration (morning or evening), eplivanserin did not impair attentional or psychomotor tasks.

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Evaluation of the interaction of repeated doses of the strong CYP3A4 inhibitor ketoconazole on the pharmacokinetic profile of the novel sleep compound, eplivanserin, in healthy male subjects

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Introduction: Eplivanserin is an Antagonist of Serotonin Two A Receptors (ASTAR) that is being developed at the 5-mg dose for chronic insomnia characterized by night-time awakenings. Eplivanserin increases slow wave sleep (SWS), and unlike benzodiazepines, does not bind to GABA receptors. *In-vitro* studies have shown that eplivanserin is slightly metabolized by CYP3A4 (fraction metabolized = 15%). This study evaluated the effect of repeated doses of ketoconazole, a strong CYP3A4 inhibitor, on the pharmacokinetic profile of eplivanserin.

Methods: Single-centre, open-label, non-randomized, 2-period, uncontrolled, single-group study, in which 12 healthy male subjects received 1 oral dose of 5 mg eplivanserin alone (Period 1, Day 1) followed 14 days later (wash-out period) by 8 once-daily oral doses of 200 mg ketoconazole (Period 2, Days 1–8), with 5 mg eplivanserin coadministered on Day 8 of Period 2. Blood samples for the assay of eplivanserin and its active N-demethyl metabolite, SR141342, were collected over a 4-day period after each eplivanserin administration. Blood sample collection for ketoconazole assay occurred over a 24-h period after the last dose of ketoconazole. Eplivanserin and SR141342 plasma concentrations were determined by a validated LC-MS/MS method and ketoconazole by a validated HPLC method using fluorescence detection. Pharmacokinetic parameters were calculated using a non-compartmental analysis.

Results: The pharmacokinetic profile of eplivanserin or SR141342 was not significantly altered by ketoconazole. Estimated ratios (coadministration/alone) for C_{max} and AUCs ranged from 0.88 to 1.05, and 90% CIs were within the bioequivalence interval [0.8–1.25], except for eplivanserin C_{max} with a ratio estimate

[90% CI] of 1.15 [1.03–1.29]. No serious adverse events were reported.

Conclusion: The 8-day repeated dosing of ketoconazole did not meaningfully alter the pharmacokinetics of eplivanserin or SR141342. Eplivanserin was well tolerated both alone and in combination with ketoconazole. Eplivanserin can be safely coadministered with any drug inhibiting CYP3A4.

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Sleep complaints and hypnotic drug use in hospitalized patients

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Objectives: Epidemiological studies have shown that sleep disturbances are especially common among older adults with physical disorders. The main aim of this study was to assess the frequency of sleep problems and hypnotic drug use in middle-aged and elderly patients who were hospitalized at acute care wards.

Subjects and Methods: The present survey was commissioned by the Ministry of Health, Labour and Welfare. A total of 522 patients (men 297, women 225, mean age 74.7 ± 10.1 years) aged 50 years or over admitted to 43 acute care hospitals in July 2007 participated in the present survey. Study subjects answered a questionnaire about their sleep habits, insomniac symptoms, daytime sleepiness, and hypnotic drug use. The presence of insomnia was defined as having one or more moderate to severe insomniac symptoms: early morning awakening, difficulty in initiating sleep, difficulty in maintaining sleep, non-restorative sleep. Patients wore a waist actigraph (Lifecorder PLUS, Suzuken Co.Ltd) for consecutive two days to estimate their objective sleep parameters calculated by a sleep/wake-scoring algorithm for this device.

Results and Discussion: Two hundreds ninety-one patients (55.7% out of 522 patients) had insomnia and 226 patients (43.3%) had moderate to severe daytime sleepiness. In insomnia patients, difficulty in maintaining sleep (66.0%) was the most frequent, followed by difficulty in initiating sleep (47.2%), non-restorative sleep (34.0%) and early morning awakening (32.4%). Objective sleep parameters confirmed that insomnia patients had significantly poor quality of sleep (Sleep efficiency, 69.0% versus 74.0% for insomnia and non-insomnia patients, $P = 0.016$; Total sleep time, 372.4 min versus 400.7 min, $P = 0.018$; Wake after sleep onset, 167.3 min versus 138.6 min, $P = 0.018$). Overall, 127 patients (24.3%) were prescribed hypnotic drugs. Regardless of type of insomnia, patients were prescribed hypnotic drugs with ultra short or short half-life that might not match their symptoms. Attention should be given to the sleep disturbances in middle-aged and elderly hospitalized patients to improve their impaired sleep, excessive daytime sleepiness, and associated deterioration of their ADL and QOL.

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Efficacy of eszopiclone in the treatment of insomnia: a subset analysis by baseline wake time after sleep onset (WASO)

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Introduction: Insomnia agents are often used for the long-term treatment of chronic insomnia. Eszopiclone, a single isomer non-benzodiazepine, has demonstrated statistically significant improvements in measures of sleep and daytime function versus placebo for up to 6 months, with no evidence of tolerance. Because WASO was not an entry criterion, subset analyses were conducted to determine the effect of eszopiclone in patients with more severe sleep maintenance insomnia.

Methods: Patients meeting DSM-IV criteria for primary insomnia entered a 6-month, placebo-controlled study evaluating the efficacy of eszopiclone 3 mg in the treatment of chronic insomnia (eszopiclone: $n = 548$, placebo: $n = 280$). Patients were grouped by baseline WASO into Low-WASO (≤ 60 min; $n = 254$) and High-WASO (> 60 min; $n = 475$) subgroups; endpoints evaluated were sleep latency (SL), WASO and total sleep time (TST).

Results: Statistically significant differences ($P < 0.003$) in favour of eszopiclone were noted between treatment groups for each subgroup at each month in all parameters. Results were similar over the 6-month treatment period ($P < 0.001$): median WASO in the Low-WASO (eszopiclone: 14 min, placebo: 24 min) and High-WASO groups (eszopiclone: 25 min, placebo: 52 min); median TST in the Low-WASO (eszopiclone: 402 min, placebo: 352 min) and High-WASO groups (eszopiclone: 388 min, placebo: 328 min). Patients taking eszopiclone in the High-WASO group had larger differences between treatments than the Low-WASO group for all parameters.

Conclusions: Eszopiclone 3 mg was effective at reducing SL and WASO, and increasing TST in patients with high and low baseline WASO. This analysis demonstrates that the efficacy of eszopiclone on sleep maintenance was preserved irrespective of baseline sleep maintenance severity.

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Long-term efficacy of eszopiclone in adults with primary insomnia: a responder analysis of subjective sleep outcomes

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Introduction: Insomnia treatments that are effective and well tolerated in the long-term are needed. Eszopiclone is a single-isomer, non-benzodiazepine $GABA_A$ receptor modulator under evaluation by the EMEA for the treatment of insomnia. Two studies examined the long-term efficacy of eszopiclone in patients with primary insomnia. The proportions of subjects that respond over time are assessed.

Methods: Data from two six-month, double-blind, randomized, placebo-controlled studies were pooled to evaluate the long-term effects of eszopiclone treatment in adults with primary insomnia. In studies 190–049 and 190–050, subjects received eszopiclone 3 mg ($n = 1141$) or placebo ($n = 475$) nightly. Subjects completed subjective assessments weekly via an interactive voice response system. Change from baseline in sleep latency (SL), wake time after sleep onset (WASO) and total sleep time (TST) were calculated on a monthly basis. Subjects responding to treatment were categorized into those who experienced an increase in TST compared to baseline of a) ≥ 30 min and b) ≥ 60 min, using an LOCF approach. Significance was calculated using a Cochran-Mantel-Haenszel test of general association.

Results: Published data demonstrate that patients receiving eszopiclone experienced significant improvements in SL, TST and WASO at each month compared to those receiving placebo. The proportions of subjects responding at each time point were

maintained throughout treatment. More subjects in the eszopiclone group than the placebo group experienced an increase in TST $\geq$30 min at each month (Months 1–6 respectively: eszopiclone 68%, 71%, 72%, 69%, 71%, 70%; placebo 38%, 42%, 43%, 43%, 45%, 45%; $P<0.0001$ at each month). Similarly, more subjects in the eszopiclone group than the placebo group experienced an increase in TST $\geq$ 60 min at each month (Months 1–6 respectively: eszopiclone 52%, 57%, 56%, 55%, 56%, 56%; placebo 21%, 25%, 28%, 27%, 28%, 28%; $P<0.0001$ at each month).

Conclusion: Approximately 70% of adults with primary insomnia experienced an improvement of $\geq$30 min in TST while receiving long-term eszopiclone treatment (3 mg day^{-1}), compared with approximately 45% receiving placebo. The proportion of responders remained consistent over the long term, with no evidence of tolerance.

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Efficacy of eszopiclone relative to zolpidem in patients with primary insomnia: a responder analysis of objective sleep outcomes

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Introduction: Zolpidem is a non-benzodiazepine $GABA_A$ receptor modulator available in the EU for the treatment of primary insomnia. Eszopiclone-a single-isomer, non-benzodiazepine $GABA_A$ receptor modulator that is effective in the treatment of sleep onset and sleep maintenance difficulties in patients with primary insomnia-is under evaluation by the EMEA for the treatment of insomnia. This double-blind, placebo-controlled, 6-way Williams design crossover study evaluated the efficacy of eszopiclone relative to placebo and zolpidem in subjects with primary insomnia.

Methods: In study 190–045, subjects received 2 nights' treatment with placebo ($n=63$), zolpidem 10 mg ($n=64$), or eszopiclone 1 mg ($n=63$), 2 mg ($n=63$), 2.5 mg ($n=65$), or 3 mg ($n=64$), in a random order with a 3–7 day washout period between treatments. The primary outcome measure was latency to persistent sleep (LPS); secondary outcomes included total sleep time (TST) and wake time after sleep onset (WASO). Sleep outcomes were assessed by polysomnography and averaged over the 2 treatment nights. A TST response was defined as an improvement of $\geq$30 min. A WASO response was defined as a decrease of $\geq$50% compared to baseline. The ITT population in each treatment group was used as the denominator in responder calculations.

Results: As previously reported, significant differences for eszopiclone 3 mg compared with placebo were seen on LPS, TST and WASO; zolpidem was significantly different to placebo on LPS and TST. More subjects in the active treatment groups than the placebo group met the TST response criterion, with the proportions by group in descending order as follows: eszopiclone 2.5 mg 86%, eszopiclone 3 mg 83%, zolpidem 10 mg 81%, eszopiclone 2 mg 78%, eszopiclone 1 mg 78%, placebo 54%. Similar results were seen with WASO responders, with the proportions by group in descending order as follows: eszopiclone 3 mg 52%, eszopiclone 2 mg 46%, eszopiclone 2.5 mg 43%, zolpidem 10 mg 42%, eszopiclone 1 mg 33%, placebo 33%.

Conclusion: Approximately 80% of adults with primary insomnia experienced an increase of $\geq$ 30 min TST during zolpidem or eszopiclone treatment.

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Effects of dopamine-agonist (pramipexole) on spinal motor neurons excitability in subjects with primary restless legs syndrome (RLS)

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Objective: To evaluate the effects of chronic treatment with dopamine-agonist pramipexole on spinal motor-neurons excitability in subjects with primary Restless Legs Syndrome (RLS).

Methods: Subjects with idiopathic RLS were consecutively recruited from outpatients referring to the Sleep Medicine Unit and tested in drug-free basal conditions and after a 1-month treatment period with pramipexole at a low standard dose (0.18 mg die^{-1}). All the subjects underwent both global clinical evaluation (including International Restless Legs Syndrome Rating Scale (IRLSRS), Augmentation Severity Rating Scale (ASRS)) and neurophysiological investigation including Hmax/Mmax ratio (indicating spinal alpha-motor neurons excitability) and tonic vibratory reflex (evaluating proprioceptive presinaptic inhibition).

Results: Data are available in 10 subjects (7 female, mean age 61.2 $\pm$ 13.4 years, IRLSRS 28 $\pm$ 7, range 18–38). At the 1-month control an important decrease in intensity of RLS symptoms (IRLSRS 6.0 $\pm$ 8.0), with no subjects reporting augmentation symptoms, was observed, paralleled by a decrease of Hmax/Mmax ratio from Soleus muscle (median reduction of 17%, range 0–68%) and an increase of proprioceptive presinaptic inhibition by tonic vibratory reflex (TVR) (median reduction of 11%, range 1–38%).

Conclusions: Our data suggest that pramipexole treatment in patients with idiopathic RLS induces a reduction of alpha motor neurons excitability in the lower limbs (decrease of Hmax/Mmax ratio). This effect could be induced by an increase of presinaptic inhibition of the propriceptive afferents at the lower limbs (increase of TVR inhibitory effect on the H reflex amplitude).The ongoing analysis is expected to enlarge the casuistic and give data at the three months treatment control.

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Enhancement of performance overnight after sleep assisted by hypnotics

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Introduction: The beneficial effect that a preceding period of sleep assisted by a hypnotic may have on performance overnight raises the question whether the performance enhancement is related to the effect of increased sleep duration or involves other mechanisms such as an excitatory 'rebound' after a period of drug-induced depression of the central nervous system. To explore this issue, performance was studied overnight after periods of sleep assisted by temazepam and zolpidem and by the shorter acting hypnotic, zaleplon.

Methods: Study 1: At the start of a 6 h sleep from 13:15, subjects (9 healthy young females) ingested temazepam (20 mg), zolpidem (10 mg) or placebo. This was followed by a 12 h work period from 20:00 and then a 4 h recovery sleep from 08:15.

Study 2: A 3.5 h sleep from 14:00 was followed by a 6 h work period from 18:00. A second 3.5 h sleep from 00:00 was followed by a second 6 h work period from 04:00 and, finally, by a 6 h recovery sleep. Subjects (12 healthy young females) completed this schedule on two occasions: (1) when zaleplon (10 mg) was taken at 14:00 and again at 00:00; (2) when placebo was taken at these times.

Results: Study 1: Compared with placebo, temazepam and zolpidem increased total sleep time (TST; $P<0.01$) and zolpidem impaired performance 6.75 to 12 h post-ingestion ($P<0.01$ up to

8.5 h; $P<0.05$ from 10.25 h). Both hypnotics then enhanced performance at 04:45 ($P<0.05$). Regression analysis showed that, even after correcting for increased sleep duration with the hypnotics, the improvement in performance remained.

Study 2: Zaleplon increased TST during the first sleep and impaired performance 4 to 6.5 h post-ingestion, compared with placebo ($P<0.05$). Thereafter, at 19:00, performance was enhanced, compared with placebo ($P<0.05$). Regression analysis showed that, when corrected for prior sleep duration, the enhancement of performance by zaleplon did not persist. There was no effect of zaleplon on TST from 00:00 and no enhancement of subsequent performance.

Conclusion: Performance enhancement after zaleplon appeared to depend solely on an increase in prior sleep duration, whereas with temazepam and zolpidem the improvement in performance could not be explained in terms of increased sleep.

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Food consumption has no effect on the pharmacokinetic parameters of a single oral 5-mg dose of eplivanserin, a novel sleep compound, after administration to healthy subjects

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Introduction: Eplivanserin, an Antagonist of Serotonin Two A Receptors (ASTAR), is being developed at the 5-mg dose for chronic insomnia characterized by night-time awakenings. Eplivanserin increases slow wave sleep (SWS) and, unlike benzodiazepines, does not bind to GABA receptors. This study assessed the effect of food consumption on the pharmacokinetic parameters of a single oral dose of 5 mg eplivanserin in healthy subjects.

Methods: Single-centre, open-label, randomized, 2-period, cross-over study, in which 20 healthy male and female subjects received a single oral 5-mg dose of eplivanserin either in fasted conditions (morning administration after overnight fast) or at the end of a high-fat breakfast (816 cal, with fat representing approximately 50%) during Day 1, Period 1. After a 13-day wash-out, Period 2, the subjects were crossed over to the other treatment condition (fasted or fed). Blood samples for eplivanserin and its active N-demethyl metabolite, SR141342, were collected over a 10 day period after administration. Eplivanserin and SR141342 plasma concentrations were determined by a validated LC-MS/MS method. Pharmacokinetic parameters were calculated using a non-compartmental analysis.

Results: The pharmacokinetic parameters of eplivanserin and SR141342 (C_{max} and AUCs) were not altered by food consumption. Estimated ratios (fed/fasting) ranged from 0.96 to 1.07 and 90% CIs were within the [0.8–1.25] bioequivalence interval, regardless of the pharmacokinetic parameter. No serious adverse events were reported.

Conclusion: Food consumption does not affect the pharmacokinetics of eplivanserin following single-dose administration in healthy subjects. Therefore, eplivanserin can be administered regardless of food intake.

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Influence of smoking and nicotinic substitution on circadian sleep and skin temperature variations under natural living conditions

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Smoking, as well as nicotinic substitution, are known to affect brain regions involved in the circadian modulation of many neurovegetative functions. The aim of this study was to examine whether smoking or nicotinic substitution had repercussions on the functional interaction between selective vasodilatation of distal skin regions and sleep processes. Thirty-three adults (age: 33 ± 9 years) have been investigated during 24 h in natural living conditions. Sleep-wake cycles were scored by actigraphy (Cambridge Neurotechnology). Skin proximal temperature (Tp) was measured by thermistors at the level of the right infraclavicular area while distal skin temperature (Td) was measured on the back of the left hand. Distal-proximal gradient (DPG, Td-Tp) was considered as an indicator of heat loss via distal skin regions. Participants were enrolled according to whether they did not smoke (NS, control group), were habitual smokers (S+) or were under a nicotinic substitution therapy (N+). Compared to controls, smoking did not modify the 24-hr time course of the DPG. Although the mean level of DPG was higher in the N+ group than in the NS group during daytime ($P = 0.007$), the level of DPG was not different anymore at sleep onset (11:30 pm ± 55 min). As a result, the N+group exhibited a lower variation of the gradient at the surrouding of sleep onset than the NS group ($P = 0.032$). Interestingly, despite these differences, nocturnal sleep/wake actigraphic parameters did not differ between the three groups. These results point out that nicotinic substitution, but not smoking, influences the time course variations of skin temperature. As sleep parameters were not modified, this suggests the actuation of compensatory mechanisms allowing to maintain the influence of thermoregulation on sleep promotion and maintenance.

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Residual effects of gaboxadol, zopiclone and zolpidem on over-the-road driving and cognition

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Residual sedation the morning after use of hypnotics is a major problem with respect to traffic safety. Gaboxadol is a GABA-agonist, binding primarily to benzodiazepine-insensitive extrasynaptic α4β3δ-, and α6β3δ-containing GABA-A receptors. After oral doses it is rapidly absorbed and eliminated ($t^{1/2}$ 1.5–2.0 h). Clinical trials did not reveal residual effects on cognitive functioning of bedtime doses up to 20 mg.

Objective: To determine whether gaboxadol would have residual effects on car driving the morning after ingestion at bedtime or later in the night.

Methods: Twenty-five healthy subjects (M/F 13/12; mean age 31.4 yrs) completed a double blind 5-way crossover study. On treatment nights they ingested capsules twice; once before initiating sleep at 11 pm and again during brief awakening at 4 am. They arose at 7 am. Treatments were: placebo at both times, gaboxadol 15 mg or zopiclone 7.5 mg at 11 pm followed by placebo at 4 am, and placebo at 11 pm followed by gaboxadol 15 mg or zolpidem 10 mg at 4 am. Zopiclone and zolpidem were included as active controls to demonstrate sensitivity of the tests and procedures. Psychomotor performance and memory were assessed at 7:30 am and driving at 9 am, using a one-hour standardized highway driving test. The primary dependent variable was Standard Deviation of Lateral Position (SDLP in cm), an index of weaving.

Results: Evening doses of gaboxadol tended to increase SDLP but the effects were only marginally significant. In addition it had minor but significant effects on speed variability and performance in a divided attention test. In contrast, evening doses of zopiclone significantly impaired performance in every test, except tracking. Following middle-of-the-night doses, gaboxadol clearly impaired driving and psychomotor performance, but not memory. Performance after middle-of-the-night doses of zolpidem was impaired in every test.

Conclusion: Gaboxadol 15 mg can produce minor residual effects on driving between 10 and 11 h after evening administration.

Sensitive individuals may occasionally experience impairment. Administration later at night is associated with moderately impairing residual effects on driving and psychomotor performance, but not on memory.

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Daytime sleepiness and performance in healthy male subjects after the evening intake of escitalopram: a randomized, double-blind, placebo-controlled study

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Using a double-blind cross-over design we investigated the impact of a single evening dose of escitalopram (ESCIT) on the nocturnal polysomnogram, daytime sleepiness (as measured by the MSLT), vigilance and cognitive performance in comparison to amitriptyline (AMI) and placebo (PLAC). Up to now, neither for AMI nor ESCIT data are available, with respect to the question whether the administration of these compounds has an impact on daytime vigilance/sleepiness as measured by an objective test like the Multiple Sleep Latency Test.

Methods: Tweleve healthy male subjects underwent 3 periods of 2 consecutive nights of polysomnography. After adaptation night and prior to the second laboratory night 10 mg ESCIT, 75 mg AMI or PLAC was administered at 9 pm Whole-night polysomnograms (11 pm–7 am) were recorded and analysed for standard sleep variables. On the following day subjective sleep parameters, a standardized test battery (d2 test, TAP) and the MSLT were conducted. One subject had to be excluded retrospectively because of a protocol violation.

Results: Regarding daytime vigilance as measured by the MSLT, wake efficiency (WE) increased significantly after the evening intake of ESCIT. In contrast, AMI led to a pronounced decrease of WE and to a marked reduction in sleep latency during the MSLT. Regarding daytime alertness there was no difference between ESCIT and Placebo (TAP test). However, AMI significantly impaired daytime alertness. Although polysomnographically determined nocturnal sleep continuity was disturbed by ESCIT and improved by AMI neither subjective sleep parameters nor processing speed and performance measured by the d2 test the following morning were impaired. In fact, processing speed and performance were significantly increased by ESCIT versus AMI.

Conclusion: After the evening intake of ESCIT daytime sleepiness measured by MSLT was reduced. Neither daytime alertness nor performance or processing speed was impaired by ESCIT. In contrast to this, AMI led to a strong impairment of vigilance and, in tendency, to a decreased daytime performance. Future studies should investigate if a SSRI induced improvement of daytime vigilance in depressed patients can also be confirmed by MSLT and whether this finding corresponds with overall better treatment outcome.

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Rotigotine transdermal patch is effective in the treatment of idiopathic RLS: results of a 6-month, multicenter, double-blind, placebo-controlled trial

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Objective: To evaluate the efficacy and safety of rotigotine transdermal patch in patients with moderate to severe idiopathic restless legs syndrome (RLS).

Methods: This was a multicenter, randomized, double-blind, placebo-controlled, 5-arm parallel-group trial with 4 fixed doses of rotigotine 0.5–3 mg 24 h^{-1} (2.5–15 cm^2). IRLS sum score and the CGI item 1 (severity of illness) were the co-primary efficacy parameters.

Results: A total of 505 patients (52 ± 13 years, 61% female) were randomized at 58 sites in the US. The mean baselines scores were 23.3 ± 5.0 for the IRLS and 4.7 ± 0.7 for the CGI item 1. For rotigotine at doses of 0.5, 1, 2, and 3 mg 24 h^{-1}, improvement net effects versus placebo after 6 months treatment were −2.2 ± 1.2, 2.3 ± 1.2, −4.5 ± 1.2 ($P<0.001$), and −5.2 ± 1.2 ($P<0.001$) in the IRLS and −0.35 ± 0.19, −0.32 ± 0.19, −0.65 ± 0.19 ($P<0.001$) and −0.90 ± 0.19 ($P<0.001$) in CGI item 1. At least one AE was reported by 84% of placebo and 88% of rotigotine patients. The most common side effects among rotigotine-treated patients were application site reaction (27.2%), nausea (21.5%), headache (17.6%) and somnolence (12.6%). AEs were usually mild to moderate in intensity and transient. Augmentation measures were generally greater in placebo patients.

Conclusion: Therapy with rotigotine transdermal patch was well tolerated and led to greater benefit on primary measures (IRLS and CGI item 1) at all doses with statistically significant and clinically relevant benefit at doses of 2 and 3 mg 24 h^{-1} over a period of 6 months compared to placebo.

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Efficacy of rotigotine transdermal patch in the treatment of idiopathic RLS: results of a 6-month, multicenter, double-blind, placebo-controlled trial in Europe

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Objective: To evaluate the efficacy and safety of rotigotine transdermal patch in patients with moderate to severe idiopathic restless legs syndrome (RLS).

Methods: Multicenter, randomized, double-blind, placebo-controlled, 4-arm parallel-group trial with 3 fixed doses of rotigotine 1–3 mg 24 h^{-1} (5–15 cm^2). IRLS sum score and the CGI item 1 were the co-primary efficacy parameters.

Results: A total of 458 patients (58 ± 11 years, 73% female) were randomized at 49 sites in 8 European countries. The mean baselines scores were 28.1 ± 6.1 for IRLS and 5.0 ± 0.8 for CGI item 1. For rotigotine at doses of 0.5, 1, 2, and 3 mg 24 h^{-1}, improvement net effects versus placebo after 6 months of treatment were 5.1 ± 1.3 ($P<0.001$), −7.5 ± 1.3 ($P<0.001$), and −8.2 ± 1.3 ($P<0.001$) in the IRLS and −0.76 ± 0.19 ($P<0.001$), −1.07 ± 0.19 ($P<0.001$) and −1.21 ± 0.19 ($P<0.001$) in CGI item 1 for rotigotine 1, 2, and 3 mg 24 h^{-1}, respectively. At least 1 adverse event (AE) was reported by 78% of rotigotine-treated patients. The most common side effects were application site reactions (42.5%), nausea (16.4%), headache (15.8%) and dizziness (5.8%). AEs were usually mild to moderate in intensity and transient.

Conclusion: Therapy with rotigotine in doses from 1 to 3 mg 24 h^{-1} over a period of 6 months was well tolerated and resulted in a statistically significant and clinically relevant reduction in the IRLS sum score and CGI item 1 compared to placebo.

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Use of natural products as sleep aids: a common practice?

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Introduction: Despite a paucity of data on efficacy and safety of natural products, their use appears to be widespread for insomnia.

The present study aimed at examining the pattern of use of natural products used as sleep aids in a population-based sample.

Methods: A randomly selected adult sample ($n = 997$; 59.9% women) from the province of Quebec completed a postal survey on sleep. Salient variables were the use of sleep-promoting products (natural products, prescribed medication, over-the-counter medication and alcohol) during the preceding year, weekly frequency of use of natural products for sleep during the past month and type of product.

Results: A total of 18.5% of respondents reported having used natural products as sleep aids in the preceding year. Of those, 10.3% ($n = 98$) relied on them exclusively, while 8.2% ($n = 78$) used them in combination with other types of sleep aids (prescribed medicines, over-the-counter medicines and/or alcohol). Among 176 subjects reporting having used a natural product in the past year, 70.3% ($n = 123$) also reported its use in the preceding month. Forty-four out of 123 subjects (35.8%) had used them for sleep three or more times a week. The most commonly used product was chamomile ($n = 46$). The next most common were the mixtures of herbal/natural compounds (valerian root, lemon balm, lavender, hops, magnesium, etc) ($n = 12$), generally sold in the form of tablets. The remaining products (valerian, St. Johns wort, homeopathic medicines, dicentra, Chinese green tea passiflora and essential oils) were used by less than 5 subjects.

Conclusion: The use of natural products as a sleep aid is a common practice in the general population. The frequent use of camomile reflects its popular reputation as a relaxing substance that facilitates sleep and its availability. Nevertheless, scientific data supporting its efficacy are lacking. In addition, the assumption that chamomile is inherently safe may be dangerous. It has been postulated that chamomile may interact with anticoagulant and antiplatelet drugs, benzodiazepines and other drugs with sedative properties.

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Nocturnal transcutaneous carbon dioxide in postmenopausal estrogen users and non-users

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Background: There is a metabolic adaptation shown as higher venous bicarbonate levels after menopause (1). We have previously shown that postmenopausal women compared to premenopausal have higher sleep-induced increase in transcutaneously measured carbon dioxide tension ($TcCO_2$) (2). Since estrogen restores bicarbonate levels (1), we hypothesized that nocturnal $TcCO_2$ should also be restored with estrogen therapy (ET).

Subjects and Methods: We recruited ten postmenopausal ET users and ten BMI matched controls through a newspaper announcement for a sleep study (age 56 ± 3 years). The study included overnight polysomnographic recording, arterial oxyhemoglobin saturation (SaO2) measurement and $TcCO_2$ measurement.

Results: Nadir SaO_2, mean SaO_2, arterial oxyhemoglobin desaturation index or apnea-hyponea index did not differ between the groups. $TcCO_2$ increased from evening wakefulness to sleep both in ET users ($TcCO_2$ difference = 0.72 kPa, $P = 0.007$) and in controls ($TcCO_2$ difference = 0.33 kPa, $P = 0.037$). Sleep induced increase in $TcCO_2$ was markedly greater in ET users than controls ($P = 0.041$) and the difference was even more significant when comparing the wake to slow-wave sleep (SWS) ($P = 0.008$). $TcCO_2$ levels in wake, SWS, REM sleep or total sleep time did not differ markedly between the groups.

Conclusions: Sleep induced increase in $TcCO_2$ is more pronounced in postmenopausal ET users than non-users. The result was contrary to our hypothesis that ET would restore menopause related increase in $TcCO_2$. Estrogen is a vasodilator, so ET usage might cause changes in peripheral microcirculation affecting transcutaneous monitoring. With this study design, however, it is not possible to prove causality and in the future placebo-controlled trial is needed.

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From 'sleep attacks' to 'better brains': exploring representations of sleep drugs in the media

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The move towards 24-h living and the increase in shift-work have raised major concerns about sleep deprivation and its impact on health and well-being. In this context, the development of novel therapeutic drugs for the treatment of sleep disorders is of importance. This paper uses UK newspaper coverage of the drug modafinil as a case study to explore the social and ethical issues surrounding pharmaceutical intervention in the sleep-wake cycle. The media operate at the interface between science and society and are a central forum for debates regarding issues relating to science, society, life-style, and most importantly, health and illness. It is mainly through the media that those outside of the scientific community become aware of scientific advances, new therapies, and the social and ethical issues regarding their use and availability. In order to gain deeper insights in how the media portray the use and abuse of modafinil and its status in science and society, metaphor analysis combined with frame analysis was used. This paper will argue that alternative ways of talking about sleep and modafinil across different contexts allowed for specific social and ethical concerns and moral obligations to be expressed. The engagement with a medical rhetoric in each of these ways of talking about sleep was intricately intertwined with the moral obligation to 'get better'. Popular accounts of pharmaceutical intervention in the sleep wake cycle could contribute to shifts in what is perceived as normal, in need of medical treatment or a lifestyle intervention and in turn influence behaviour.

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Efficacy of SSRI in primary insomnia treatment

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Sedating antidepressants are commonly used in primary insomnia treatment even though it is not supported by clinical trial data according to good clinical practice. Trazodone, mirtazapine, doxepine and amitriptiline have almost dominated insomnia therapy in US (Walsh 2004). In Poland the small doses of mianserine are also used in pharmacotherapy of insomnia (Sobanska 2006). Some pat mechanisms causing insomnia are identical as those met in depression (Bonnet 1998, Vgontzas 1987, Richardson 2001). These theoretical premises also encourage using sedative antidepressants in insomnia treatment Selective serotonin reuptake inhibitors (SSRIs) are usually not recomended in primary

insomnia treatment. However, facts that SSRIs increase melatonin secretion (Brzezinski 1997) and there is psychological advantage of taking them in the morning encouraged us to try SSRIs in primary insomnia treatment. Additionally an increase of SWS in cats has been described during administration of citalopram. The aim of this work is comparison of escitalopram, citalopram, and trazodone efficacy in chronic insomnia treatment.

Methods: We analysed case reports of: 35 patients (19–84 years) treated with citalopram (5–20 mg in the morning), 22 patients (21–83 years) treated with escitalopram (5–10 mg in the morning) and 27 patients (18–75 years) treated with trazodone 50–150 mg in the evening,

Results: Citalopram therapy: 30 patients reported improvement, 4-lack of improvement, 1-worsening. Escitalopram therapy: 20 patients reported improvement, 1-lack of improvement, 1-worsening. Trazodone therapy: 25 patients reported improvement, 2-worsening. Side effects were usually of mild intensity and lapsing in character. Some persisting side effects were eliminated after dosage correction. Pharmacotherapy lasted maximally 20 weeks and improvement persisted also after finishing the treatment.

Conclusions: 1. Low doses of escitalopram and citalopram are also effective in primary insomnia treatment 2. The treatment of primary insomnia with antidepressants seems to be safe due to very few mild side effects.

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Eszopiclone improves the quality of PSG: a prospective, randomized, placebo-controlled trial

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Introduction: Poor sleep during PSG can result in unsatisfactory studies. We hypothesized that premedication with eszopiclone (esz) would improve sleep duration and continuity,improving PSG quality and facilitating better CPAP titrations.

Methods: We conducted a prospective, double-blind, randomized, placebo-controlled trial assessing the quality of PSG with esz premedication. We compared sleep latency, efficiency, total sleep time and apnea-hypopnea index between eszopiclone 3 mg or matching placebo. We also compared rates of inadequate studies between groups, defined as insufficient sleep time (<120 min or sleep efficiencies $<70\%$) or incomplete CPAP titrations (>5 events/hr on the highest CPAP or complete intolerance). Lastly, we evaluated CPAP compliance data.

Results: We enrolled 226 subjects, 113 esz, 113 placebo. The esz group experienced reduced sleep latency (21.7 versus 32.6 min, $P = 0.014$), improved sleep efficiency (87.6 versus 78.1%, $P < 0.001$), less WASO (39.2 versus 64.5 min, $P < 0.001$) and prolonged sleep time (346.5 versus 312.2 min, $P < 0.001$). Sleep efficiencies $<70\%$ were more common with placebo (21.2 versus 7.1%, $P = 0.004$). Esz facilitated greater ablation of events during CPAP titration. Residual events were less (5.7 versus 11.9, $P = 0.02$) and incomplete CPAP titrations were less (31.1% versus 48.0%, $P = 0.04$) with esz. Both nonusable (7.1 versus 2.7%, $P = 0.22$) and poor quality studies (46.0 versus 26.5%, $P = 0.004$) were more common with placebo. Esz had a NNT of 5 to prevent one poor quality sleep study and 23 to prevent one nonusable study. Side effects were uncommon and did not differ between groups. Those receiving esz during PSG were more likely to start CPAP therapy (68.6 versus 56.5%, $P = 0.14$) and used CPAP more in the first month. Pct of days (80.0 versus 72.2%, $P = 0.20$) and hrs of CPAP used/night (4.77 versus 4.23, $P = 0.24$) were higher with esz. CPAP compliance, defined as use >4 h/nt and $>50\%$ of nights was also better in the esz group (54.1 versus 37.1%, $P = 0.16$).

Discussion: Pretreatment with esz improved PSG quality and CPAP titrations. Esz may improve pts overall experience in the sleep lab and decrease the need to repeat PSGs. Esz use during PSG also tended to improve initial CPAP tolerance and compliance, likely resulting from a better initial experience with CPAP or improved titrations.

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Efficacy of circadin in elderly insomniacs – double blind, placebo controlled, sleep laboratory study

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Background: Circadin is a newly developed prolonged release oral formulation of melatonin that mimics the physiological melatonin production profile. Since the melatonin secretion decreases with age, and endogenous melatonin affects sleep in man, substitution therapy in insomniacs aged 55 years and older would be beneficial.

Aim: This study was performed to investigate the effect of 2 mg Melatonin prolonged release (Circadin®) on the sleep/wake cycle in out-patients with insomnia, age ≥ 55 years. Sleep was assessed by means of polysomnography, all-night sleep EEG spectral analysis, actimetry wake EEG and sleep/wake quality questionnaires.

Design: This was a double-blind, placebo-controlled, parallel-group sleep laboratory study. The study consisted of a 2-week single-blind placebo run-in period, followed by a 3-week, double-blind, placebo-controlled treatment period and finally a 3-week withdrawal period. The study included 40 healthy men and women, aged ≥ 55 years, with a diagnosis of primary insomnia according to DSM-IV criteria (307.42).

Results: By the end of the 3-week treatment period, Circadin® showed efficacy on the variables assessing sleep induction. Sleep onset latency (SOL) was significantly shortened ($P = 0.011$) 7 min versus baseline 9 min versus placebo. Similarly, a decrease was seen in the Duration of Wake Prior to Sleep Onset (DWAPSO) and in percentage of time spent asleep (DWAPSOP). During this period, DWAPSO and DWAPSOP decreased by approximately 50% versus baseline and versus placebo. No effects on sleep structure or sleep architecture were seen. Half of the patients reported substantial improvement in quality of sleep at home with Circadin® versus 15% with placebo ($P = 0.018$). By the beginning and the end of the run-out period, no significant differences were observed between the two groups on variables assessing sleep induction and maintenance. Circadin was safe and well tolerated.

Conclusions: -Circadin® was superior to placebo in sleep induction and sleep quality during the 3 week treatment phase.-Upon discontinuation of treatment, the sleep parameters slowly returned to values close to the baseline level. There was no evidence of rebound effects. Circadin® was safe and well tolerated.

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Efficacy of circadin in elderly insomniacs – morning psychomotor performance

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Background: Circadin® is a newly developed prolonged release formulation of melatonin mimicking the physiological melatonin production profile. It is developed for insomnia in patients aged 55 years and over. Since insomnia is associated with significant decrease in daytime vigilance, the effects of Circadin on daily psychomotor and neurocognitive functioning were investigated.

Aim: This study was performed to investigate the effect of 2 mg melatonin prolonged release (Circadin®) on the sleep/wake cycle in insomniac out-patients, age ≥ 55 years. Vigilance and cognitive

skills were assessed by means of psychomotor and neurocognitive tests derived from the Leeds psychomotor test battery (vigilance and arousal) and TEA battery (attention).

Design: Double-blind, placebo-controlled, parallel-group design, sleep laboratory study. The study started with a run-in of 2 weeks (single-blind with placebo treatment), followed by a treatment period of 3 weeks (double-blind, placebo-controlled) and finally a 3 weeks withdrawal period (no treatment). The study included 40 healthy male and female, aged ≥ 55 years, suffering from primary insomnia according to DSM-IV criteria (307.42).

Results: At the end of the 3 weeks of treatment, Circadin® induced a clear positive effect on variables assessing daytime vigilance. A significant treatment effect for the Critical Flicker Fusion Test (CFF) is observed with an increased score under Circadin® versus placebo, at end of treatment ($P = 0.031$) and late withdrawal ($P = 0.038$). A significant treatment effect for the Total Reaction Time (TRT) parameter is observed with a decreased score in the Circadin® group as compared to the placebo group: end of treatment ($P = 0.014$), early withdrawal ($P = 0.026$) and late withdrawal ($P = 0.035$), suggesting CNS arousal and improvement of the reaction time. No rebound effects were observed.

Conclusions: Treatment with Circadin® was superior to placebo, in improving daytime psychomotor and neurocognitive functioning in insomnia patients aged 55 years and older. This is furthermore objectified by the fact that after stopping the active treatment, these parameters are slowly returning to values close to the ones observed at baseline.

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Substance abuse among insomnia patients taking a nonbenzodiazepine receptor agonist, benzodiazepine, or melatonin receptor agonist

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Objectives: To assess the occurrence of substance abuse claims among insomnia patients prescribed a nonbenzodiazepine receptor agonist (nBZRA), benzodiazepine (BZD), and melatonin receptor agonist (MRA).

Methods: A retrospective matched cohort design was used with data from Florida Medicaid recipients aged 18 to 64 years old. Insomnia patients initiating therapy with nBZRA, BZD, or MRA between 7/1/2002 and 3/31/2006, without a previous history of substance abuse, were included in this analysis. Each MRA patient was matched to 3 nBZRA and 3 BZD patients based on demographic and clinical (history of insomnia, depression, anxiety) characteristics. Treatment exposure was determined by service dates and days of medication supply from pharmacy claims. Substance abuse claims related to sedatives and hypnotics were identified using the International Classification of Diseases 9th edition Clinical Modification (ICD-9-CM) codes for the same time frame. Rates of substance abuse (SA) were calculated as the number of patients with a claim for SA per 100 patient-years of treatment exposure.

Results: After matching, a total of 980 patients were identified and included in this analysis (140 MRA, 420 nBZRA, and 420 BZD). The mean age was 46 years; 64% were female, 57% were Caucasian, 50% had comorbid depression, and 14% had comorbid anxiety. The mean Charlson comorbidity score was higher for MRA patients (1.4) than nBZRA or BZD patients (0.6 and 0.7, respectively, $P < 0.01$). There was no evidence of substance abuse among the MRA cohort. The SA rate per 100 patient-years of exposure was 1.84 and 2.51 for nBZRA and BZD patients, respectively.

Conclusions: Results from this study suggest that patients taking a MRA used fewer medical services for substance abuse than those taking an nBZRA or BZD. However, no definitive conclusions can be drawn due to the small number of patients included in the analysis. Further studies will be needed to confirm these findings.

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Sleep and respiratory response to a simulated altitude of 3810 m: no evidence of respiratory depression with hypnotics

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Introduction: Disturbed sleep at altitude is a common feature of acute mountain sickness and hypnotic drugs have been used to treat this problem. However, the respiratory depressant effect of hypnotic drugs at altitude is controversial. Limited experimental protocols are possible with altitude experiments in the field, between group comparisons are the norm and dose response studies are impractical. An altitude chamber allows a within subject cross over design and the ability to study the effect of hypnotic dose on sleep and respiration.

Methods: Six healthy male volunteers (age 19–23 (mean 20.9) years, weight 57–95 (mean 74) kg) took part in a study involving ten experimental nights each separated by at least one week. The ten nights began with an adaptation night recorded in a sleep laboratory, followed by a baseline night in a hypobaric chamber at around sea level (122 m (749 torr)). Six nights were then recorded in the hypobaric chamber at a simulated altitude of 3810 m (473.8 torr) during which temazepam (10, 20, 30 mg), diazepam (10 mg) or matching placebo (on two nights) were taken in a double blind, cross over design. Another sea level night in the chamber and a final night in the sleep laboratory completed the study. Polysomnographic sleep measures, respiratory frequency, ECG, arterial oxygen saturation and respiratory mass spectrometry were recorded throughout the night.

Results: Diazepam (10 mg) and temazepam (20 & 30 mg) increased sleep efficiency compared with placebo ($P < 0.05$). Diazepam and the highest dose of temazepam also ameliorated the increase in wakefulness seen with altitude ($P < 0.05$). Both drugs attenuated the reduction in slow wave sleep at altitude ($P < 0.05$). Maximum arterial oxygen saturation fell from 98.2% to 80.6% on ascent to altitude ($P < 0.001$), and end tidal $PaCO_2$ and PaO_2 were also reduced ($P < 0.001$). Diazepam restored end tidal $PaCO_2$ to sea level values. Number of breaths per minute were increased by diazepam and temazepam 30 mg when compared with placebo. ($P < 0.01$).

Conclusion: There was no evidence of any respiratory depressant effects of temazepam at doses up to 30 mg. Indeed, both temazepam (30 mg) and diazepam increased respiratory rate at altitude compared with placebo.

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Effects of intravenous corticotropin-releasing hormone upon sleep EEG in young healthy women

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In young healthy male subjects the intravenous administered neuropeptide corticotropin-releasing hormone (CRH) decreased slow wave sleep (SWS) and rapid eye movement (REM) sleep. A sexual dimorphism was shown in sleep endocrine studies with the neuropeptides growth hormone releasing hormone (GHRH) and ghrelin. GHRH enhanced SWS in young males, whereas in young women SWS was reduced. In contrast to male subjects ghrelin had no sleep promoting effect in female subjects. We aimed to clarify whether a gender dimorphism exists in the effects of CRH on sleep EEG. In the present single-blind study we examined the effect of pulsatile administration of 4×50 μg CRH (intravenous injection at

22:00, 23:00, 00:00 and 01:00) or placebo on sleep EEG. Eight young healthy women were included according to a randomised schedule. Each subject underwent two sessions and to minimize the influence of gonadal hormone activity the sleep EEG recordings took place during the follicular phase. In accordance to the findings in young men CRH induced a decrease of stage 3 (S3) sleep (CRH: S3 sleep mean = 33,63 min SEM 6,01 min; placebo: S3 sleep mean 44,94 min SEM 3,73 min), but in contrast wakefulness increased in the second half of the night, whereas REM sleep was not affected by CRH. Sleep period time and sleep efficacy index were decreased by trend. The study demonstrated that systemic CRH administration impairs sleep in women.

Sleep Deprivation

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Chronic sleep restriction and glucose homeostasis in wistar rats

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Restricted and disrupted sleep is an increasing problem in our modern society. Epidemiological studies suggest that there is a connection between changes in sleep duration and an increased risk in obesity and diabetes. There is also one study in humans in which was shown that acute sleep restriction may reduce glucose tolerance, the first step in the development of (pre)-Diabetes. We decided to investigate the possible effects of sleep restriction on glucose metabolism. Rats were cannulated in the jugular veins to allow stress free glucose infusion and frequent blood sampling. After recovery, they were subjected to a schedule of chronic partial sleep deprivation (SR) allowing only 4 h of rest per day (at the beginning of the light phase) for 8 days. Sleep deprivation was achieved by placing the animals in slowly rotating drums. A forced activity (FA) group, who had to walk twice the speed in half the time, served as controls. This group was allowed to sleep for at least 14 h per day. All animals were subjected to a series of three intravenous glucose tolerance tests (IVGTT) to establish the effects of sleep restriction on glucose regulation. These IVGTT's were given in the baseline period before chronic sleep restriction (day 0), after 8 days of sleep restriction (day 8) and after 4 days of unlimited recovery sleep (day 12). The results show that there were no differences in the glucose and insulin profiles during the IVGTT's that were performed at day 0 and day 12. Both sleep restriction and forced activity led to somewhat lower insulin profiles at day 8, reflecting the increased physical activity in both groups. The most interesting finding was a significantly increased blood glucose response in the sleep restricted animals, a phenomenon that did not occur in the FA controls. The impaired glucose tolerance after sleep restriction is markedly similar to the data observed in a relative acute study in humans. Further research is necessary to investigate the underlying mechanisms.

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Sleep related car crashes : risk perception and sleepiness at wheel coping strategies

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Sleepiness is often a contributing factor in car crashes. Despite drivers under 30 years of age are particularly prone to sleep-related accidents in the early morning [1], they often underestimate potential hazards in the road environment and overestimate their driving ability [2]. The aim of the study is to examine which factors are associated with the risk perception to have night-time car crash in young drivers and to evaluate the strategies most commonly used to counteract sleepiness at the wheels. 1123 young drivers (41,8% males; mean age = 21,04, SD = 1,65), with at least 6 months driving experience participated to the study. The questionnaire, individually administered, evaluated 1) night-time driving and the related risk perceptions 2) previous experience of sleepiness at the wheels and about the strategies used to cope with it. A linear regression analysis pointed out that males are less worried about night-time car crashes than females (b = 0.07). Such concerns decrease with the increasing of night-time driving (b = – 0.12), whereas the frequency of episodes of driving impaired by sleepiness increase the perception of this risk (b = 0.14). The 51,47% of the participants answered that they "would continue driving but do something in order to cope with the sleepiness at wheel", whereas 48% indicated that they "would stop driving and do something to cope with the sleepiness at wheel". The preferred coping strategies were: "Opening windows" (18,10%), "Increasing the effort and attention" (13,25%), "Stop and taking a coffee" (13,20%), "Stop and washing the face" (10,19%). A logistic regression analysis showed that the risky decision to continue driving while impaired by sleepiness is positively and linearly related to the frequency of night-time driving (Wald = 15.40, gdl = 2; $P < 0.001$). Our results indicate that the frequency of night-time driving influences risk perception and worries: the perceived likelihood of having a sleep-related car crash and the counteract sleepiness with safe strategies are lower for those who report driving at night more frequently. 1. McConnel et al. (2003), Behavioral. Sleep Medicine, 1 (3): 171–183. 2. Gregersen, N.P., Bjurulf, P. (1996). Accident Analysis & Prevention, 28, 2:. 229–241.

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Changes of EEG correlation during MWT in sleep-deprived subjects

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The objective of this study was to assess changes of spatial EEG correlation strength between wakefulness and sleep in twelve healthy sleep-deprived subjects aged 22 to 28 years. Each subject underwent a Maintenance of Wakefulness Test (MWT) with four trials after a night of total sleep deprivation and had been instructed to immediately indicate perception of sleepiness through pressing a button. Spatial EEG correlation strength was measured by a linear multi-variate and frequency selective method. In the 44 MWT trials when S1 was reached we observed, that from lights off to onset of the first epoch of sleep stage 1, spatial EEG correlation strength decreased significantly in the δ (1–4 Hz) band and non-significantly in the β band (13–20 Hz). From lights off to first occurrence of microsleep, spatial EEG correlation strength decreased significantly in the δ and β band ($n = 45$). Spatial EEG correlation strength in theδband was significantly higher during 30s following lights off, when subjects later failed to indicate perception of sleepiness before microsleep or falling asleep compared to those MWT trials when sleepiness was accurately indicated prior to sleep onset.

Conclusion: Spatial EEG correlation strength is a powerful tool to assess neuronal network dynamics in the transition from wakefulness to sleep. As such it revealed frequency-specific changes and was associated with accurately timed indication of sleepiness.

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Interruption of sleep pattern before mating and during the first week of pregnancy impairs the offspring living ability: comparison of Long-Evans and Wistar rats

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Sleep pressure increases during the first week of pregnancy both in Long-Evans and Wistar rats (Almirall et al. 2004). It was shown also that gently sleep deprivation (SD) of Wistar rats before mating or during the first week of pregnancy significantly increases the offspring mortality (Pigareva, 2004). With the same method, Long Evans rats were subjected to gently SD from 11:00 until 14:00

during 3 consecutive days before mating (group 1) or during the first week of pregnancy (group 2). In order to achieve the total SD the following manipulations were used: moving of the food pellets in the food tray, opening or horizontal rotation of the cage and handling of the rat. Control rats were placed in the same room but their sleep was not interrupted. Statistical analysis was performed using two-ways ANOVA and Fisher test for post-hoc. The number of pups per litter did not differ in experimental and control groups. However, the number of dead pups during 3 postnatal weeks was more in group 1 ($F = 3.99$, df = 1;44, $P = 0.05$) and especially in group 2 ($F = 27.3$, df = 1;44, $P < 0.00001$) in comparison with the control group. In group 2, this difference became significant already to postnatal day 7. Maximal pups mortality in both experimental groups of Long-Evans rats was observed during the first postnatal week; the same was observed in Wistar rats. However, in Wistar rats, the total percentage of pup's death was higher after SD before mating than in the case of SD during the first week of pregnancy. Long-Evans rats appeared to be more sensitive to the same sleep interruption procedure and their behaviour during lactation had prominent individual differences. All rats of group 1 and most of them in group 2 had long-lasting circling, ''tail carrying'' and ''pup carrying'' behaviour. Such behaviour was very rare in Wistar lactating rats. Possible connection of observed types of behaviour in Long Evans rats with SD before the pregnancy or during the first week of pregnancy needs the special investigation.

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Does sleep deprivation affect task switching performance?

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Neural systems of prefrontal cortex (PFC) involved in executive functions are particularly susceptible to sleep deprivation. As a consequence, several neurocognitive functions result impaired by acute sleep loss: attention, divergent thinking, decision making, response inhibition. In the present study we investigated the effects of sleep loss on the executive control processes as assessed by a task switching procedure, that require individuals to perform two different tasks in an intermixed fashion. Eighteen subjects participated to Experiment 1, that investigated the effect of sleep deprivation on the task set reconfiguration component of task switching, and 18 ss. to Experiment 2, that focused on the decay component. Each experiment comprised 2 groups: one performed task switching before and after a normal nocturnal sleep (control group), the other before and after a night of total sleep deprivation in the laboratory (experimental group). Dependent variable was the switch cost (SC), measured as the difference in reaction times (RT) between switch and repetition trials. Preliminary analyses of variance confirmed for both experiments that switch trials had slower mean RTs compared to repetition trials. Moreover, analyses of variance on mean SCs showed a significant GROUP*DAY interaction only for Experiment 2, indicating an increase of switch cost after sleep deprivation. Such an increase disappeared after one night of recovery sleep. The ability to rapidly and flexibly adjust behavior to changing environmental demands is a defining characteristic of cognitive control and represents one of the most sophisticated capabilities of the human beings. This skill seems to be reduced after sleep deprivation, although one recovery night is sufficient to return to optimal levels of performance. The difference between experiment 1 and 2 suggests that sleep deprivation specifically affects decay component of task-switching capability.

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The effects of self-awakening on sigma band power before awakening

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Introduction: Self-awakening that wakening by oneself at a predetermined time, has been reported to reduce sleep inertia after awakening (1) EEG activity before self-awakening was analyzed to clarify the psychophysiological mechanisms of this effect.

Methods: Undergraduate and graduate students ($n = 10$) in good health participated in an experiment that was conducted for 5 consecutive nights: (1) adaptation night. (2) forced-awakening night, and (3–5) self-awakening nights. EEG power spectra in sleep Stage 2 and stage REM during 90 min before forced- and self-awakening were calculated.

Results and discussion: Sigma band power that reflects sleep spindles gradually decreased in the self-awakening night, duiring 20 min of stage 2 before awakening, whereas it did not change as a function of time in the forced awakening nights. Previous studies have reported that sleep spindles were involved in maintaining sleep (2). Based on the results of this study, is concluded that self-awakening reduces the sleep maintaining function before awakening, and thereby attenuate sleep inertia.

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The effect of repeated short sleep deprivations on sleep and the sleep EEG

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Sleep regulation is realized by homeostatic and circadian processes. The homeostatic component is reflected by slow-wave activity (SWA) in the NREM sleep EEG, while high frequency activity (>10 Hz, HFA) is thought to be influenced by the circadian factors. We investigated whether daily changes in sleep and HFA are independent of changes in SWA. Rats ($n = 4$) were implanted with EEG and EMG electrodes and kept in 12 h:12 h light/dark cycles for the recovery period. Subsequently the animals adapted to constant dark conditions (DD) for at least 1 week. A baseline (BL) day was recorded followed by ''short-day protocol''-2 h sleep deprivation followed by 2 h rest for 2 days. The vigilance states were determined and EEG spectral analysis between 0.1–25.0 Hz was performed. The amount of sleep over 24 h of the ''short-day protocol'' was less ($43.3 \pm 1.7\%$ SE) compared to baseline ($51.5 \pm 1.2\%$, $P < 0.005$, t-test). Circadian changes in vigilance states was reduced to 25% of baseline ($P < 0.05$, t-test). SWA (1.1–4.0 Hz) in NREM sleep did not show a significant circadian modulation ($P > 0.5$, ANOVA 4-h intervals) during the protocol, while the power density in spindle range (11.1–15.0 Hz) and frequencies between 15.1–25.0 Hz showed strong circadian modulation ($P < 0.05$, ANOVA 4-h intervals) which did not differ from baseline ($P > 0.5$, ANOVA). Analysis of the time course of SWA and power density in the spindle range in the first 7 min of a NREM sleep episode confirmed these results, with no circadian

modulation in SWA but circadian changes in the spindle range and a time course within the NREM sleep episode identical to baseline. The present data show that, in a contrast to SWA, HFA is not influenced by sleep homeostatic mechanisms and displays significant circadian modulation with an endogenous origin.

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Dynamic changes in neurotransmitter levels in the basal forebrain during and after sleep deprivation

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Wakefulness is maintained by several collateral and overlapping neurotransmitter systems, including the cholinergic, noradrenergic and serotonergic systems. The basal forebrain (BF) participates in the control of vigilance state through its cortical cholinergic, GABAergig and glutamatergic projections. Prolonged waking accumulates sleep pressure in the BF by increasing adenosine concentration. Adenosine is an inhibitory neuromodulator, which is known to decrease the firing rate of the waking-promoting neurons in the BF, Thus, during sleep deprivation (SD) the increased adenosine levels promote sleep. However, the animals are able to stay awake, suggesting increased activity of the wakefulness-maintaining system to counteract the effect of sleep pressure. The BF receives projections from all major waking-inducing neurotransmitter systems. The relative contribution of these neurotranmitters in maintaining wakefulness during SD has not been previously explored. In order to study the dynamic changes in neurotransmitter level in the BF during and after SD, male Han-Wistar rats were subjected to a 6 h SD by 'gentle handling'. In vivo microdialysis was used to sample the BF extra cellular space. Samples for neurotransmitter level measurement were collected before, during and after SD and the EEG and EMG were recorded continuously. Using HPLC an increase in 5-HIAA was found during SD, decreasing again during recovery sleep. SD progressively increased the 5-HIAA concentration every following hour of SD in the BF. During recovery sleep a steady decrease of 5-HIAA towards baseline level was seen. These findings are in accordance with previous research where SD significantly increased the 5-HIAA/5-HT ratio in tissue samples from the frontal cortex, hippocampus, hypothalamus and brain stem indicating increased 5-HT turnover in those areas.

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Critical periods of vulnerability to sleep during total sleep deprivation or partial sleep deprivation

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Very few sleep deprivation studies were performed while the EEG of the subjects was continuously recorded. However it is the only method making it possible to control with certainty extra sleep outside the scheduled sleep period. The aim of this study is to compare sleepiness between subjects under total deprivation and subjects under restriction through continuous EEG recording. 20 women aged 20–30 years, healthy and non smoker were included in the study after a careful selection. 10 women participated to the Partial Sleep Deprivation (PSD) in which they were admitted to the Sleep Laboratory for one Baseline Night (BN)- (11 pm–7 am), three nights of Sleep Restriction (01 am–05 am) and one Recovery Night (RN). The other 10 were included in the Total Sleep Deprivation (TSD) in which the subjects had to stay in the laboratory for two BN, 40 h of Sleep Deprivation and one RN. Continuous EEG recordings were performed day and night in both studies. Vigilance was estimated with the EEG recordings that were controlled every day to detect potential sleep episodes at inappropriate time. Subjects did not fall asleep during the baseline day in both studies, but fell asleep during all the 40 h of TSD and during the day following the third restriction night. In both studies 60% of the subjects fell asleep during a few minutes. There was no significant difference between the two groups in the number of sleep episodes and their duration (mean duration: 5 ($\pm$ 5) minutes for 2,3 ($\pm$ 2,8) sleep episodes in TSD against 6,5 ($\pm$ 9,8) minutes for 1 ($\pm$ 1,1) sleep episodes in PSD). However the distribution of the sleep episodes differed in the two studies: in TSD the majority of sleep episodes appeared in the afternoon and in the evening (after 31 h–40 h of wakefulness). In PSD all sleep episodes appeared in the morning after awakening between 5 am and 8 am; and no one in the afternoon or evening. Critical periods of vulnerability to sleep appeared in the afternoon and evening after 31 h–40 h of wakefulness during TSD and in the morning after awakening during PSD.

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Deficits in sustained attention during wakefulness have little in common with ESS global ratings of sleepiness

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We studied the maintenance of simple attention in 58 consecutive sleep disorders patients. 19 of these patients were restudied at least once after treatment. Trait ratings of fatigue and sleepiness were obtained with the Epworth Sleepiness Scale (ESS) and Fatigue Impact Scale (FIS). State assessments of alertness during testing were elicited along the continuum of "very alert" to "fighting sleep" with a 100 mm visual analog scale (VAS). Sustained attention was assessed from responses to visual stimuli presented at either 3 second intervals ($n = 68$) or at random intervals between 3–10 seconds ($n = 75$) over 20 min. Two tests were performed at each visit. The number of missed responses (lapses) and subjective reports were modeled using the General Estimating Equation (GEE) (R statistical language) and reported as the robust Z score and associated *P*. value. The median number of lapses was 13 (IQR range 3–45, max 165). Expressed metaphorically as the distance traveled at 90 km hr^{-1}: 50% of the tests resulted in total travel greater than 1 km and 25% between 3 and 12.5 km during attentional "blindness". While attention performance was predicted by state "alertness" (VAS: Z -2.53, *P*. 0.01), trait assessments of fatigue and somnolence were less informative (FIS: Z 1.8, p. 0.07/ESS: Z 1.2, *P*. 0.2). Test protocol type had no influence on these relationships. These results suggest that retrospective global subjective ratings of sleepiness from the ESS may greatly underestimate clinically significant deficits in the maintenance of wakeful attention and raises the question: "Is the ESS a suboptimal measure of the burden of sleep disorders and of the efficacy of their treatments?"

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The restorative value of short sleeps in on-board rest facilities

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Introduction: In many industries, shiftworkers have the opportunity to supplement their normal home sleep with sleep at work. In some cases, particularly in the long-haul transport industries, sleep at work may actually occur in on-board rest facilities. There are research data and anecdotal reports suggesting that the restorative value of sleep is influenced by the sleep environment. The purpose

of this study was to compare the restorative value of 'on-board sleep' and 'bed sleep'.

Methods: Data were extracted from a data set that contained sleep/wake information for over 400 airline pilots. Participants kept a self-report sleep diary and wore a wrist activity monitor for at least two weeks. Participants rated their level of fatigue at the start and end of sleep periods using the 7-point Samn-Perelli Fatigue Checklist (1 = fully alert, 7 = completely exhausted). The restorative value of sleep was calculated as the difference between self-rated fatigue at the start and end of a sleep period (range = – 6 to+6). Two groups of sleeps were selected from the database: on-board sleeps and bed sleeps. To match the groups, bed sleeps were only selected if time in bed was less than the mean plus two standard deviations of time in bed for the on-board sleeps.

Results: There were 2,217 on-board sleeps, with an average (± st.dev.) time in bed of 2.36 h (± 1.18 h), total sleep time of 1.72 h (± 1.11 h), and recovery value of 0.90 (± 1.13). There were 3,079 bed sleeps with an average time in bed of 2.36 h (± 1.24 h), total sleep time of 1.83 h (± 1.15 h), and recovery value of 1.29 (± 1.11).

Conclusions: The current analyses indicate that sleep obtained in on-board rest facilities has approximately 70% the recovery value of duration-matched bed sleeps. This difference may be due to psychological factors (e.g. difficultly relaxing the mind while at work) and/or environmental factors (e.g. comfort of the rest facility). Issues related to the restorative value of sleep should be taken into account when planning on-board rest opportunities for airline pilots and other transport workers.

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Sleep related arousals caused by different types of train

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The expected development of railway transportation in the next few years might be a potential risk factor for people living alongside the rail tracks, especially at night. Nocturnal exposure to noise induces sleep disturbances especially in terms of sleep fragmentation. The main purpose of this study was to compare the effects of different types of train (freight, automotive, passenger) on arousal from sleep. In particular, we investigated the contribution of the physical characteristics of the train noises (intensity, rise time, duration) as a function of age and sleep stage. Twenty young (25.8 years ± 2.6) and 18 middle-aged (52.2 years ± 2.5) healthy subjects participated in three whole-night polysomnographic recordings including one control night (35 dB A), and two noisy nights with equivalent noise levels of 40 or 50 dB (A), respectively. The results showed that railway noise produces micro-arousals in addition to those occurring spontaneously. EEG arousals increased with noise intensity. They were the highest in S2 and the lowest in REM sleep. Micro-arousals (3–10 sec) occurred at a rate of 25–30%, irrespective of the type of train. Awakenings (>10 sec) were produced more frequently by freight train than by automotive and passenger trains. Arousal onset latency increased gradually from automotive to passenger to freight. Age-related sleep disturbances were not aggravated by railway noise, suggesting that older people show a similar level of sleep dependent noise sensitivity compared to juniors, perhaps because their sleep is more fragmented leading them to hear noise while awake. In conclusion, microscopic detection of sleep fragmentation may provide advantageous information on sleep disturbances caused by environmental noises. To determine the critical threshold for intermittent noise, physical parameters such as duration and rise time (progressive increase in noise intensity) should be taken into account, in addition to the already proposed factors such as the number and maximum levels of auditory stimulus.

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Selective slow-wave-sleep deprivation induces lapses of attention in psychomotor vigilance tasks

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Loss of sleep leads to reduced vigilance. We investigated the effect of partial sleep deprivation in healthy well-sleeping elderly on two tasks of psychomotor vigilance, one requiring an immediate response to the target stimulus and the other requiring a decision before responding. We developed a slow-wave-sleep selective sleep deprivation procedure, using auditory stimuli delivered to the subject based on the slow-wave density in the EEG of the subjects: We recruited 13 healthy well-sleeping elderly subjects who spent two nights in the sleep laboratory while we recorded their polysomnogram; we repeated the measurement with an interval of 5–7 weeks. On one of the occasions, balanced across subjects, we administered partial sleep deprivation for two consecutive nights. On each of the sessions we administered the two vigilance tasks on separate days, in a balanced order across subjects. Selective sleep deprivation in healthy well-sleeping subjects resulted in a higher number of vigilance lapses across the two tasks, but not in a change in reaction times for the correct responses. Our results corroborate and extend the findings of increased number of lapses after sleep deprivation in healthy young subjects.

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Effects of sleep restriction of subjective and objective vigilance measures

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This study investigated the effects of 5 consecutive nights of a mild sleep restriction and two nights of recovery on subjective and objective vigilance measures. Nine young healthy volunteers (males, aged between 18–30 y.o.) took part in the study. Participants, under constant PSG monitoring, spent 11 consecutive nights and days at the sleep laboratory (1 adaptation night, 2 baseline nights, 5 sleep restriction nights, 3 recovery nights). In baseline and recovery conditions time in bed was 8 h night^{-1} (11.00 pm–7.00 am), during the sleep restriction phase time in bed was 5 h (1.00 am–6.00 am). PVT (Psychomotor-vigilance task) was taken as objective vigilance measure. Subjective vigilance measures were the Global Vigor-Affective Scale (GVA), and the Stanford Sleepiness Scale (SSS). PVT and alertness-sleepiness scales were administered four times per day (9.00 am, 1.00 pm, 5.00 pm, 8.00 pm). Data were analysed by a series of univariate ANOVAs. Results show a general negative effect of sleep restriction procedure on all vigilance measures, in particular on tests performed on the first part of the day. As long as nights of sleep restriction augment the negative effect increases (9.00 am: PVT mean RT, $P<0.05$; PVT 10% Slowest RT, $P<0.05$; GVA, $P=0.06$; SSS, $P<0.05$). Comparing recovery with baseline values objective vigilance levels are still impaired (9.00 am: PVT mean RT, $P<0.05$; PVT 10% Slowest RT, $P<0.05$; 1.00 pm: PVT mean RT, $P<0.01$; PVT 10% Slowest RT, $P<0.01$). On the contrary subjective vigilance

measures did not differ from baseline values. This study simulated a week were people are slightly sleep deprived during the week days and recover on week-end. Results are alarming. Even thought after recovery nights participants assessed them-selves alert and not sleepy, two 8 h sleep nights are not sufficient to recover the impairment on objective vigilance provoked by preceding sleep loss. Discrepancy between subjective and vigilance measured should be furthermore investigated.

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Efficacy of olfactory stimulation following one night of sleep deprivation

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Introduction: Sleep-loss impairs vigilance, subjective well-being and cognitive functioning. The present study investigated whether periodic olfactory stimulation (OS) with rosemary scent, for which an activating effect has been shown, counteracts increased sleepiness.

Methods: Twelve healthy subjects participated in a repeated measurement design consisting of 3 conditions: (i) after a night with sufficient sleep (Baseline), (ii) after 24 h awake without OS (Sleep Deprivation), (iii) after 24 h awake and OS with rosemary scent (Rosemary). In intervals of 5 min, a 1 min stream of scented or plain air was administered to the subjects through a modified oxygen mask. We used standardized subjective (Karolinska Sleepiness Scale), physiological (pupillography) and cognitive instruments (verbal fluency test, Mackworth Clock).

Results: Subjective sleepiness was increased significantly after a night of sleep-loss, the olfactory stimulus had no effect on subjective measures. The changes in pupillary diameter (Pupil-Unrest-Index) did not differentiate between the three conditions ($M \pm SE$: Baseline: 4.7 mm $min^{-1} \pm 0.7$, Sleep Deprivation: 5.6 mm $min^{-1} \pm 1.0$, Rosemary: 5.5 mm $min^{-1} \pm 0.7$). Divergent thinking ability, assessed with percentiles in the verbal fluency test, was not affected by sleep deprivation, rosemary even impaired category fluency tendentially ($P<0.10$) (Baseline: 51.2 ± 8.0, Sleep Deprivation: 63.6 ± 9.0, Rosemary: 44.8 ± 8.3). Both reaction time and performance accuracy were impaired significantly in the sustained attention test (Mackworth Clock) following sleep-loss, with rosemary demonstrating no improving effect (RT: Baseline: $0.49s \pm 0.02$, Sleep Deprivation: $0.56s \pm 0.01$, Rosemary: $0.58s \pm 0.02$; Lapses: Baseline: 3.3 ± 1.4, Sleep Deprivation: 26.2 ± 5.3, Rosemary: 29.5 ± 6.1).

Conclusion: The results revealed a substantial negative impact of sleep deprivation in different domains of sleepiness. These findings are consistent with previous studies. Periodic olfactory stimulation with rosemary did not prove to be an effective countermeasure to vigilance decrements after one night of sleep-loss.

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Sleep deprivation as an antidepressant treatment following chronic mild stress: effects on translation factor EIF4E and EEF2 activity

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Onset of action of antidepressant drugs are typically delayed, where several weeks of treatment usually requires for achieving a therapeutic response. In contrast, a single night of sleep deprivation can rapidly, if transiently, reverse symptoms of depression in humans. While slow actions of antidepressant drugs have underwent extensive research, the rapid effects of sleep deprivation are little understood. Several lines of work suggest that chronic antidepressant treatment requires upregulation of brain-derived neurotrophic factor (BDNF) and enhanced signaling through the BDNF receptor, TrkB. In the adult rat brain, BDNF regulates protein synthesis-dependent changes in synaptic strength through modulation of gene transcription, as well as through post-transcriptional effects on mRNA translation. In the present report, an animal model of depression, chronic mild stress (CMS) was used to determine the effects of total sleep deprivation. Previously, we have shown that BDNF levels are downregulated following CMS. In healthy outbred rats, we have found that chronic, but not acute, administration of the SSRI, fluoxetine, modulates the activity of translation initiation factor 4E (eIF4E) and elongation factor 2 (eEF2) in a brain region-specific manner. Here, we examined the effects of CMS (4 weeks) and subsequent sleep deprivation (8 h) on the phosphorylation state of several translation factors (eIF4E, eEF2, cytoplasmic polyadenylation element binding protein (CPEB)). The results suggest that translation factor activity is modulated by chronic mild stress, and that these effects are reversed, at least in part, by sleep deprivation.

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Sleep loss produces false memories

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People sometimes claim with high confidence to remember events that in fact never happened, typically due to strong semantic associations with actually encoded events. Sleep is known to provide optimal conditions for consolidation of memories for long-term storage, whereas sleep deprivation acutely impairs retrieval of stored memories. Here, focusing on the role of sleep-related memory processes, we tested whether false memories can be created (a) as enduring memory representations due to a consolidation-associated reorganization of new memory representations during post-learning sleep and/or (b) as an acute retrieval-related phenomenon induced by sleep deprivation at memory testing, possibly via adenosinergic mechanisms. According to the Deese, Roedinger, McDermott (DRM) false memory paradigm, subjects learned lists of semantically associated words (e.g., ''night'', ''dark'', ''coal'',. . .), lacking the strongest common associate or theme word (here: ''black''). Subjects either slept or stayed awake immediately after learning, and they were either sleep deprived or not at recognition testing 9, 33, or 44 h after learning. Sleep deprivation at retrieval, but not sleep following learning, critically enhanced false memories of theme words. This effect was abolished by caffeine administration prior to retrieval, indicating a critical involvement of adenosinergic mechanisms in the generation of false memories associated with sleep loss.

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Changes of delta and spindle oscillations in response to sleep deprivation are correlated

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Introduction: The human sleep EEG is characterised by the occurrence of distinct oscillatory events such as delta waves, sleep

spindles, and alpha activity. Several studies demonstrated their specific response to sleep deprivation by using spectral analysis or by studying the events. On average, an increased incidence of delta oscillations and a decreased spindle density was reported. We investigated to which extent these changes are correlated taking into account inter-individual variation.

Methods: Sleep EEG data of 27 healthy young males were analysed (baseline and recovery sleep after 40 h of prolonged wakefulness; C3-A2 derivation, sampling frequency 128 Hz). Oscillatory events were detected using a method based on estimating autoregressive (AR) models on overlapping 1-s segments. In each subject we determined both the change in event density after sleep deprivation and the ratio of spectral band power (recovery/baseline).

Results: A positive correlation ($r = 0.48$, $P < 0.05$) between the changes in event densities of delta oscillations and sleep spindles was observed. Individuals showing a stronger than average increase in the density of delta oscillations exhibited a lower than average decrease or even an increase in the density of spindles. This correlation was most pronounced in sleep stage 2 between delta oscillations and fast spindles (12.75–16.5 Hz) ($r = 0.74$, $P < 0.05$) and was only observed in the event analysis and not in the corresponding band power.

Conclusions: Our results question the picture of a complementary relationship between delta oscillations and sleep spindles. Moreover, our results demonstrate the usefulness of event based methods for analysing human sleep EEG.

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An integrative role of the median preoptic nucleus in sleep deprivation and recovery induced by low ambient temperature

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Introduction: Cold exposure selectively reduce REM sleep occurrence and, when ambient temperature (Ta) is very low, it also decreases delta power density [1]. These changes are concomitant with a modification of cellular activity in the preoptic-anterior hypothalamic area [2]. In order to extend the map of cellular activity for a model of sleep deprivation based on cold exposure, we have investigated the expression of c-Fos and P-CREB in several brain regions. Here we present the results concerning the median preoptic nucleus (MnPO), which is implicated in the regulation of body osmolality, body temperature and sleep [3,4].

Method: Twenty-four male albino rats were used. Animals were randomly assigned to the following experimental conditions: i) control: 5 h or 24 h at the normal laboratory (nl) Ta of 23.0 ± 1.0 °C; ii) exposure: 5 h, 24 h, or 48 h at Ta −10.0 ± 0.5 °C; iii) recovery: 5 h at nl-Ta after 24 h or 48 h of exposure. Brains were fixed with 4% p-formaldehyde and 40 μm coronal sections were alternately processed for c-Fos and P-CREB immunohistochemistry. Each fifth section was stained with cresyl violet for the anatomical identification. c-Fos positive nuclei and the extension of P-CREB stained area were counted within standardized grids on digital images of sections. The rostral, caudal ventral [5], and caudal dorsal nuclear subdivisions were separately examined. Data were statistically assessed by means of ANOVA.

Results: In the whole MnPO, P-CREB but not c-Fos expression was higher in control 5 h than in control 24 h. c-Fos expresion was significantly higher during both exposure and recovery with respect to control levels. P-CREB expression was significantly higher during exposure, but significantly lower during recovery with respect to control levels.

Conclusion: The results suggest that MnPO may be activated by both the ambient condition and the resulting changes in sleep pressure.

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Concomitant paradoxical sleep deprivation potentiates reserpine-induced orofacial dyskinesia in mice: role of striatal catalase

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Paradoxical sleep deprivation (PSD) in rodents induces striatal dopaminergic supersensitivity (SDS) as well as brain oxidative stress. In parallel, tardive dyskinesia has been related to both SDS and striatal oxidative stress. Concerning this last issue, we have demonstrated that striatal catalase activity is particularly important to avoid reserpine-induced orofacial dyskinesia (RIOFD) (a rodent model of tardive dyskinesia). Within this context, we have recently verified that previous PSD potentiated RIOFD without modifying SDS. The aims of the present study were three-fold: 1) to investigate whether concomitant PSD would also potentiate RIOFD, 2) to verify the motor specificity of such an effect and 3) to determine a possible involvement of the stress induced by the PSD procedure and/or of striatal catalase activity in such a potentiation. Male Swiss mice were submitted to PSD for 96 h using the method of multiple platforms in a water tank. Stress control (SC) mice were kept in their home-cages with daily exposures for 15 min to the same method (days 1 to 4). Control (CT) animals were maintained in their home-cages. Immediately before the beginning of PSD or SC, animals of the 3 groups (PSD, SC or CT) received a first sc injection of saline (SAL) or $0.25\,mg\,kg^{-1}$ reserpine (RES) followed by a second identical injection 48 h later (days 1 and 3 of SD, respectively). Thus, the 6 groups were: PSD-SAL, PSD-RES, SC-SAL, SC-RES, CT-SAL and CT-RES. 24 h after the second SAL or RES injection (day 4 and, thus, immediately after the 96-period of PSD), orofacial dyskinesia was quantified in wire mesh cages and general motor activity in an open-field. In a second experiment, instead of behavioural quantification, mice were sacrificed and striatal catalase activity was quantified. Results showed that the PSD-RES group presented higher frequency of vacuous chewing movements than all the other groups and had a significant decrease in catalase activity. However, there was no difference in open-field immobility among the different groups. Our data show that concomitant PSD potentiates RIOFD. This potentiation is not related to: 1) a general motor activity effect, 2) the stress of the PSD procedure, but may be related to a lower activity of striatal catalase.

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Sleep deprivation effects on postural control vary during aging

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Introduction: Falls increase with age and cause significant injuries in the older population. While a few studies suggest that sleep

influences postural control, the impact of age-related changes in sleep mechanisms on postural control is still unknown. This study aimed to determine whether age modulates the interactions between sleep deprivation (SD), attention, and postural control.

Methods: Eight young (mean age 24,8; SD 1,9) and nine older adults (mean age 64,4 ; SD 4,0) stood still on a force plate in two counterbalanced sleep conditions: after a night of sleep and after a night of total SD (25 h of wakefulness). Two hours after wake time, center of pressure (CoP) displacements were measured in six postural conditions: eyes open (EO) and eyes closed (EC), while doing an interference task, a control task, or no task. Three-way ANOVAs (2 age groups * 2 sleep conditions * 6 postural conditions) were executed on anteroposterior CoP range and speed parameters.

Results: Only older subjects presented an increased CoP range after SD in the "EO-control task" condition and in all EC conditions (age*sleep conditions*postural conditions interaction $P<0.002$; all contrasts $P<0.05$). SD increased CoP speed in the "EO-no task" condition and in all EC conditions for all subjects (sleep*postural condition interaction $P<0.007$; all contrast $P<0.005$).

Conclusions: SD increased CoP speed in both age groups. However, in older subjects, the CoP did not only move faster, but also shifted further away, suggesting an even higher risk of crossing postural stability boundaries. Importantly, while the effects of SD on CoP range seemed to depend on tasks and visual input, CoP speed reacted to SD even when visual information was available and no cognitive task was performed, revealing a direct impact of SD. These results suggest that SD may be a significant factor putting older people at higher risk of falling.

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Redefining the PVT lapse in terms of duration & eyes open/closed

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Introduction: The Psychomotor Vigilance Task (PVT) lapse is usually defined as a response longer than 500 ms. This cut-off is arbitrary, and an assessment of what a participant is doing during the lapse may reveal further discrimination of the level of participant 'disengagement' during these events. In turn, we propose that this will provide further criteria for categorising PVT responses in relation to sleepiness-impaired performance.

Methods: Sixteen healthy, young adult (24.4 y $\pm$ 3.6) normal healthy sleepers (8 h $\pm$ 1 h), without complaint of daytime sleepiness (<2 naps/week^{-1}; ESS ≤ 10; bihourly KSS) underwent two extended 30 min PVT sessions, at 22.00 h (ALERT) and again at 04.00 h (SLEEPY). Video-data (birds-eye and frontal-view) was used to classify each lapse (≥ 500 ms) as occurring with eyes open (EO) or eyes closed (EC). Other lapses due to distraction were excluded (2.4%).

Results: Repeated measures three-way ANOVA for lapse (EO versus EC), sleepiness (Alert versus Sleepy), and PVT epoch (3×10 min bins) showed significant main effects ($P \leq 0.005$) together with a significant lapse×sleepiness×time ($P = 0.013$) interaction. EO lapses remained stable over PVT epochs, whereas EC lapses increased. Further analysis of lapse duration showed: no reaction time effect of sleepiness for EO (Av. 728 ms for alert versus 744 ms for sleepy), significant effect for EC (Av. 3061 msec versus 4207 ms). There were clear changes in the EO versus EC nature of lapses: those above 3200 ms were 95% likely to be EC, whereas those between 500–600 ms were 95% likely to be EO. We provide probabilities of EC/EO for the transition between these two extremes of lapse durations.

Conclusions: Notwithstanding different time of day effects between the conditions and that sleep loss was not severe, these findings point to the potential usefulness of a further sub-division of lapses beyond the usual dichotomy of lapse/no lapse, based only on a 500 ms criterion. We propose redefining the lapse to express magnitude of lapse (i.e. mild, moderate, etc) given the likelihood of varied associated behaviour (i.e. EO Vs EC). This study provides further insight into developing sleepiness and its measurement.

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Desiring more sleep: links between sleep deficit and MSLT and PVT scores

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Introduction: Current literature relying on MSLT-reported findings suggests many healthy adults are accruing a chronic sleep debt (i.e. sleeping ≤ 8 h night^{-1}) as determined by the increased tendency to fall asleep in the MSLT laboratory setting. Our previous findings from 10,800 participants suggested those who desired more sleep, generally were not considered 'sleepy' using subjective measures. Here, we address reported sleep need in healthy volunteers, and assess its relationship to established objective sleepiness measures: the PVT and MSLT.

Methods: Forty-four healthy young (21–25 y) adult, good sleepers (7.4 h actigraphy-determined), who were non-nappers and not complaining of daytime sleepiness (Epworth Sleepiness Score) ESS underwent standard MSLT (10:00, 12:00, 14:00, 16:00) and extended PVT testing (30 min–16:30). They also self-reported sleep need (SN) by questionnaire which was categorised as 'Sleep Deficit' (TST $<$ SN), 'Nil' (TST = SN) and Sleep Plus (TST $>$ SN).

Results: Participants had an average MSLT score of 14.40 min and small PVT impairment (av.1 lapse every 6.5 min). Of these, 15.9% complained of sleep debt, compared with 54.6% nil and 29.5% sleep plus. TST for these groups were significantly different (6.58 h, 7.37 h, and 8.12 h respectively) however MSLT scores (14.49 min, 13.35 min, 16.34 min) or PVT were not different ($P>0.15$).

Conclusion: For average 7.4 h sleepers with no complaint of daytime sleepiness there was no difference in MSLT or PVT-determined sleepiness between those who self-reported a sleep debt versus those who did not.

Acknowledgment: This supports previous findings that the 'desire' for more sleep may not be synonymous with the 'need' for more sleep due to increasing daytime sleepiness.

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Extended driving impairs nocturnal driving performances

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Though fatigue and sleepiness at the wheel are well-known risk factors for traffic accidents, many drivers combine extended driving and sleep deprivation. Fatigue-related accidents occur mainly at

night but there is no experimental data available on the relationship between duration of driving and nocturnal accidental risk. The study objective is to determine whether 2, 4 and 8 h of nocturnal driving affect differently driving performance. 14 young healthy men (mean age [± SD] = 23.4 [± 1.7] years) were recruited. Participants drove in 3 nocturnal driving sessions (3–5 am, 1–5 am and 9 pm–5 am) on an open highway. Inappropriate line crossings (ILC) in the last hour of driving of each session (3–5 am, 1–5 am and 9 pm–5 am), sleep variables, self-perceived fatigue and sleepiness were analyzed. Compared to the 3–5 am driving session, the incidence rate ratio of inappropriate line crossings increased by 2.6 (95% CI, 1.1 to 6.0; $P<0.05$) in 1–5 am driving session and by 4.0 (CI, 1.7 to 9.4; $P<0.001$) in 9 pm–5 am driving session. Compared to the reference session (9–10 pm), the incidence rate ratio of inappropriate line crossings were 6.0 (95% CI, 2.3 to 15.5; $P<0.001$) in the 3–5 am driving session, 15.4 (CI, 4.6 to 51.5; $P<0.001$) in the 1–5 am driving session and 24.3 (CI, 7.4 to 79.5; $P<0.001$) in the 9 pm–5 am driving session. Self-rated fatigue and sleepiness scores were both correlated to driving impairment in the 1–5 am and 9 pm–5 am driving sessions and increased significantly during the nocturnal driving sessions compared to the reference session. At night, extended driving impacts on driving performances and therefore should be limited. Revision of driving recommendations should take into account these new findings to reconsider the maximal nocturnal non stop driving duration.

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Sleep deprivation affects memory formation and adaptation: studies on maze learning and reversal learning in mice

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Sleep loss attenuates hippocampus-dependent memory formation. In a series of experiments we examined the effects of sleep deprivation (SD) on both memory formation and adaptation. Mice were trained to locate a food reward in one of two accessible arms of a Y or T shaped maze. To assess the role of sleep, half of the group was sleep deprived for 5 h following each training session, a phase critical for memory encoding and sensitive to sleep loss. When animals had mastered the task, the training was followed by: 1) brain collection for molecular analysis; 2) a probe trial to test the strategy that was used for learning (starting from the arm opposite of the original start arm); and 3) reversal training to asses memory flexibility (same start arm, food relocated to the previously non-baited arm). SD during the training phase did not appear to affect performance directly: control and sleep deprived mice performed equally well. However, SD prevented the training-induced MAPK activation that was seen in the hippocampus of control mice, suggesting that SD indeed affected hippocampal plasticity-related signalling. Moreover, a probe trial at the end of the training phase showed that SD mice used a different strategy to locate the food. Instead of a spatial, hippocampus dependent strategy, they used a response based, presumably striatum dependent strategy. Finally, mice that were previously sleep deprived during the training phase had a significantly reduced performance during subsequent reversal training. Perhaps the response based learning strategy that SD mice had adopted during the training phase made them less flexible during the subsequent reversal training. In conclusion, these results suggest that SD impairs hippocampus function and thereby forces subjects to rely on other brain regions and different strategies. This may initially prevent a decrease in performance at the behavioural level, but it may hamper subsequent adaptation of acquired memories when conditions change.

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Effects of sleep deprivation to ability of speech perception

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Sleep deprivation conduct to changes of cognitive efficiency (Schmidt et al. 2007). Our study investigated effects of prolonged wakefulness to speech processing, in particular speech perception. Based on the theory of Borbély (1982, see Schmidt et al. 2007) we predicted a circadian oscillation of speech perception which cannot explained by effects of vigilance or sleepiness. A 40 h Quasi-Constant Routine protocol (QCR) was conducted which started in the morning at 8:00. According to a cyclic schedule, eleven subjects (mean age 24.9) performed an auditory speech perception task as part of a cognitive test battery every 3 h during 40 h of constant wakefulness. External environs conditions were constant with dim light (~10 Lux), room temperature and failure of any time information. At the beginning of each hour subjects got is caloric meals (~100 kcal). To determine variations of alertness, Karolinska Sleepiness Scale and different Visual Analogue Scales were conducted hourly. Status of vigilance was tested by Psychomotor Vigilance Test every three hours. Circadian phase was estimated from salivary melatonin at 1-hr intervals and body temperature as continue measure. The mean melatonin onset (melatonin concentration >3 pg mL^{-1}) was measured at 22:30 (SD 96 min). The results revealed a daily variation of cognitive performance and confirmed our hypothesis of circadian oscillation in speech perception. Best performance was found in the evening. During the night performance decreased significantly with a nadir in the early morning. This central cognitive slowing during the night was not correlated with psychomotor vigilance, sleepiness or body temperature. After the circadian nadir speech performance increased again and indicates a circadian drive. The combination of central slowing in speech perception, sleepiness and decrease of vigilance under sleep deprivation seems to be an indicator of a general decrease in cognitive functioning during the night.

Reference: Schmidt C. et.al.; 2007. A time to think: Circadian rhythms in human cognition. In: Cognitive Neuropsychology 24 (7): 755–789

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The recognition of facial emotions under conditions of sleep deprivation

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Introduction: Individuals with sleep deprivation, which is associated with fatigue, moodiness, difficulty with concentration, memory impairment and disorientation, have been observed to experience impaired recognition of negative emotions. This study investigated the influence of sleep deprivation upon the recognition of six basic facial emotions including emotions such as anger, fear, etc. towards the end of suggesting the possible effects of such impairment upon social interaction.

Methods: Five healthy subjects who had been deprived of sleep for one night and also 5 age matched control subjects were recruited. Subjects were shown a standardised set of 6 basic facial emotions (anger, disgust, fear, happiness, sadness and surprise) and three neutral faces for a total of 39 stimuli, on a PC using the SuperLab software. They were asked to rate each face according to intensity of emotion on a scale of 1 (not at all) to 5 (most). The experimental

session consisted of a brief practice session and six study-test blocks.

Results: The subjects with sleep deprivation as a group were significantly impaired in recognizing anger [3.33 (IQR 2.67–3.83) versus 4.17 (IQR 3.67–4.42); $P = 0.047$] and fear [3 (IQR 1.92–3.67) versus 4 (IQR 3.83–4.17); $P = 0.016$] compared to controls, even though individual responses ranged from severely impaired to normal.

Conclusions: This study confirms that sleep deprivation impairs recognition of facial emotions, especially anger and fear. This may affect their interpersonal communication.

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Effects on maintenance of wakefulness test of recovery sleep dose following sleep restriction

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Little is known about the sensitivity of the Maintenance of Wakefulness Test (MWT) to differing sleep period lengths (TIB) following chronic sleep restriction. This study investigated the effect of varying TIB sleep doses on a night following 5 nights of sleep restriction (SR). $N = 118$ healthy subjects (age = 30.12 ± 6.98 yr, 64f) participated in a controlled laboratory protocol. Subjects underwent 2 nights of baseline sleep (TIB = 10 h) followed by 5 nights of SR (TIB = 4 h) and a night of varying time in bed for recovery sleep (R1). On R1 subjects were randomized to one of six TIB sleep doses (0 h $n = 13$; 2 h $n = 18$; 4 h $n = 24$; 6 h $n = 16$; 8 h $n = 17$; 10 h $n = 21$ TIB). Modified single trial (30 min) MWTs were conducted between 1430 h–1600 h on the day after the second baseline night, after the fifth SR night (SR5) and after R1. Sleep latency was defined as time to the first appearance of a brief sleep (10sec microsleep). $N = 9$ served as 10 h TIB per night control subjects. MWT sleep latency (± SD) after 5 nights of SR was 10.48 ± 8.6 min, which differed significantly from baseline 19.12 ± 10.3 min ($P < 0.001$). At SR5, sleep latency was shorter in the sleep restricted group (10.48 ± 8.6 min) versus the control group (22.26 ± 9.32 min; $P < 0.01$). R1 sleep doses of ≤6 h TIB (0 h, 2 h, 4 h, 6 h) yielded MWT sleep latencies significantly below those at baseline (all $P < 0.05$). R1 0 h and 2 h TIB decreased ability to stay awake significantly below that on SR5 ($P < 0.05$). R1 10 h TIB improved ability to stay awake significantly above SR5 ($P < 0.05$), however 8 h TIB did not ($P > 0.05$). The MWT was sensitive to SR and to the dose of subsequent TIB for sleep. However, MWT showed significant recovery only after a sleep dose of 10 h TIB. Analyses are underway to determine the nature of physiological sleep obtained in the 10 h TIB.

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Distinct topographical patterns in the dynamics of sleep homeostasis

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Introduction: EEG slow-wave activity (SWA) is a marker of nonREM sleep intensity and serves as an indicator of sleep homeostasis (Process S). SWA shows a frontal predominance and its increase after sleep deprivation is most pronounced in frontal areas. The spatial distribution of SWA is characteristic for an individual and may reflect traits of functional anatomy. Parameters of the homeostatic Process S were mainly derived from average data and for just a few derivations. We aimed at quantifying inter-individual variation in the parameters of Process S and to investigate their spatial distribution.

Methods: We analyzed sleep recordings of two data sets (27 EEG electrodes, $n = 8$; 60 EEG electrodes, $n = 4$) recorded during baseline and recovery sleep after prolonged wakefulness. The homeostatic Process S was modeled by a saturating exponential function during waking and an exponential decline during sleep. Empirical mean SWA per NREM sleep episode at episode midpoint served as reference for the parameter estimation. Parameters were estimated by minimizing the mean square error (MSE) between data and simulations. In individuals, the MSE was multiplied with an additional term to restrain the time constants to a physiological range.

Results: The decrease and buildup of Process S were slowest in fronto-central areas and the fastest dynamics were observed in parieto-occipital (decrease) and frontal (buildup) areas. For both, the buildup and decrease, significant topographic differences were observed. However, distinct individual patterns were observed. The difference between the upper and lower asymptote of Process S showed a similar spatial distribution as SWA. The best fit of Process S with empirical data was observed in fronto-central areas and the worst fit in temporal areas.

Conclusions: Our data provide an additional indication of regional differences in sleep homeostasis and support the notion of local aspects of sleep regulation.

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Recovery of neurobehavioural function and sleep following acute sleep loss

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Introduction: While there has been a significant effort directed toward understanding the manner in which fatigue accumulates, few studies have systematically described the recovery of neurobehavioural function in response to sleep loss. Even fewer studies in this area have included a control condition (i.e. no sleep loss), defining recovery as a return to pre-sleep loss levels of functioning. This approach does not take into account possible changes in function arising from spending time in an artificial, controlled environment, such as a sleep laboratory.

Methods: Forty-three subjects were sleep-deprived for one (moderate SD) or two (severe SD) nights, followed by five consecutive recovery sleep opportunities of either 6-hrs (0200–0800 h) or 9-hrs (2300–0800 h). Fifteen control subjects were allowed seven consecutive nine-hour sleep opportunities (2300–0800 h). While awake, participants completed 2-hourly batteries including a Psychomotor Vigilance Task (PVT) and a Visual Analogue Alertness Scale (VAS). Multiple Sleep Latency Tests were conducted daily (MSLT, 1000 h). Polysomnographic recordings were conducted during all sleep periods.

Results: Preliminary analyses (ANOVA with planned contrasts) defined recovery as a return to control condition levels (i.e. no significant difference, $P < 0.05$). Relative to control, sleep loss produced significant changes in all measures of waking function ($P < 0.05$). Following sleep loss (moderate and severe SD), PVT scores recovered following one sleep opportunity (9 h or 6 h). In the

groups with 9 h sleep opportunities post-SD, VAS scores recovered after one (moderate and severe SD), and MSLT scores after one (moderate SD) or three (severe SD) nights. In the groups with 6 h sleep opportunities, VAS scores recovered after five nights following moderate SD, and after only two nights following severe SD. MSLT scores in the 6 h groups did not recover.

Conclusions: Results indicate differential recovery among measures of waking function. Data collection continues. Further analyses will investigate recovery in the larger data set including several neurobehavioral tasks and examine recovery sleep parameters (duration and composition) relative to the control condition.

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Sleepiness is not always perceived before falling asleep in healthy sleep deprived subjects and in sleepy patients

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Objective: We prospectively evaluated the spontaneously perceived sleepiness (SPS) prior to sleep onset during Maintenance of Wakefulness Test (MWT) in young healthy sleep deprived subjects and in sleepy patients.

Method: 28 young healthy students (mean age 22.4 years; 13 females) after a whole night sleep deprivation and 159 patients (mean age 39.8 years; 59 females) with sleepiness of various origin underwent 4 MWTs. They received the instruction: ''Indicate your earliest symptoms of sleepiness and try to stay awake as long as possible!'' Over sleep (OS) and microsleeps (MS) of at least 3 seconds duration were scored separately.

Results: Overall 17 of 28 healthy subjects (60.7%) and 64 of 159 patients (40.3%) presented either a MS- or a OS fragment before indicating SPS at least in one of 4 MWT-trials. In both healthy subjects and patients, females demonstrated a better awareness of SPS than male subjects.

Conclusion: Our unexpected finding is in sharp contrast to the general assumption that nobody can fall asleep without prior awareness of sleepiness while driving. If the results will be confirmed in larger series, far reaching consequences will ensue. 1. The simple advice to sleepy subjects that they should not drive when sleepy would no longer be adequate. 2. Motor vehicle crashes due to microsleeps could no longer be judged as due to ''reckless driving'' in all cases. 3. Prevention strategies against sleepiness induced motor vehicle crashes would have to include efforts toimprove perception of SPS.

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Speech degradation with sleep restriction and recovery

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''Slurred speech'' with sleep loss has been anecdotally reported but difficult to quantitatively measure in the lab. Though few studies have examined the issue, Harrison and Horne (1997) found that intonation (i.e. pitch range and melody) was rated worse following 36 hours of total sleep deprivation. We assessed speech precision during sleep restriction and recovery. Eleven males and 13 females [mean (SD) age = 25 (6.5) years] were assigned to either an Extended [10 hours time in bed (TIB)] ($n = 12$) or Habitual [Mean (SD) = 7.09 (0.7)] ($n = 12$) sleep group for one week followed by one baseline night, seven sleep restriction nights (3 hours TIB), and five recovery nights (8 hours TIB). Throughout baseline and restriction at 0800, 1700, and 0300 and Recovery at 0800 and 1700, volunteers were recorded reading a standard passage. Landmarks based on acoustically abrupt speech events (as with consonant release for sounds p, t, k, b, d, g) and total voice-onset time (time to start phonation at the beginning of a syllable) are indicative of speech precision and were analyzed using non-parametric Fisher Sign Tests on combined sleep groups comparing the effect of day. Total number of landmarks and total duration of voice onset time decreased ($P < 0.05$) as a function of sleep restriction. This pattern persisted into recovery, and neither of the two speech variables returned to baseline. An effect of time of day was evident such that both landmark and voice onset time were worst in the morning testing sessions. This is the first study to quantify a deterioration in articulatory precision of speech with sleep restriction, with effects persisting into recovery. Thus, chronic sleep loss may disrupt the sensory and motor systems involved with speech production, impairing communication. The pattern of degradation is similar to that seen on cognitive performance tasks (Rupp et al., 2008), suggesting sleep restriction may have pervasive effects on a variety of functions, and that several nights of normal sleep may be needed to effect full recovery. These findings highlight the importance of sleep in situations in which precise communication is necessary, and suggest that speech recordings may be a useful tool in assessing sleepiness in real-world situations.

Instrumentation-Methodology

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Newly developed waist actigraphy and its sleep/wake scoring algorithm

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Objectives: Various types of actigraphy and their sleep/wake scoring algorithms have been developed and used in many sleep researches. Agreement rates of S/W determination between actigraphy and PSG have been reported 91.2–96.3%. The aim of this study was to determine an algorithm for a newly developed waist actigraphy (Lifecorder PLUS, Suzuken Co.Ltd) that is inexpensive (10000 yen = \$100 = €65 = £50) and available for large scale surveys.

Subjects and Methods: Young healthy volunteers (men 20, women 11, mean age 31.7 yrs, mean sleep efficiency 93.5%) who reported no major medical or psychiatric problems underwent one-night simultaneous monitoring of PSG and Lifecorder (LC) in a sleep laboratory. LC is able to assess exercise intensities of the longitudinal axis every 4 seconds that are successively converted to 10-step ascending scale data and to store the mode values every 2 min for over 2 months. We collected 2-minute-epoch data of sleep-wake status determined by PSG and exercise intensity measured by LC for 31 nights. Using exercise intensity at estimating epoch (X3), and at 4 min before (X1), at 2 min before (X2), at 2 min after (X4), at 4 min after estimating epoch (X5), we set a composite variate: $Z = A1^*X1+A2^*X2+A3^*X3+A4^*X4+A5^*X5$. Sleep/wake scoring algorithm for LC was determined by discriminant analysis to obtain maximum agreement rate between sleep (0)/wake (1) status judged by PSG and Z value (if $Z \geq 1$, 1; if $Z < 1$, 0).

Rusults and Discussion: We obtained the following sleep/wake scoring algorithm for LC: $Z = 0.635^*X1+0.427^*X2+0.701^*X3+0.805^*X4+0.718^*X4$. Overall agreement rate of S/W determination between LC and PSG was 86.9 ± 8.9 (SD) %. Sleep parameters judged by LC and PSG were as followed: total sleep time, 376.3 versus 401.2 min; sleep efficiency, 86.9 versus 93.5%; wake after sleep onset, 59.9 versus 29.2 min. Agreement rate for stage Wake, stage 1, stage 2, stage 3+4, and stage REM were 58.2%, 60.6%, 89.3%, 99.2%, and 90.1%, respectively. We could obtain high concordance rate for sleep/wake scoring algorithm for LC that is comparable to currently available actigraphy. Future study should be focused on availability of this device for patients with sleep disorders including insomnia, sleep related breathing disorders, and parasomnias.

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Normal values of polysomnography in children

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The purpose of our study is to develop normative Dutch polysomnography (PSG)reference values. We tried to delineate these values in a comprehensive group. Up to now normative values are known only in small groups of children and in most cases only for certain aspects of sleep. Retrospectively we obtained from our database all healthy children from the last six years. Included were all children in whom PSG was performed on request of the parents. Only those children were used for the database of normal values who already on beforehand were considered as probably normal en in whom sleep related respiratory disorders were excluded by the PSG itself and who did not use medication (N = 80, Age 2–16 years). No PSG was performed on a night when a child had fever, signs of respiratory or other infection. All measures were digitized by using commercially available PSG systems. In addition to central and occipital electrodes, EMG and EOG (as recommended in the Rechtschaffen and Kales rules), airflow with nasal pressure, chest and abdominal wall movement by strain gauges, snoring by piezo snore sensor, heart rate by electrocardiogram and saturation by pulse oximetry were measured in all children. Conventional criteria set of Rechtschaffen and Kales were used to extract the usual sleep variables. All data stratified for age, will be presented in detail. Our study was a cross-sectional analysis. Although this set-up is less useful in a study of the development of sleep, the data can still be screened for this purpose. For example: the sleep latency, stage 1 and 2 and REM duration increased with age as SWS diminished. This is in accordance with generally accepted (but only substantiated in a limited way in the literature) ideas on the development of sleep during the ages 2–16 years. The values found in the oldest group are very close to those thought to be normal for young adults. As a final remark, we think that normal sleep in children merits much more study, especially to clarify features of sleep at different ages and the relevance that those features have for health and development.

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Validation of the Dutch occupational impact of sleep questionnaire (OISQ)

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Background: Sleep problems are often under-diagnosed, but may have a profound impact on work performance. The purpose of this study was to validate the Dutch version of the Occupational Impact of Sleep Questionnaire (OISQ).

Methods: A total of 555 adults with a regular daytime job completed the OISQ. In addition, the also completed the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS) and the SLEEP-50 questionnaire.

Results: 443 surveys were included in the analysis (220 men and 223 women). The Dutch OISQ had high reliability (Chronbach's alpha = 0.96). OISQ scores correlated significantly with scores on the SLEEP-50 questionnaire, ESS, and PSQI ($P < 0.0001$). Mean score on the OISQ was 14.0. Poor sleepers (OISQ score around 20) had approximately double the OISQ score as good sleepers (OISQ score around 10), irrespective of this classification was based on self-ratings, PSQI-scores or SLEEP-50 scores.

Conclusion: The Dutch OISQ is a highly reliable and valid tool to examine the occupational impact of sleep.

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Arousability and insomnia: validation of the Italian version of the arousability predisposition scale (APS)

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Arousability has been described as a predisposing factor for insomnia (e.g. Lundh, Broman, 2000). Coren (1988) supposed that

insomnia could be predicted by a long term stable trait of hyper-arousability. In order to assess this hypothesis, the author developed a 12 items self-report scale (Arousability Predisposition Scale, APS) and found it to be a good predictor of sleep disturbances. The aim of this study was to validate an Italian version of the APS in a sample of 348 participants (61.0% F, 36.7% M) categorised on the bases of the self-reported quality of their sleep in three groups: good sleepers (GS), people with subthreshold insomnia (SI) and people with insomnia (PI). Participants were recruited among family physician patients from three central Italy areas. First it was conducted an explorative factorial analysis applied to the items of the APS (method Maximum Likelihood). Based on the scree test, one factor was chosen accounting for the 38.04% of the total variance. Two items with communalities lower than 0.25 were excluded. In order to confirm this 10-items monofactorial solution, structural equation models were conducted and results showed good indices of fit (RMSR = 0.064; CFI = 0.95; TLI = 0.93). The Chronbach's alpha indicated good reliability ($\alpha = 0.86$). The test resulted also valid as indicated by the differences on the total score among the three Groups ($F(2,328) = 24.84$, $P < 0.001$; GS: $M = 14.82$, SD = 6.31; SI: $M = 17.53$, SD = 6.97; PI: $M = 22.66$, SD = 7.13). Validity is also evidenced by high correlations with a subscale of arousability (.65) of another independent measure (Rome Arousability Scale, RAS, Violani et al. 2006). A brief and easy to use scale of Arousability as the APS has been found to be effective and predictive of insomnia also in the Italian version.

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Can assessment by pulse oximetry be useful outside the setting of sleep disordered breathing?

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Pulse oximetry is widely used in the assessment of suspected sleep apnoea based on visual analysis of the saturation trace. The accompanying heart rate trace may be assessed for increased heart rate variability suggestive of arousals due to the OSA or if the saturation trace is unremarkable, due to increased upper airway resistance or other sleep pathologies. We report here 6 patients with snoring and sleepiness who underwent overnight home pulse oximetry which demonstrated isolated increased heart rate variability (i.e. with an unremarkable saturation trace). This increased heart rate variability was confined to only a part of the night in each case. Later polysomnography showed the increased heart rate variability to be due to periodic limb movements in all six patients. Subsequent review of PSGs from the last 50 patients with PLMD seen at this centre showed the same phenomenon in most. **Conclusion:** Pulse oximetry may identify patients without obstructive sleep apnoea who should undergo PSG.

P420

Issues in digital signal recording and analysis: what does the sampling rate "do" ?

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A decade or two ago, the technical demands for recording sleep were considerable: ink ran dry, paper jammed, ... always at the precise moment you dozed off! Today, this technology is largely "hermetically sealed" in digital systems with users having little exposure to the principles which they are based on. This can foster misunderstandings of the requirements for adequate recording quality and misinterpretations of the scientific literature. For example: Why is the sampling rate meaningful? The faithfulness of "drawing" a signal using "individual dots" depends on the number of dots. One measure of faithfulness is the % error of reconstructed frequencies from the original signal (fo) sampled at rate (fs): = [(fo * (fo/fs)]/ (fo * 2 * 100). Another fs dependent measure is the % amplitude error of the sampled signal: = 100 * sin[pi/ (fs/fo)] The Nyquist sampling theorem describes artifacts (aliases) in sampled data when the signal contains frequency components greater than fs/2. Accordingly any such frequencies must be strictly removed using filtering (anti aliasing). All filtering comes with the penalty of distortions of both signal amplitude and phase over the range of "desirable" frequencies, and of spurious responses to transients. But as the sampling rate increases in relation to the highest frequency of interest, these signal distortions can be minimized. What then is a minimum acceptable sampling rate for the accurate frequency measurement of the sleep EEG ? If we are interested in waveforms up to 15 Hz, then a minimum sampling rate of 500 samples sec^{-1} is required to achieve an accuracy of 95%. Sampling at 100 s sec^{-1}, a 12 Hz waveform is reproducible to only 76% accuracy, effectively blurring the borders between alpha and sigma. In terms of spectral power, a 14 Hz spindle sampled at 100 s sec^{-1} results in >42% amplitude error. I encourage you to explore these concepts using your own examples! While these brief comments can only hint at some of the complexities involved-the implicit message here is that our field will benefit as technical practice standards and editorial guidelines evolve to better address these issues.

P421

Sleep stages and automatic overnight cortisol sampling

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Sleep and the hypothalamic-pituitary-adrenal (HPA) axis have a complicated relationship that is the subject of much research. Plasma cortisol is the end point which is often used to investigate the HPA axis response to stressful stimuli. An automated blood sampling machine has been used at Bristol University in the investigation of the rat HPA axis for a number of years (Windle et al. 1997) and the technology is now developed so that automated sampling can be carried out in humans. A peristaltic pump is linked to a computer and fraction collector designed to enable the collection of multiple samples of small volumes blood at specified time points over a long period of time i.e. 24 h. The objective of this study was to pilot the use of automatic blood sampling overnight for cortisol assay synchronized with polysomnography in 6 normal subjects, to assess the minute by minute effect of sleep stage on cortisol measures, and to compare plasma cortisol and salivary cortisol on awakening. Six healthy volunteers slept in the sleep laboratory. They were prepared for polysomnography (PSG) and had an indwelling cannula connected 'through the wall' to the sampling machine. Blood samples (1 mL) were taken every 10 min, synchronised with the PSG recording. Samples were later assayed for cortisol. Sleep was scored and the cortisol levels related to different sleep stages Cortisol levels fell during the first few hours of sleep and then showed a rise independent of sleep stage about halfway through the night, consistent with the literature. In addition, both awakenings and REM sleep tended to increase cortisol level. An increase in cortisol similar to that seen in the normal wakening response could be found from any stage of sleep and at any time of day/night. The automatic sampling method was reliable and effective in obtaining frequent cortisol samples without interfering with sleep. There was evidence of both circadian and sleep-stage-dependent regulation of night-time cortisol level.

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Wireless body area network for sleep staging

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As focus shifts towards portable and personalized health monitoring, body area networks are becoming increasingly important inside and outside the clinical environment. In this work, a Wireless Body Area Network (WBAN) is evaluated for sleep staging applications. The proposed system emerges from new technologies for autonomous wireless sensors developed at the Holst Centre. It relies on a proprietary ultra-low-power Application Specific Integrated Circuit (ASIC) for the acquisition of bio-potential signals. The wireless sleep staging prototype consists in a network of three low-power wireless sensor nodes, for the recording of 2 channels EEG, 2 channels EOG and 1 channel EMG. Each node is able to acquire and amplify two bio-potential signals, pre-process them and send them wirelessly to a receiver located within 10 meter range. Each node is miniaturized such that it can be fully integrated in a simple head-band. Clinical evaluation of the system is performed at the Vésale Hospital (Charleroi, Belgium), on a population of 12 healthy volunteers. Each volunteer is monitored for a complete night, during which the 5 physiological signals are recorded using the wireless BAN prototype and a reference system. The two systems are set-up in parallel, and all electrodes are duplicated. The recordings are manually analyzed to obtain the hypnograms for both systems, from which a set of features is extracted, including: latency of sleep stages, time spent in different sleep stages and number of microawakenings. These features are then used as input to the Wilcoxon signed rank test, in order to evaluate whether information from the two systems are statistically equivalent. First results indicate that the sleep stages inferred from the WBAN system correlate with those inferred from the reference system. This suggests that the proposed wireless sleep staging prototype has similar performances when compared to standard systems, while having the potential to enhance patient comfort and mobility.

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Pitfall of automatic sleep stage detection

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The major challenge in polysomnographic (PSG) analysis is finding the compromise between the speed and the accuracy of determination of sleep parameters. All laboratory PSG acquisition software incorporates algorithms for some level of automated scoring. However, for sleep stage scoring at least, the implemented set of algorithms is not accurate enough, and data are usually additionally scored by sleep technicians. In this study, we discuss results of automated stage scoring, generated with commercial software for Alice4 (Respironics, USA), and MEPAL (MAP, Germany) devices, on visually-scored test databases. Test databases contain 30s epochs of PSG signal from S1, S2, SWS and REM sleep stages, derived from 20 healthy male subjects, as well as epochs from 18 male patients with obstructive sleep apnea. All epochs are equally scored by 2 independent experts. Sensitivity and specificity of automatic detection for particular sleep stage and for particular subject group is discussed.

P424

Diffusion entropy analysis of sleep EEG

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Fourier spectral analysis of EEG has been almost synonymous with quantitative analysis of sleep for over three decades. From this perspective, the Fourier spectrum of stage 4 sleep, dominated by delta waves, suggests rather mundane quasiperiodic dynamics. On the other hand, much more complex spectrum of wake EEG is traced to intricate, presumably stochastic, fluctuations of wake EEG. We revisit the problem of randomness in sleep analysis using a recently develop technique of diffusional entropy (DE). In this approach, dynamics of an EEG recording are quantified by temporal evolution of a properly defined entropy. In particular, we study the growth of diffusional entropy of wake and stage 4 EEG. We find that in both cases, after approximately 1s, the initial growth of entropy is arrested. Interestingly enough, the saturation level of entropy for stage 4 sleep is two times larger than that of wake state. The high value of entropy may indicate predominantly stochastic character of delta waves in deep sleep. The existence of partial ordering in wake EEG underlies much lower values of diffusional entropy.

P425

Comparison of EEG data referenced to linked mastoid and average reference

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Introduction: EEG signals depend on the choice of the reference. In studies of topographical differences it is common to re-reference signals to an average reference. To examine the effect of this procedure we compared linked mastoid recordings with average reference data.

Methods: Baseline polysomnographic recordings (12 h time in bed) of 11 subjects from a previous study (Tucker et al. 2007; JSR 16, 170–180) were investigated. Four derivations (Fz, C3, C4 and Oz) were recorded against linked mastoid. Sleep stages were scored according to Rechtschaffen and Kales for 30-s epochs. EEG signals were re-referenced to the average of the four derivations. Power density spectra were determined for 30-s epochs (FFT, 4 s sub-epochs, cosine taper, 1 s overlap) and averaged across artifact-free vigilance states.

Results: Re-referencing to average reference reduced total power (0.75 to 30 Hz) in the waking, NREM sleep and REM sleep EEG at Fz, C3 and C4, but not at Oz. The fast spindle peak (>12 Hz) was reduced in all recordings. Six subjects showed in addition slow spindle activity (peak <12 Hz) in the frontal derivation that was independent of the reference. The alpha peak in the waking EEG was increased relative to the background activity in all derivations of the average reference data. Analysis with different number of electrodes contributing to average reference are ongoing.

Summary and Conclusion: The use of an average reference resulted in reduction of total power relative to the linked mastoid reference, except in the occipital derivation. Importantly, EEG topography differed between the two procedures, and rhythmic activity patterns were affected. The choice of reference is an important factor and caution is needed in the interpretation of topographical differences.

P426

Nonlinear dynamical analysis of EEG in sleep: a review of current literature

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Progress in the study of complex nonlinear dynamical ('chaotic') systems has led to the development of a variety of methodological tools for the analysis of nonlinear dynamics in time series data. Several of these methods have been applied to study changes in EEG and MEG dynamics related to perceptual processing, cognitive tasks, brain pathology (e.g. Alzheimer's disease), as well as states such as anaesthesia and sleep. The first published study to apply such measures on the human EEG had in fact involved sleep recordings (Babloyantz, Salazar, & Nicolis, 1985), and since then an increasing number of studies have used nonlinear analysis methods to investigate changes in brain dynamics during sleep. A summary of the underlying concepts and some of the methods used for nonlinear time series analysis will be presented, and the current literature of nonlinear sleep EEG research will be reviewed. Findings from these studies suggest that nonlinear measures of sleep EEG can provide additional information not accessible with linear (e.g. frequency-based) measures, and may also be better at discriminating between certain sleep stages (e.g. stages 1 and 2). Despite these promising findings however, there is a notable lack of studies applying nonlinear EEG methods to investigate sleep pathology; the potential use of these methods for the diagnosis of certain sleep disorders, and their role in understanding the brain dynamics underlying healthy and pathological sleep will be discussed.

Babloyantz, A., Salazar, J. M., & Nicolis, C. (1985). Evidence of chaotic dynamics of brain activity during the sleep cycle. Physics Letters, 111A (3), 152–156.

P427

Comparison of sleep parameters obtained by means of actigraphs and sleep-wake diaries

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Both actigraphy and sleep-wake diaries are methods often used in adolescents' sleep studies. However, there is a lack of data about their agreement in estimates of sleep parameters over longer period. Diary data on bedtime and wake-up time are regularly used to restrict actigraphic scoring. One alternative is to use actiwatch devices that allow for manual marking of these events. In this study we compared actigraphic and diary measurements of sleep in a group of adolescents over two weeks, using manually entered markers of bedtime and wake-up time for restriction of actigraphic scoring. During two consecutive weeks 21 secondary-school students (11 girls), aged 15–17 years, kept sleep-wake diaries and wore actigraphs (Actiwatch® Score, Mini Mitter Company, Inc). The participants marked the time of going to sleep and time of waking-up by pressing the marker button on actigraphs certain number of times. Good correlations between actigraphic and diary data were found both for schooldays (s) and weekends (w) for sleep onset ($rs = 0.98$; rw = 0.97), sleep offset ($rs = 0.96$; $rw = 0.95$), and sleep duration ($rs = 0.84$; $rw = 0.86$). Methods were not correlated for parameters of sleep latency, number and duration of night awakenings. Comparisons of mean values of sleep parameters between two methods showed somewhat different results for schooldays and weekends. On schooldays actigraphs indicated earlier sleep onset and earlier sleep offset than diaries. Both on schooldays and weekends actigraphs recorded shorter sleep duration, greater number and duration of night awakenings than diaries. In conclusion, actigraphs and sleep-wake diaries yielded similar estimates of sleep timing and sleep duration of adolescents over period of two weeks. In contrast, the methods did not agree in estimations of sleep latency and indices of night awakenings.

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P428

Assessment of a wireless dry headband technology for automatic sleep monitoring

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Introduction: A wireless headband system has been developed for monitoring sleep. The dry fabric sensors acquire EEG, EOG and EMG in a single channel from the forehead and transmit the data to a base station for processing automatically by a neural network. The aim of the current study was to compare sleep measures derived from polysomnography (PSG) and from the wireless system.

Methods: Three healthy female subjects (ages 25, 33 and 38) participated. Subjects were co-monitored in a sleep lab for two nights each by the wireless and standard PSG systems. Wireless system data were captured at 128 samples per second with a 12 bit A-D converter. PSG records were visually scored according to Rechtschaffen & Kales and compared to the automatically scored data from the wireless system. The following parameters derived from the records were assessed: Sleep onset latency (SOL) to 3 continuous epochs of sleep, wakefulness after sleep onset (WASO), total sleep time (TST), and sleep efficiency (SE).

Results: Preliminary findings suggest that sleep measures were reasonably similar for PSG versus the wireless system: SOL 26.6 ± 9.3 versus 26.8 ± 3.7 min, WASO 59.9 ± 12.7 min versus 69.8 ± 21.8 min, TST 326 ± 22.5 min versus 307.9 ± 30.1 min, SE $81 \pm 3\%$ versus $76 \pm 5\%$, respectively (Mean ± SEM).

Conclusion: Ongoing data collection and analyses are needed to further evaluate the ability of the wireless system to distinguish among sleep stages. Low cost, portable, easy to use, sleep monitoring technologies may have utility as research and educational tools.

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P429

Differences between spontaneous autonomic activation, PLM events and apnea events using the Watch-PAT00 channels

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Introduction: The Watch PAT (WP100) is an ambulatory device intended for diagnosis of obstructive sleep apnea (OSA), based on the PAT, oximetry and actigraphy signals. Since both sleep apnea and PLM events are associated with increased sympathetic activity we attempted to show differences in various parameters of the Watch-PAT channels.

Methods: 22 OSA suspected patients (21 M), aged 51 ± 11 with BMI 31 ± 6 underwent full night standard PSG recording in the sleep lab with simultaneous WP100 recording. Mean PSG scoring of AHI was 15 ± 14 and PLM index 17.8 ± 22. The related changes in signals recorded by the WP100 were quantified. The data was then compared between apneas, PLMs and spontaneous autonomic events which are defined by PAT amplitude decrease

coupled with increased pulse rate. Those changes in PLM and apnea events were normalized by the mean value of the changes in spontaneous events for each patient.

Results: PAT Amplitude Reduction :1.21 SE 0.048 1.44 SE 0.067* 1 SE 0.027* Increase in heart rate:1.47 SE0.053 1.604 SE0.073* 1 SE 0.029*, Time Difference Between Peak pulse Rate and Peak PAT Amplitude:2.4 SE 0.17 S −0.15 SE 0.22 S* −1.23 SE 0.06 * S. Actigraph Normalized Energy (a measure of the amount of movement):2.035 SE 0.39 1.764 SE0.54 1 SE0.22*, Time Between Max PAT Amplitude And Movement: 4 ± SE 0.30 S 6 SE 0.39 S* 4 SE 0.102 S, All values are for PLM apnea and spontaneous respectively. (* stands for significance $P < 0.05$ compared to PLM). SE is the mean Standard Error provided by Matlab Multcompare (ANOVA)

Conclusion: Utilizing indirect physiological signals such as general movement (actigraphy), pulse rate and neuro-vascular signal (PAT),we found that apnea and spontaneous autonomic activation are morphologically different from PLM. The autonomic system reacts in a hierarchic way to apnea, PLM events and spontaneous modulation.

P430

A new method for detecting body position during sleep

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Introduction: The gold standard to measure body position in a sleep lab is a video recording of the patients' position. For the ambulatory setting, the method most commonly used is an electromechanical body position sensor made of moving elements that switch positions attached to the patient chest. We have developed a new method based on a 3-axis accelerometer in a small housing driven by a miniaturized electronic circuit. The accelerometer measures the acceleration in each axis and a small microprocessor integrated in the device transforms the projection of the gravity in the direction of the body position in a 3 axis system. From the gravity vector the body position is computed with high precision.

Methods: Eight patients were tested awake while maneuvering positions in a documented controlled manner ($n = 5$) and during sleep in a sleep lab ($n = 3$) with simultaneous recordings of the tested device and video-camera. An epoch by epoch comparison of the position was performed between the two methods.

Results: The total agreement between the tested device and video-camera was 82% for a total accumulated 2798 epochs in the sleep lab and 512 epochs in the controlled maneuvering. The agreement for each position was 78%, 79%, 87%, 55% and 90% in the sitting, left side, right side, prone and supine postures respectively.

Conclusion: We conclude that the new sensor can detect the five basic postures with a higher accuracy than the conventional sensor (for which we recently reported less than 70% total agreement). Future studies should test the ability to measure mixed ("in between") positions that are undetectable with the standard sensors.

P431

Assessment tools for sleepiness: advantages of simultaneous measurement techniques

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Investigations on physiological, neuropsychological and behavioural correlates of sleepiness have frequently been accomplished. Considering sleepiness is not a unitary concept that can reflect essentially different states (Cluydts et al. 2002), the single use of instruments or subsequently measure by test batteries leads to conflicting results. The parallel registration of behavioural observation (yawning, oculomotor activity, eye closure, head movements, actigraphy), electrophysiological measures (wake-EEG, microsleep episodes, polysomnography, cerebral evoked potentials) and performance tasks (reaction times, errors, missing reactions, time on task decrements) is necessary to gain more valuable data. In many studies on sleepiness, reaction time measurement systems-based on PC registration-are a common instrument to determine attention, vigilance and cognitive skills. For our purpose we implemented Presentation®, a stimulus delivery and experimental control software system, developed by Neuorobehavioral Systems Inc. Presentation was designed for behavioural and physiological experiments that collect fMRI, ERP, MEG, reaction time or electrophysiological data. It provides the best possible timing accuracy and timing verification on standard hardware and is completely programmable by PC. We present some technical solutions, how established sleepiness assessment instruments for sustained attention-like the Psychomotoric Vigilance Task and the Macworth Clock-can be simulated with Presentation. This allows testing of performance under strictly standardized conditions in connection with EEG and video recording at the same time. Some case reports will be presented to illustrate the specific properties of these united measurement techniques in sleep deprived subjects. These examples reveal the advantages of simultaneous recording of performance measures, behavioural observations and EEG data. It is of great value to bring together the diverse measurement methods in one experimental design to gain more detailed and precise findings about the different aspects of sleepiness. Furthermore, using Presentation based tests, the same technique or paradigm can be used in EEG as well as in fMRI studies.

P432

Detection of sleep stages using peripheral arterial tone (PAT) signal

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Introduction: We previously described algorithms that differentiate between wake and sleep and detect REM sleep stage using Arterial Tone (PAT) and actigraphy. We further developed the algorithms for full sleep stages stratification that can now differentiate between light, deep, REM and wake stages

Methods: 49 (40 males) subjects undergoing simultaneous PSG and PAT recording were used as a training set for the algorithms development. A separate set of 54 subjects (38 males) was used for validation. Different characteristics of the PAT amplitude and the pulse rate in the time and frequency domains were extracted. The main characteristics in the frequency domain were derived for frequency ranges corresponding to respiratory, baro-receptor, thermoregulation and hormonal ranges: 0.4–0.15 Hz (HF), 0.15–0.04 Hz (LF), 0.04–0.015 Hz (VLF) and 0.015–0.005 Hz (ULF) respectively.

Results: Overall sensitivity, specificity and agreement of the automatic algorithm to identify standard 30sec epochs of light and deep sleep stages were 66%, 89%, 82% % and 65%, 87%, 80% for the training and validation sets respectively. The validation set showed a very little degradation compared to the training set. Together with the already existing algorithms for REM and wake detection we propose a near-full sleep stages detection based on the PAT and Actigraphy signals only. The total agreement of detecting the 4 stages (wake, light, deep, REM sleep) is 68% which is slightly below the reported inter-scorer variability of 69.3%. The Kappa Cohen coefficient is 0.48 (moderate).

Conclusion: The PAT signal coupled with actigraphy signal gives a reasonable accuracy in detecting sleep stages.

P433

Predicting aircraft noise induced changes in sleep structure with Markov models

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Introduction: This investigation quantitatively assessed the effects of the introduction of a noise-free period at Frankfurt Airport between 11 pm and 5 am on sleep structure.

Methods: A six state (Wake, S1, S2, S3, S4 and REM) Markov state transition sleep model was built. Transition probabilities between states were calculated for both noise-free and noise conditions with autoregressive multinomial logistic regression based on polysomnographic laboratory studies, where 125 healthy subjects were investigated for 13 consecutive nights. First-order Monte Carlo simulation trials were performed for modelling a noise-free night and three noise scenarios: (1) traffic at Frankfurt Airport on 16 August 2005, (2) as (1), but flights between 11 pm and 5 am cancelled and (3) as (2), with flights between 11 pm and 5 am from (1) rescheduled to periods before 11 pm and after 5 am.

Results: The results of the models indicate that there will be a small benefit for airport residents compared to the current situation without a ban of air traffic in terms of sleep structure even if all traffic is rescheduled to periods before 11 pm and after 5 am (average time spent awake −3.2%, S1 −4.6%, S2 −0.9%, S3+3%, S4+9.2%, REM+0.6%, number of sleep stage changes −2.5%). This benefit is likely to be outweighed by the increase in air traffic during shoulder hours, especially for those who choose to or have to go to bed before 10:30 pm or after 1 am.

Conclusion: Alternative strategies might be necessary to both guarantee undisturbed sleep of airport residents and to minimize economic and legal disadvantages accompanied by a ban of air traffic between 11 pm and 5 am. The models developed in this investigation may serve as a valuable tool for optimizing air traffic patterns at airports, and therefore guide political decision making.

P434

Real-time automatic measure of drowsiness based on a single EEG channel

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Introduction: In modern societies, lack of sleep is often due to an increase of work pressure and abnormal work schedules and associated to increased daytime drowsiness. Electroencephalography (EEG) is a widely recognized clinical measure for drowsiness monitoring. However, this technique remains invasive, complex and difficult to implement in the working environment. Therefore, the simplification of EEG recording was our primary goal. The purpose of this study was to develop an automatic algorithm for the online measure of drowsiness based on a single channel recording.

Method: 19 volunteers (aged 30 ± 6 years, 12 women) were monitored during 2 h while driving a car-simulator. Recorded channels included EEGs (C3, O1, P3, Fz referenced to A2, bipolar CzPz, C4O2), EOGs (vertical and horizontal leads), and ECG. The Objective Sleepiness Score (OSS) [1] stood for the visual reference. This scale defines 5 states of drowsiness that can be merged to define 2 or 3 different states of drowsiness. The developed algorithm analyzed the single EEG signal CzPz, without any expert input. The real-time analysis was simulated by providing the algorithm with incremental EEG data. The algorithm was tuned using data from 14 subjects and then evaluated using data from 5 other subjects. The evaluation was assessed by comparing automatic and visual scoring on a 20-second epoch-by-epoch basis.

Results: On the evaluation data, agreements between OSS and automatic analyses obtained 89%, 87% and 75%, when scoring drowsiness on 2, 3 and 5 states respectively. They reached 94%, 92% and 77% respectively on the whole cohort data.

Conclusion: This study shows that the information contained in a single EEG channel is sufficient to obtain a diagnosis of drowsiness similar to the one obtained by a visual approach examining several EEG and EOG traces. A follow-up study on a larger cohort is underway to affirm these first results.

Acknowledgment: Grant This work was supported by the French Defense DGA n°0534061004707565.

[1] Muzet A, Pebayle T, Otmani S, Peters B, Nikolaou S, Bekiaris E. Preventing driver drowsiness at the wheel: can steering grip sensor measurement contribute to its prediction? Proc. of 4th Eur. Congress and Exhibition on Intelligent Transport Systems and Services, Budapest, 24–26 May 04.

P435

Exploring the determinants of sleep duration: an analysis of time use diaries utilizing multilevel models

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Introduction: Despite the increasing number of time use surveys in Western societies, there have been few attempts to analyze such studies to investigate the relationship between sleep duration and sociodemographic as well as lifestyle factors. Furthermore, the few existing studies analyze sleep duration only at the individual level failing to take into account that the multi-stage sampling followed in most time use surveys leads to dependent observations that render single-level inferential procedures unsuitable.

Aims and Data: This paper follows a multilevel modelling approach in order to analyze time use data to investigate the determinants of sleep duration. Multilevel modelling is a statistical methodology for analyzing data with a hierarchical structure considering different levels as distinct sources of variability. We analyze data from the ONS 2000 UK Time Use Survey which contains a representative sample of individuals over 8 years old that completed time use diaries over two days, a weekday and a weekend day (n of level 1 = 19898). The survey has a strict hierarchy structure with individuals (n of level 2 = 10381) nested within households (n of level 3 = 4919) and households nested within areas (n of level 4 = 591). We develop a four-level model predicting individuals' sleep duration that takes into account the contextual effects of the family and the area where an individual lives. A series of sociodemographic and lifestyle factors is included in our model that makes use of fixed and random effects coefficients.

Results: Our null random intercepts model finds significant variability in sleep duration between individuals (ICC: 13.8%*), between households (ICC: 13.9%) and between areas (ICC: 0.8%). The results point towards the significance of the context on the determination of an individuals' sleep duration which has hitherto been neglected by sleep analysts.

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MORPHEE: an internet patient file with polysomnographic and CPAP devices automated data transfer

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Introduction: MORPHEE is an internet network for medical data of sleep patients aimed at sharing patient care among sleep health professionals in order to achieve good clinical outcomes. It has included more than 1600 patients since its opening in 2006 in the Paris area.

Objective: Diagnosis (polysomnography) and therapy (Positive Airway Pressure) PAP devices differ from a manufacturer to another and use different output data formats. Improving data management will help clinicians and health care providers to assess compliance, evaluate therapy efficiency and to determine appropriate interventions. Thus, there is a need to standardize these reports and to allow their automated transfer and processing into a secured web based server.

Methods: The polysomnographic analysis software (CIDELEC) exports the results in XML CDAR2 format in full and summarized formats. The therapy devices (RESPIRONICS) export the technical data, settings and compliance results in a standardized XML format too. These files are automatically sent via https transfer into the corresponding patient file. The data are then incorporated in the structured patient file which is operated and hosted by SANTEOS. The securely shared access is open to affiliated professionals via a simple internet explorer. The exported data include standardized results and additional optional data for each device. These internet applications are suited for all sleep data analysis software and therapeutic devices following standard XML format (HL7 rel2).

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Epworth Sleepiness Scale: clinical and polysomnographic Determinants

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Although daytime sleepiness is commonly associated with obstructive sleep apnoea (OSA), the relationship between OSA severity and subjective sleepiness has been documented elusive. This study aimed to identify clinical and polysomnographic determinants of subjective sleepiness among patients suspected of having OSA. A sleep clinic-based sample of 915 patients was interviewed with a structured questionnaire and underwent diagnostic overnight polysomnography. Subjective sleepiness was quantified by Epworth Sleepiness Scale (ESS). Excessive daytime sleepiness (defined as ESS score >10) was present in 38.8% of patients. In multiple linear regression analysis, respiratory disturbance index [used to define (whenever respiratory disturbance index was >5) and quantify OSA], depression and diabetes were the most important determinants of ESS score accounting for 16.5%, 10.6% and 5.6% of its variability, respectively. Chronic obstructive pulmonary disease (COPD), stroke, heart disease, alcohol use and body mass index were less important determinants of ESS score explaining 0.5–2.8% of its variability. In conclusion, OSA should not be considered the sole potential cause of increased subjective sleepiness in patients suspected of having OSA. Primarily depression and diabetes, but also COPD, stroke, heart disease, alcohol use, and increased body mass index may contribute to increased subjective sleepiness.

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Epworth sleepiness scale discriminiation thresholds reported to sleep parameters

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Discrimination threshold of Epworth Sleepiness scale is frequently defined as a value $>=10$. This seems to be in agreement with the Johns findings (1) But a second cutting point of 14 was evoked in the same paper. The mean of our work consist to iteratively determine the best cutting edge of ESS in regard with objective sleep parameters.

P439

Detection of sleep and wake stages based on jaw movement analysis

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The aim of the study was to evaluate mandible activity as an alternative method to wrist actimetry in order to differentiate sleep from wake states. Mandible activity sensors measuring the space between the anterior edges of upper and lower jaws were used. Implemented in a portable monitoring system of type 3 (PM3, Somnolter® NOMICS, Liège, Belgium), they were primarily adopted to detect breathing effort during sleep. In order to improve the accuracy of the monitoring device, specific signal features (amplitude and wavelet-based complexity measure of movements) corresponding to wake or to sleep states were defined as recognition patterns for an automatic analysing.

Method: The distance-meter is composed of 2 small magnetometers fixed, parallel to each other, on the midline of the face; one on the forehead and one above the chin. It allows a continuous recording of the elevations and depressions of the mandible. After storage, the digitalized signal was submitted to automatic analysis. An algorithm was built from a previous database of a set of different awake and asleep subjects. Consecutive unselected patients entered the study between December 2007 and February 2008. Full-night polysomnography and mandible activity recordings were realized in the Sleep Center of the University hospital. The Total Sleep Times obtained by manual scoring (TSTpsg) and by automated mandible activity analysis (TSTjaw), between lights-off and light-on were compared. Linear correlation analysis and two-tailed student t test for paired data were applied.

Results: Twenty patients-3 females and 17 males-mean age 53 year-old (SD $\pm$ 11,6; range 32–73) provided the set of data. The primary diagnoses were OSA syndrome (11 patients), insomnia (8), and Restless Leg Syndrome (1). A linear regression analysis between TSTjaw and TSTpsg led to the equation TSTjaw = 1.66+0.61 TSTpsg ($r = 0.65$; $P = 0.0021$). The p value of the Student t test was 0.0078 for $t = 2.97$. The 95% confidence interval ranged from 0.26 to 1.49.

Conclusions: An automatic processing of mandible movements appears as an acceptable means in order to assess sleep and wake period times in human beings, in different pathological situations.

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Who's training the techs: a look at the United States model

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Recently, the Board of Registered Polysomnographic Technologists (BRPT), the American Academy of Sleep Medicine (AASM) and the American Association of Sleep Technologists (AAST) have combined forces to create a trained sleep technologist. This includes learning modules provided by the AASM and/or other training programs up to and including an Associate's Degree in Polysomnographic Technology. The history of how this happened and the value of a technologist with formal training are part of this discussion. This represents a change from on-the-job training to formal programming.

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Evaluation of a new simplified polysomnographyc system for the diagnosis of sleep disordered breathing

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Introduction: Full Nocturnal Polysomnography (PSG) is the gold standard to diagnose Sleep Disordered Breathing (SDB). However, given the high prevalence of SDB new portable diagnostic devices are needed. OBJECTIVE: To compare the sleep variables and respiratory events measured with PSG and with a portable cardio-respiratory polygraph SOMTE (PSG-PS). The recording of sleep variables in the PSG-PS is limited to only two channels (EEG and EOG).

Methods: Nocturnal PSG and PSG-PS were simultaneously performed in 37 adult patients with clinical symptoms of SDB. Data were scored by two independent observers. Paired *T*-test was used to compare sleep parameters and respiratory events. Sensitivity and specificity were calculated for 3 cut-off points (>5, >15, >30) of the AHI. To determine the agreement between the two scorers the Kappa coefficient was calculated.

Results: Thirty-seven adult patients (24 men; mean age 55,1 $\pm$ 11,5, body mass index 27,3 $\pm$ 3,9 and BMI 28,9 $\pm$ 6,1, Epworth 10 $\pm$ 8,0. The mean duration of recordings were 442,4 $\pm$ 46 min. There were no differences between PSG y PSG-PS in sleep efficiency (1stobserver, PSG: 68,3 $\pm$ 19,0, PSG-PS:68,4 $\pm$ 19,7 and 2ndobserver, PSG: 69,1 $\pm$ 18,5, PSG-PS:71,0 $\pm$ 17,6), REM sleep time (1stobserver, PSG: 40,5 $\pm$ 29,3, PSG-PS:43,9 $\pm$ 29,5 and 2ndObserver, PSG: 41,6 $\pm$ 26,8, PSG-PS:40,3 $\pm$ 25,3), NREM sleep time (1st-observer, PSG: 255,7 $\pm$ 74,4, PSG-PS:253,2 $\pm$ 78 and 2ndobserver, PSG: 261,0 $\pm$ 75,6, PSG-PS:270,9 $\pm$ 76,9) and AHI (1stobserver, PSG: 20,5 $\pm$ 18,0, PSG-PS:17,7 $\pm$ 16,6 and 2ndobserver, PSG: 19,4 $\pm$ 16,5, PSG-PS:16,1 $\pm$ 14,4) For a cut-off point of 5, PSG-PS showed a sensitivity and specificity, 93,3% and 86,7% for 1stobserver and 87,5% and 100% for the 2ndobserver. For a cut-off point of 15, for 84,2% and 100% for 1stobserver and 78,9% and 94,4 for the 2ndobserver. For a cut-off point of 30, 55,6% and 96,4% for 1stobserver and 66,7% and 100% for the 2ndobserver. The kappa coefficient for the AHI was 0,78 for PSG and 0,61 for PSG-PS.

Conclusion: This preliminary results suggest that PSG-PS may be a useful system for the diagnosis of SDB.

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Sleep classification according to AASM and Rechtschaffen & Kales: effects on sleep scoring parameters

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Objective: To investigate differences between visual sleep scorings according to the classification developed by Rechtschaffen and Kales (R&K, 1968) and scorings based on the new guidelines of the American Academy of Sleep Medicine (AASM, 2007).

Methods: This report is based on the analysis of 72 all-night sleep recordings of healthy subjects and patients (38 females and 34 males) aged between 21 and 86 years. Polysomnographic recordings were scored visually according to the R&K and AASM rules by experienced sleep scorers. Descriptive data analysis was used to compare the resulting sleep parameters.

Results: While sleep and REM latency, total sleep time and sleep efficiency were not affected by the classification standard, the time (in minutes and in percent of total sleep time) spent in sleep stage 1 (S1/N1), stage 2 (S2/N2) and slow-wave sleep (S3+S4/N3) differed significantly between the R&K and the AASM classification. While light and deep sleep increased (S1 versus N1 (+10.6 min./+2.8%): $P<0.01$; S3+S4 versus N3 (+9.1 min./+2.4%): $P<0.01$), stage 2 sleep decreased significantly according to AASM rules (S2 versus N2 (-20.5 min./-4.9%): $P<0.01$). Moreover, wake after sleep onset was significantly prolonged by approximately 4 min ($P<0.01$) according to the AASM standard. Interestingly, the effects on stage REM were age-dependent. No effects of sex and diagnosis were observed.

Conclusion: The study shows significant and age-dependent differences between sleep parameters derived from conventional visual sleep scorings on the basis of R&K rules and those based on the new AASM rules. Thus, new normative data have to be established for the AASM standard.

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A novel interactive dual-task performance test of alertness designed using open-source gaming software: usability design and proof-of-principle

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Goal: Assessment of alertness while simultaneously performing two differing repetitive tasks is relevant to many current ergonomic activities affected by sleep pathologies. The goal of this project was to develop an interactive test of alertness based on open-source gaming software that could monitor for lapses in selective attention while performing a visuospatial psychomotor task.

Process: A 10 m gaming task ("Tetralert", based on the game Tetris) was instrumented to record alertness-related parameters such as reaction times and lapse percentages for a simultaneous numeric go-no-go task, consisting of an irregularly occurring (every 3–10 secs)numeric target. A data analysis and visualization package was developed to enable rapid visualization of test results. Trial tests were performed and user feedback was gathered in a usability

design process to modify and/or add various task functionalities. Proof-of-principle data was then collected for 6 healthy subjects (3M,3F, mean age = 37) with no underlying sleep pathologies, all tested between 15:00 and 17:00.

Results: (mean and standard deviation shown) Reaction Time- Visuospatial (RT-V) = 1.15s ± .67s Reaction Time-Selective Attention (RT-A) = 1.22s ± .55s Lapse Percentage: 3.46% ± 3.01%

Conclusions: Via usability design process, we were able to develop an interactive test of alertness for assessing dual-task neuroergonomic performance. We speculate that the low percentage of lapses in normals suggests this may be a useful measure of selective attention worth comparing to patients with sleep disorders.

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Improvement in polysomnographic sleep quality with a mattress cooling device

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Introduction: Ambient temperatures above (Libert. Sleep 1988;195) and below (Haskell. EEG Clin Neurophysiol 1981;494) the thermoneutral range disrupts human sleep suggesting that microclimate manipulations may affect sleep.

Methods: Randomised crossover trial to evaluate the effects on sleep quality of a novel mattress topper, capable of bed cooling (Morphy Richards Ltd, Mexborough UK). Recruits included insomniacs ($n = 4$) and normal sleepers ($n = 8$). The device consists of a free-standing, external air-conditioning unit which circulates temperature-regulated air through conduits within the topper. Subjects were acclimatised to polysomnography on a baseline night, before undergoing two further nights of 22-channel polysomnography under conditions in randomised order; one of ambient air circulated through the mattress topper, and one of circulated air cooled to 3–5 °C below room temperature. After each night, subjective ratings of mood (UWIST mood adjective checklist) and sleep satisfaction (five-point Likert scales of sleep quality, refreshment, comfort and noise) were completed. Polysomnography was scored blind by registered technologists, and both objective and subjective variables from ambient and cooled nights were compared by Wilcoxon tests.

Results: Ten of 12 subjects (4F, mean age 36 ± SD 8 yrs, body mass index 28 ± 7 kg m^{-2} and Epworth sleepiness score 4 ± 3 points) completed the three-night protocol. Five subjects underwent the cooled condition first and five the ambient condition. Of 12 polysomnographic outcome variables, three were significantly improved in the cooled bed condition; total sleep time (cooled versus ambient median 432 versus 383 mins; $P = 0.04$), sleep efficiency index (83 versus 74%; $P = 0.05$) and arousal index (23 versus 27 per h slept; $P = 0.02$). No significant differences in subjective ratings were noted.

Conclusions: This preliminary study of mixed subjects with and without sleep difficulties shows that a bed-cooling device objectively improves sleep quality.

P445

Automatic sleep classification according to the AASM standard: validation study of the AASM version of the somnolyzer 24×7

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Introduction: In 2005, we presented the first validation study of the Somnolyzer 24×7 for the classification of sleep according to Rechtschaffen and Kales based on 286 PSGs from 94 healthy subjects and 49 patients with sleep disorders (Anderer et al. Neuropsychobiology 2005;51:115–113). The validity of this R&K version was recently confirmed by Svetnik et al. in 164 PSGs from 82 subjects in a clinical trial using zolpidem in a model of transient insomnia (Sleep 2007;30:1562–1574). In June 2007, we adapted the Somnolyzer 24×7 to score according to the new AASM rules (Iber et al. 2007; American Academy of Sleep Medicine) and performed thereafter a validation study presented in this paper.

Methods: The validation study is based on the analysis of 72 PSGs from the SIESTA database (56 healthy subjects, 16 patients, 38 females, 34 males, aged between 21 and 86 years). PSGs were scored visually according to the AASM rules by experienced sleep scorers after a two-day training symposium on the new rules and automatically by the AASM version of the Somnolyzer 24×7 with subsequent structured quality control. Visual scorings as well as Somnolyzer quality controls were performed independently by at least two experts, out of 8 sleep experts from 4 sleep centers.

Results: In the quality control process, the two sleep experts corrected 4.2% and 4.1% of the automatically assigned epochs, resulting in a reliability between two Somnolyzer-assisted scorings of 98% (Cohen's kappa: 0.97). In contrast, the reliability between the two visual scorings was 82% (Cohen's kappa: 0.76). The agreement between Somnolyzer 24×7 and first scoring was 81% (kappa: 0.74), between Somnolyzer 24×7 and second scoring 81% (kappa: 0.74).

Discussion: The validation study of the AASM version of the Somnolyzer 24×7 revealed an overall epoch-by-epoch agreement comparable to that published for the R&K version (80%, kappa: 0.72) and most importantly comparable to the inter-rater reliability between two human experts. Two Somnolyzer-assisted scorings, however, resulted in an inter-rater reliability close to 1.

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Sensitivity and specificity of visual and automatic detection of cortical arousals in sleep

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Introduction: Cortical arousals in sleep are important markers of sleep disruption and/or physiological indicators of the regulation of the sleep process. In the new rules for the scoring of sleep, EEG arousals define the end of a period of stage N2 sleep (Silber et al. 2007, American Academy of Sleep Medicine) and thus a valid and robust automatic identification method is urgently needed.

Methods: In the present study, arousals were visually identified independently by two experts and automatically detected by Somnolyzer 24×7 in 60 PSGs from the SIESTA database (53 healthy subjects, 7 patients, aged 21 to 86 years). The automatic algorithm compares the pattern of 9 EEG frequency bands between a 10-s baseline and a 3-s test window by a series of linear discriminant analyses to identify abrupt and transient (between 3 and 30 s) changes in EEG frequency. The prior probability for an arousal event is increased if chin EMG amplitudes increase, and reduced if the baseline EEG activity resembles wake EEG or a probable sleep spindle is identified in the test window. Validation was performed on a 30-s epoch basis. Since both scorers were equally experienced sleep experts, detection by the automatic

algorithm was assigned as true positive if at least one expert had marked an arousal in the same 30-s epoch.

Results: Epoch-by-epoch comparisons between the experts resulted in a sensitivity of 72.4% with a specificity of 95.6%. The comparison between Somnolyzer and expert scorings showed a sensitivity of 79.9% with an equally high specificity of 96.3%. Interestingly, the automatic scoring showed higher performance in all sleep stages, but specifically in slow-wave sleep (70.8% sensitivity and 99.4% specificity for visual scorings; 92.3% sensitivity and 98.7% specificity for automatic scorings).

Discussion: The observed inter-rater reliability in the present study is comparable to previous reports (Bonnet et al. 2007 J Clin Sleep Med 3:133–145). By varying the prior probability for the occurrence of arousals, the automatic detection system can be optimized for the purpose of the study (maximal sensitivity or specificity or equal weights for sensitivity and specificity).

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Multiple indicator prediction of sleepiness: implications for driver fatigue warning systems

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Driver fatigue is an established risk factor for vehicle accidents on the road. The present study summarizes predictive models of sleepiness in a HI-FI moving base driving simulator (Volvo 850) using the best subset of a large number ($n = 33$) of candidate physiological and behavioural indicators of sleepiness. The study included 14 randomly selected, healthy drivers that were examined during a baseline condition with normal (8 h) sleep and a partial sleep condition with 4 h sleep. Each condition included 6 one-hour driving session evenly distributed across the 24 h-day. During the drive EEG, EOG and driving performance were continuously collected and sleepiness ratings were obtained with 10-minute interval using the Karolinska Sleepiness Scale (KSS, 1 = very alert, 9 = very sleepy). Prior to analyses, 10 min means were calculated for the indicators and KSS was scored as a dichotomous variable indicating severe sleepiness (KSS $\geq$ 8). Data was analysed using General Estimation Equations (GEE), Generalized Linear Mixed Model (GLMM) and a Mixed Latent Class Model (MLCM) using a logistic link function. Univariate mixed effect logistic models were used to pick three of the best indicators for further analysis. The predictors described the amplitude/peak closing velocity of eye blinks, blink duration and lane drifting calculated as the standard deviation of lateral position ($P < 0.001$). The GEE predicted 81% of the observations, the GLMM 83% and the MLCM with 4 classes 85% ($P < 0.001$). The main difference between the models was the distribution of errors between subjects. The GEE showed zero sensitivity for 36% of the subjects but the same estimate fo GLMM and MLCM was only 7%. The sensitivity for GLMM was 47% and for MCLM 58%. The latter was chosen as the final model. Specificity was estimated at 93%. The results suggests that it is possible to detect close to 60% of severe sleepiness events from eye blink and driving performance data while maintaining a low false alarm rate (7%). This approach relies on statistical models that explicitly models individual differences within a mixed model approach that classifies the subject into one of four possible groups.

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Dissociable effects of recent and enduring sleep quality on reported everyday affect and function: a structural equation modeling approach

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Introduction: Surveys reporting sleep quantity and sleep quality frequently make claims that imply a causal relationship between poor sleep and everyday functioning. Few of these studies incorporate formal measures of sleep, cognitive function or psychological well-being, and fewer still attempt to control for the contaminating effects current mood and recent sleep may have on how people regard the effects of enduring sleep patterns on well-being and performance. None use statistical techniques which are capable of distinguishing between mere associations and truly causal relationships. Here we report an attempt to address these issues in an extended survey of almost 2000 British residents.

Method: The self-reported long-term sleep quantity, quality, and difficulties, recent sleep quality, current mood and long-term emotions (Positive And Negative Affect Schedule), psychological well-being (General Health Questionnaire), and cognitive function (Cognitive Failure Questionnaire), of 766 males and 919 females (aged between 12 and 91 years) were modeled using Structural Equation Modelling (SEM).

Results: As might be expected, reports of current and longer term affect and sleep were closely correlated. However, the modeling approach adopted here enabled us to quantify the independent effects of long-term sleep reports on self-reported long-term psychological well-being and cognitive function. These were greater than their indirect effects, as mediated through current mood and recent sleep. People with long-term sleep problems were far more likely to report poorer cognitive functioning and mental health, even when the effects of short-term sleep quality and current were controlled. These effects were similar for men and women.

Conclusion: Persistent sleep problems contribute to poor long term psychological well-being and cognitive function and these effects are in part independent effects of current mood and sleep.

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Sleep onset detection using sequential spectral analysis

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The wake-sleep transition is not clear-cut but characterised by a period of gradual change operating at every level of biological organisation & involving a progressive reduction in the arousal level, until the attainment of definite sleep. Along with EEG changes, studies have shown that there are also gradual physiological, cognitive & behavioural changes. So where on the arousal continuum does the moment of sleep onset (SO) occur? There is no clear consensus on this point. For some, based on the criterion of alpha reduction, SO is defined as the onset of stage 1. The majority, however, situate SO at the first appearance of a sleep spindle or a K-complex, i.e. at the start of stage 2 (S2). Both definitions have the limitation of relying solely on a visual appraisal of the EEG with the possible subjective error that this may entail, added to the random variation in the time of appearance of these markers. A more precise way to pinpoint SO is to use the information contained in the spectral power time courses, particularly sigma (11–16 Hz). Although all frequencies in the range 1–28 Hz show gradual changes in power across the wake-S2 interval (De Gennaro et al. 2001), the sigma band shows an abrupt rise at S2 onset, giving a more objective criterion,

agreeing with that described by the neuronal transition probability (NTP) model. Using a 20s resolution, the sigma time course was obtained from the start of the recording to the end of the first episode of S2 in 20 healthy subjects aged 20–30 y. The power gradient was fitted over 1 min intervals (3 epochs) starting at each successive epoch. When this gradient reached a maximum (preceding the first peak in sigma power) it was extrapolated back to the horizontal line representing the mean sigma level preceding the start of the sigma rise. The crossing time gives the best estimate of the moment of SO. Preliminary results show that SO calculated in this way is on average quite close to the visually detected SO, with the former lagging the latter by 42 ± 16s. To conclude, automatic detection of SO is more reliable, more precise and less time consuming than visual appraisal and can be easily extended to detect NREM sleep onset in the later cycles. This is a considerable asset when modelling sleep structure.

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Automatic sleep stage detection pitfall

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The major challenge in polysomnographic (PSG) analysis is to find the compromise between the speed and accuracy of sleep process description. Commercial software for PSG analysis is designed in such a way to allow real-time analysis of data, a preferred option if there is a technician on-site. However, when post-acquisition analysis is considered, and higher accuracy is demanded, manual scoring is a must following the Guidelines for Accreditation of the Sleep Centre, and the implemented sets of algorithms are not satisfactory.In this study we discuss results of automated stage scoring, generated with commercial software for Alice4 (Respironics, USA), and MEPAL (MAP, Germany) devices on our visually-scored test databases built upon hardware/OS/application interface: DualCore processor, 2 GB RAM/Linux/MATLAB which shortens the computation time of post acquisition analysis from 12 h on common PC, to 20 min. Test databases contained epochs of PSG signal from: S1, S2, SWS, and REM sleep stages derived from 20 healthy male subjects, as well as sleep stages from 20 OSA male patients. Sensitivity and specificity of automated detection of particular sleep stages and for particular condition is discussed. A novel approach for semi-automatic polysomnographic analysis proposed in this study is optimized with the data_quantity/(time*accuracy) parameter in non-cluster environment and can be used for scientific, as well as for clinical application in sleep medicine.

Physiology-Neurophysiology

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Striking alterations of EEG and sleep patterns in transgenic mice expressing a mutant prion protein linked to inherited Creutzfeldt-Jakob disease

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An inherited form of Creutzfeldt-Jakob disease (CJD) is linked to the D178N/V129 mutation in the prion protein (PrP) gene. We have generated transgenic mice [Tg (CJD)] that express the mouse homologue of this mutation (D177N/V128). Tg (CJD) mice synthesize a misfolded form of the mutant protein which is aggregated and protease resistant. Immunohistochemical analyses of the brain of Tg (CJD) mice revealed gliosis and PrP deposition in several brain areas, including the hippocampus, neocortex, and cerebellum. Tg (CJD) mice developed memory impairment and a progressive neurological disorder characterized by ataxia, clasping of the hind limbs and kyphosis. Since alterations in EEG and vigilance are part of the clinical presentation of CJD, EEG and sleep patterns were investigated in the mutant mice and compared to those of Tg mice that overexpress wild-type PrP (WT) and remain healthy [Tg (WT)]. 6 Tg (WT) and 7 Tg (CJD) mice were anesthetized and instrumented for chronic EEG recordings, using standard techniques. Body movements were detected by means of an infrared sensor. Mice were individually housed in soundproof rooms, and maintained on a 12 h light:dark cycle, at an ambient temperature between 23 and 24 °C. The amount of time spent in REM sleep was significantly reduced in Tg (CJD) mice ($0.9 \pm 0.4\%$ of recording time during the light phase and $0.3 \pm 0.2\%$ during the dark phase) in comparison to Tg (WT) mice ($5.7 \pm 0.9\%$ of recording time during the light phase and $2.4 \pm 0.3\%$ during the dark phase). Bursts of high voltage, 5 Hz polyphasic complexes and sawtooth waves at 3 Hz were present in the EEG recordings of Tg (CJD) mice, but not of Tg (WT) mice. We propose that Tg (CJD) mice establish the first transgenic animal model of a genetic prion disease recapitulating cognitive, motor and neurophysiological abnormalities of the human disorder.

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Processing of sounds during slow wave sleep in humans: an EEG/fMRI study of auditory stimulation in non-REM sleep

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Introduction: The present study aimed at identifying the neurophysiological responses associated with auditory stimulation during deep non-rapid eye movement (NREM) sleep using simultaneous EEG/fMRI recordings. It was reported earlier that auditory stimuli produce bilateral activation in auditory cortex, thalamus, and caudate during both wakefulness and NREM-sleep (Portas et al. 2000). However, due to the spontaneous membrane potential fluctuations of both thalamic and cortical neurons, cortical responses may be highly variable during deep NREM sleep. Here we now intended to examine the modulation of cerebral responses to tones depending on the phase of the slow oscillation using simultaneous EEG/fMRI.

Methods: Seven healthy young subjects were scanned successfully during NREM-sleep in the first half of the night in a Siemens Allegra 3T scanner (EPI sequence:32 slices, voxel size:$3.4 \times 3.4 \times 3$ mm, TR:2460 ms, TE:40 ms, FA:90°). Subjects were not sleep-deprived. After removing scanner and ballistocardiogram artifacts we automatically identified those sounds which were presented around the peak negativity of stage 3 and 4 NREM-sleep. These detected sounds as well as sounds occurring before and after the peak negativity of slow waves were then entered as regressors of interest in fMRI analyses.

Results: Our study characterizes the neural correlates of slow oscillations correlated to auditory sensory stimulation during natural S3/4 NREM sleep. Preliminary results are consistent with the hypothesis that brain responses during deep NREM-sleep vary as a function of the fluctuating state of thalamo-cortical circuits (Massimini, Rosanova & Mariotti, 2003; Rosanova & Timofeev, 2005). In accordance with Massimini and colleagues larger evoked responses are observed at the negative slope of the slow oscillation. The presence of short temporal windows during which the brain is open to external stimuli is consistent with the fact that even during deep sleep meaningful events can be detected (Portas et al. 2000).

Conclusion: Altogether, brain responses during NREM sleep appear to be non-stationary and highly dependent upon the phase of the slow oscillation which may determine the faith of incoming stimuli while asleep.

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Brainstem activation precedes K-complexes in humans

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K-Complexes (KCs) are the electroencephalographic (EEG) hallmark of slow wave sleep (SWS) or non-REM sleep both in humans and in animals. During KCs, the cerebral cortex is considered to be diffusely upregulated. Although an inherent slow rhythm (<1 Hz) in the cortex is proposed to underlie its generation, subcortical mechanism has not been investigated. Here, we investigated temporally changing brainstem activation pre- and during KCs in humans ($n = 11$). The investigation was carried out by continuously delivering acoustic signals (binaural 85-dB clicks at the rate of 20 times/s) while recording EEGs for spontaneous KCs. Then, brainstem auditory evoked potentials (BAEPs) were analyzed sequentially pre- and during KCs offline. The background of the procedure is that BAEPs are far-field evoked potentials; therefore, they are not affected by the level of cortical activities. Two parameters (amplitude and area) of wave-III and -V were measured, and tested for the temporal significance by oneway repeated measure ANOVA. Amplitude of wave-III showed a transient acceleration before the onset of KCs (initial dip around -1.5 s with succeeding summit around -1.0 s), while both parameters of wave-V showed a sustained acceleration throughout KCs (initial dip around -1.5 s). Results signify the subcortical mechanism for KCs other than the cortical mechanism. Thus, during KCs the cortex will be activated diffusely through the brainstem activation, and probably this underlies the mechanism for memory consolidation in SWS.

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Effect of voluntary attention on EEG activity during REM sleep

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In the previous event-related potential (ERP) study, we found occipital P400 during REM sleep demonstrates larger amplitude

when participants were required to pay attention to the presented tone stimuli while asleep, in comparison with the passive condition (Takahara et al. 2006). As for the background EEG activity, it was speculated that the alpha band would indicate higher activities when paying attention to the stimuli, which were supposed to be related to attention and arousals (Klimesch et al. 1988, 1998). The purpose of this study was to investigate the effect of voluntary attention on EEG activities during REM sleep. Pure tones of 1000 Hz (90%) were used as standards and 2000 Hz (10%) as deviants (Odd-ball paradigm). Stimulus duration was 50 ms with interstimulus intervals of 1450 ms. All the stimuli were presented through fixed earphones. In the attentive condition, the participants were told to detect the deviant stimuli through the night. On the other hand, in the passive condition, they were only hearing them. EEG data were digitized every 5 ms. Data obtained from the first REM sleep cycle were not used for analysis. A fast Fourier transform (FFT) analysis was carried out on each REM sleep EEG segment (1024 points) previously selected, the power spectrum being computed with a resolution of 0.2 Hz. They were averaged every 6 segments. As a result, the EEG spectrum band power in alpha 2 was significantly higher in the attentive condition compared with that in the passive condition. This indicated a proof of sustained attention during the attentive night session when the participants were instructed to pay attention to the external stimuli during REM sleep; raising alpha band activities in background EEG. This is consistent with our previous ERP results.

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Time estimation ability and increased cerebral blood flow in the right frontal lobe area during sleep period before waking

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Humans have the ability to estimate the amount of time during sleep period without referring to actual clock time (Aritake, S et al. 2004). The aim of this study was to investigate whether and what to extent cerebral blood flow (CBF) and sleep structures change during sleep period preceding anticipated wake time (predetermined wake time) by using near-infrared spectroscopy (NIRS) and polysomnography (PSG). Nine healthy volunteers participated in the consecutive two-night crossover sessions; 1) the subjects were instructed to wake up at 3:00 am at bedtime ('request' night), and 2) the subjects were instructed to wake up at 8:00 am at bedtime, but were unexpectedly woken at 3:00 ('surprise' night). When the subject could self-awaken at 3:00 before and after 30 min, it set as 'succeed'. Simultaneous measurement of PSG and CBF at 40 places in the region of prefrontal lobe using NIRS instrument (OMM-3000, Shimadzu, Kyoto, Japan) were performed throughout sleep period in the two sessions. This study has been approved by ethical committee of NIMH, NCNP, Japan. Four subjects successfully could self-awaken ('succeed') at predetermined time and 5 subjects failed to ('fail') in the 'request' night. There was no significant difference in any sleep parameters between the 'succeed' and 'fail' groups, except for increased the amount of REM sleep during 15 min before waking for the 'succeed' group. In the meantime, CBF in the region of right prefrontal cortex gradually increased only in the 'succeed' group in the 'request' night. By contrast, in the 'surprise' night, CBF showed no increase in both the two groups. The present findings suggest that CBF elevation in the right frontal lobe could precede and promote the anticipated sleep termination in humans.

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Dementia biomarkers related to sleep spindle morphology

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Aim: Sleep may be fragmented in dementia. Assuming that sleep spindles may play a role in inducing and maintaining sleep as well as in cognition, their study in dementia should be of interest. We report on the quantification of sleep spindle morphology in search of novel biomarkers in dementia.

Methods: Night sleep EEG data from 3 subjects with dementia (59–71 yrs) and 3 age-matched controls were obtained through standard procedures. The dementia subjects were drug-naïve in-patients and were diagnosed for dementia through standard neuropsychological procedures. The dementia cases had various etiologies (progressive supranuclear palsy, posterior cortical atrophy and fronto-temporal dementia). Visually well-defined sleep spindles from several sleep stage 2 epochs were chosen for analysis. The spindle waveforms were processed automatically for instantaneous envelope (IE) and instantaneous intra-spindle frequency (IF) estimation, and six parameters were obtained quantifying IE and IF characteristics. The dementia and control groups were compared in terms of these parameters.

Results: Two parameters were found to be statistically different between the two groups; one, quantifying the average amplitude of the spindle envelope (of higher value in the control group, indicating more spindle power), and another, quantifying instantaneous intra-spindle frequency dynamics (of higher value in the dementia group,indicating more intra-spindle frequency ''instability'').

Conclusions: The results indicate the possibility of extracting dementia biomarkers related to sleep spindle morphology. These biomarkers imply differences in sleep EEG generation mechanisms between dementia and control subjects. Accordingly, the spindle power parameter difference implies a possible difference in cortical neural dynamics (e.g., synaptic loss in the dementia group), while the intra-spindle frequency parameter difference implies a possible difference in thalamo-cortical neural dynamics (e.g., compromised capability of thalamic ''pacing'' in the dementia group).

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Sleeping outside the box: short sleeping sloths stress the importance of neurophysiological experiments in the wild

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Insight into the functions of sleep may be obtained by comparing sleep in different types of animals. Historically, technological limitations restricted electrophysiological recordings of sleep to the unnatural laboratory environment. Herein we demonstrate the feasibility of performing minimally invasive surgeries and subsequent electrophysiological recordings of sleep in animals in the wild. Three adult female sloths were studied at the Smithsonian

Tropical Research Institute in Panama. The sloths were caught in the rainforest canopy. Silver-silver/chloride wire electrodes were inserted under the skin overlying the cranium to record EEG activity from the anterior and posterior cortex of each hemisphere. The wires were connected to an EEG data logger (developed by A. Vyssotski) that recorded four channels at 100 samples per second for up to 5 days. The logger was glued on top of the head. This 1 h procedure did not require general anesthesia. After attaching a radio collar and activity data logger, the sloths were released back into the rainforest. Sloths were recaptured 3 or 5 (N = 2) days later. We obtained a total of 12.8 d of continuous recordings. For each sloth, all data starting 24 h after release was scored for wakefulness, slow-wave sleep and REM sleep in 10 s epochs. Reported values are mean ± s.e.m. The quality of the EEG signals remained high throughout all recordings, and each state was readily identifiable. The sloths spent 59.87 ± 2.13% (14.37 ± 0.51 h) of the time awake, 32.44 ± 2.83% (7.78 ± 0.68 h) in slow-wave sleep and 7.70 ± 1.11% (1.85 ± 0.27 h) in REM sleep. REM sleep encompassed 19.45 ± 3.54% of total sleep time. Sloths in the wild slept only 9.63 h during a 24-h day. In contrast, an EEG study of captive sloths of the same species reported 15.8 h of sleep per day. Our preliminary study demonstrates the feasibility of recording sleep in wild animals living in their natural habitat, and questions whether data obtained from laboratory studies reflects the expression of niche-adapted sleep.

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Cortical plasticity induced by transcranial magnetic stimulation during wakefulness affects EEG activity during sleep

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Introduction: Sleep electroencephalogram (EEG) brain oscillations in the slow-frequency range increase/decrease locally after tasks involving circumscribed cortical regions. It has been hypothesized that these changes reflect plastic re-organizations, triggered by learning and mediated by long-term potentiation (LTP), which may regulate local sleep need. Here, we test the hypothesis that waking potentiation of synaptic transmission in the motor cortex affect EEG activity in specific cortical circuits during subsequent sleep. Waking potentiation has been obtained by a Hebbian stimulation paradigm inducing cortical plasticity in humans, which resembles associative timing-dependent LTP. The paradigm consists of repetitive pairing of median nerve stimulation with transcranial magnetic stimulation over the controlateral motor cortex, which increases cortical excitability at interstimulus intervals of 25 ms (paired associative stimulation at 25 ms, PAS-25). Cortical distribution of sleep EEG power following PAS-25 has been compared to that following a control paradigm with intervals of 50 ms (PAS-50).

Methods: We recorded full night EEG in ten healthy subjects undergoing a four-day sleep study. In the third and fourth nights, subjects were submitted to a presleep PAS-25 or to a PAS-50. Experimental manipulation of corticospinal tract excitability induced a 48% increase in amplitude of motor evoked potentials (MEPs) only with PAS-25. This waking LTP-like potentiation affected delta and theta power, in both NREM and REM sleep. Slow-wave activity (SWA) increases in some frontal and prefrontal derivations and decreases at sites neighboring and controlateral to the stimulated left motor cortex. The magnitude of increased PAS-25 MEP amplitude also predicts enhancements of SWA in prefrontal regions.

Conclusions: An increased synaptic strength, presumably induced by the LTP-like paradigm, leads to changes in local sleep regulation, as indexed by SWA. Enhancement and depression of SWA have been interpreted in terms of a simultaneous activation of both excitatory and inhibitory circuits consequent to PAS-25.

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Opposite behaviour of neocortex and hippocampus in the interhemispheric dialogue: a human stereo-EEG single case

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Previous studies showed a rhythmic oscillation in the low delta range during REM sleep in the human hippocampus. Compelling evidence point to the involvement of slow rhythms in the processes of memory consolidation and post-learning plasticity. The almost unique opportunity to record two homologue bilateral cortical and hippocampal derivations without EEG alterations in an epileptic patient undergoing presurgical evaluation allowed us to investigate the interemispheric communication within slow-frequency rhythms across the sleep wake cycle. We recorded intracerebral (bilateral hippocampal and frontal neocortical derivations) stereo-EEG of a night of sleep and of the preceding wake. In order to investigate the behaviour and phase relationship of slow rhythms across different derivations, power and coherence analyses, analysis of waveform triggered around (± 1 sec) the negative peak of slow waves (0.5–2.0 Hz) and cross-correlation analysis were carried out. In neocortical leads, delta power was lower during wake and REM sleep than during NREM sleep. Interemispheric coherence of low-delta showed a similar pattern, with high levels during slow-wave sleep concomitant with a phase synchronization of delta waves. Hippocampal derivations showed a very different pattern. Low-delta power was high during all three states, indicating that low-delta is a peculiar feature of human hippocampal EEG activity during all physiological states. Interemispheric coherence showed an opposite pattern to neocortical derivations, with slightly higher levels during wake and REM sleep and, unexpectedly, very low levels during NREM sleep. The latter result points to an inter-hippocampal functional disconnection during NREM sleep. Between neocortical and hippocampal leads no phase modulation and coherence emerged in the low delta range, indicating a functional differentiation between neocortical and hippocampal slow rhythms. Hippocampal bilateral delta synchronization during wake and REM sleep could have a role in the encoding memory process, and it could be the human equivalent of the animal hippocampal theta rhythm. The de-synchronization of Delta oscillations between the two hippocampi during NREM sleep is a novel and unexpected finding that deserves further investigation.

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Sleep deprivation decreases phase-shift responses of circadian rhythms to light in the mouse: a role for histamine?

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Homeostatic and circadian processes together regulate the sleep-wake cycle. The exact nature of the relationship between the pacemaker system and sleep-wake cycle is unknown, although evidence shows that the two systems interact in a complex relationship to influence each other and modulate the daily cycle of activity and rest. There is evidence that the circadian pacemaker

is primarily synchronized to the daily light-dark cycle. However, it is also known that the phase-shifting and synchronizing effects of light can be modulated by behavioural factors. The present experiments examine the effects of sleep deprivation on the response of the circadian pacemaker to light, and test the possible involvement of histaminergic input from the tuberomammillary nucleus in mediating the effects of sleep deprivation on the circadian clock. Photic phase-shifting of the locomotor activity rhythm was analyzed in mice transferred from a light-dark cycle to constant darkness, and sleep-deprived by gentle handling for 8 h, from Zeitgeber Time (ZT) 4 to ZT 12. Phase-delays in response to a 10-min light pulse at ZT 14 were reduced by almost 40% in sleep-deprived mice compared to control mice, while sleep deprivation without light exposure induced no significant phase-shifts. Sleep deprivation between ZT4 and 12 did not reset the mouse circadian clock. Sleep deprivation was no longer able to attenuate phase delays to light when mice were treated with mepyramine (a specific antagonist for the histamine H1 receptor, microinjections aimed at the suprachiasmatic nucleus) at ZT8. Phase delays to light in animals not sleep derived were unaffected by mepyramine. Cimetidine, an antagonist of the H2 receptor had no effect on the ability of sleep deprivation to attenuate phase delays to light. Taken together, the present results indicate that sleep deprivation can reduce the light-induced phase-shifts of the mouse suprachiasmatic pacemaker. It is possible that this is due to changes in histamine transmission associated with the loss of sleep.

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Does REM sleep contribute to sleep homeostasis?

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An unanswered question on sleep regulation regards the role of REM sleep (REMS). Most studies on homeostatic aspects of sleep regulation have been focused on non-REM sleep (NREMS), while the role of REMS has been neglected. Since the evaluation of EEG changes induced by extended waking provides the most grounded approach to this issue, we studied a large sample of healthy subjects within a sleep deprivation protocol, considering a full-scalp topography.

Methods: The sleep EEG of 40 subjects (age = 24.6 yrs) was recorded from 19 derivations in 3 nigths (adaptation, baseline -BSL-, recovery after 40 h of sustained wakefulness -REC-). EEG power was calculated across the 0.50–25 Hz range (resolution = 1 Hz), separately for REMS and NREMS. Statistical comparisons between REC versus BSL were calculated for 1-Hz power maps of NREMS and REMS, yielding a full-scalp topography of homeostatic changes in both states. Finally, the magnitude of changes in NREMS and in REMS was correlated.

Results and Conclusions: NREMS: Power maps of BSL reveal stable patterns within different frequency ranges, and maxima and minima exhibited the typical features of power spectra in NREMS. The delta and alpha ranges exhibit a frontal midline predominance and minima over the temporal regions. In the theta band, the highest values are seen at the fronto-central midline areas, while sigma power shows centro-parietal maxima. The statistical maps of the REC versus BSL differences reveal topography-specific increases from 0.5 to 12 Hz and decreases from 13 to 16 Hz. REMS: Power maps of BSL also reveal that the 0.5–7 Hz range exhibits fronto-central midline maxima and minima over the temporal areas, while the highest values of the alpha band are seen at the parietal-occipital areas. The statistical maps of the REC versus BSL differences point to topography-specific increases from 0.5 to 7 Hz and decreases from 8 to 11 Hz. Hence, the 1–7 Hz range shows significant and topography-specific increases as a consequence of sleep deprivation, shared by NREMS and REMS. On the other hand, the topography-specific changes in the 8–11 Hz range show a clear dissociation. Correlational analyses confirm the extistence of a tight relationship between changes in NREMS and REMS, suggesting a homeostatic role also for REM sleep.

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The evolutionary origin of NREM and REM

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The evolutionary origin of the mammalian sleep has been hotly debated. Most hypotheses forwarded up to now were incomplete as they only speculated on the evolution of NREM and REM, but not on their distribution in a sleeping episode. We present here a likely scenario for the evolution of the mammalian sleep from the reptilian active state. As the electrophysiological signs of sleep are unreliable in non mammals, only behavioral and physiological aspects of sleep will be considered. In mammals, NREM behavior involves the search of a thermoneutral niche, the adoption of a stereotypic posture and remaining immobile, with only small correcting movements. The physiological control works in closed loop mode. Phasic REM consists in a series of eye movements and muscular twitches which are considered as exploratory and startle responses. Tonic REM shows a total muscular block. The physiological control works in open loop mode. Active reptiles cyclically alternate between basking and goal directed behavior. Basking involves the search of a suitable place to warm the body and remaining immobile with only small correcting movements. The physiological control works in closed loop mode. After reaching the preferred temperature, the animal enters in goal directed behavior with bursts of motor activity interspersed with startles and exploratory behavioral arrests, always under open loop physiological control. Our group proposed that the mammalian sleep evolved from the reptilian activity (Nicolau et al. 2000). Here we complete the hypothesis proposing that the basking behavior evolved into NREM, while the startles and behavioral arrests were the primitive phasic REM and the ongoing goal directed behavior gave origin to tonic REM after developing a strong motor inhibition. The hypothesis explains the alternations between NREM and REM, their neurological features, the ontogenetic development of sleep and the relations between sleep and thermoregulation. The sleep appeared as a side result of developing the cortical wakefulness, a state of unprecedented features in pre-mammalian animals.

Nicolau, et al. (2000) Why we sleep: the evolutionary pathway to the mammalian sleep Prog Neurobiol 62: 379–406.

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Short-term regulation of homeostasic functions by the metabolic status of the liver

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The liver plays a central role in the maintenance of the body energy metabolism. According this fact, we put forward the hypothesis that the hepatic energy status could trigger adjustments in feeding and vigilance behaviours, occurring in the maintenance of energy homeostasis. In 15 instrumented adult Sprague-Dawley male rats, the hepatic energy metabolism was pharmacologically reduced with 2,5-anhydro-D-mannitol (2,5-AM), which specifically inhibits

carbohydrate metabolism in hepatocytes and thus stimulates food intake (FI). Feeding, vigilance patterns and internal temperatures (liver (TLiver), cortex (Tcor) and brown adipose tissue (TBAT) temperatures) were recording during for 4 h immediately after intraperitoneal injections of saline (control) or 3 different concentrations of 2,5-AM (200, 400 and 600 $mg.kg^{-1}$) administered in random order. Data with 2,5-AM were compared to control (= saline injection) with repeated measures ANOVA followed by paired t tests. Results showed that, after injection of 200 $mg.kg^{-1}$of 2,5-AM, hyperphagia (+195%, $P<0.0001$) occurred although vigilance pattern did not change. In contrast, with 400 mg $kg^{-1}$of 2,5-AM, the increase in FI (+170%, $P=0.002$) was accompanied by a greater duration of wakefulness (+25.84%, $P=0.007$) associated with a decrease in non-rapid eye movement sleep (NREMS, −14% of the control, $P=0.018$). Hepatic and cortical temperatures decreased simultaneously (TLiver: −0.48 °C, $P=0.026$ and Tcor: −0.36 °C, $P=0.023$). With 600 mg $kg^{-1}$of 2,5-AM, eating behaviour was no more modified (t14, $P=0.22$) but the depression of NREMS duration persisted ($P=0.003$). Brown adipose tissue temperature (−0.37 °C, $P=0.0080$), hepatic (−0.59 °C, $P=0.022$) and cortical (−0.49 °C, $P=0.010$) temperatures fell. These results corroborate our hypothesis that changes of hepatic energetic metabolism by 2,5-AM can trigger isolated t or concomitant changes in the vigilance, feeding and thermoregulation functions, mainly involved in the energy homeostasis regulation.

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Nocturnal pulse wave attenuation is associated with daytime blood pressure in a population based cohort

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Objective and Background: Pulse wave amplitude (PWA) derived from the digital vascular bed has been used in sleep studies. We assessed the relationship between nocturnal PWA attenuation and daytime blood pressure (BP).

Methods: 81 subjects (46 men; age 60 ± 7 yrs; body mass index [BMI] 28.2 ± 4.3 $kg\,m^{-2}$; apnea hypopnea index [AHI], 25.4 ± 22.6 events h^{-1}; systolic BP 137 ± 15 mmHg; diastolic BP 79 ± 7 mmHg) recruited from a population based cohort underwent simultaneous ambulatory polysomnography (PSG) and peripheral arterial tonometry (PAT) recording. Episodic attenuations of PWA derived from the pulse waveform of PAT signal were identified and characterized. Generalized least squares regression model was used to identify the association between PSG indexes, PWA attenuation (PWA.att) and the daytime BP.

Results: We found PWA.att, oxygen desaturation index (ODI), and AHI, but not arousal index predicted daytime BP. Systolic/diastolic BP was predicted by PWA.att ($P=0.02$/$P=0.005$), oxygen desaturation index (ODI) ($P=0.03$/$P=0.03$), AHI ($P=0.03$/$P=0.11$). The association between PWA.att and daytime BP was independent of gender, age, AHI, ODI and use of antihypertensive medication, but proportional to BMI (systolic/diastolic BP $P=0.004$/$P=0.01$). However, there was no direct interaction between the effects of PWA.att and BMI.

Conclusions: Overnight magnitude of PWA attenuation, presumably reflecting nocturnal sympathetic reactivity, was associated with daytime BP. This measure of autonomic tone in sleep may provide novel insights into cardiovascular risk classification.

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Thermoregulatory drive of liver upon food intake and vigilance in rat

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In a new concept of hepatic thermo-control upon feeding behaviour, it has been shown that rats stopped eating when the hepatic temperature reached 39.3 °C. We suggest that the thermal drive from the liver plays a major role in the main functions managing energy balance such as feeding (energy input) and vigilance (energy storage). To test this hypothesis, the liver temperature has been artificially increased at 40 °C and 40.5 °C from 12 pm to 4 pm in order to analyse the repercussions of the hepatic thermal drive on feeding and vigilance states. Fifteen adult Sprague Dawley rats were implanted for polysomnographic study. Three temperature probes were placed into cortical layers, brown adipose tissue (BAT) and between 2 hepatic lobes, respectively. The hepatic probe was associated with an electric servo-controlled resistance, which gradually increases its temperature. Food intake, vigilance states and temperature changes were analysed when the liver was heated and compared to control situation (= non-heated liver) with ANOVA followed by an unpaired t test. Results show that the increase of hepatic temperature induced a decrease in total food intake quantity compared to control (−83% at 40 °C: $P=0.004$ and −92% at 40.5 °C: $P=0.015$). A negative 'temperature-dependence' relationship was established between food intake and hepatic temperature ($r^2=0.214$, $P=0.004$). In the same way, the total duration of wakefulness decreased (−26% at 40.5 °C: $P=0.001$) at the expense of slow wave sleep (+11%: $P=0.0003$), without any change of paradoxical sleep. A negative temperature-dependant relationship was found with total duration of wakefulness ($r^2=0.11$, $P=0{,}042$). In conclusion, the present results show behavioural adjustments in feeding and vigilance functions when the thermal hepatic load is changed, giving evidence that the liver thermal load could act upon 2 homeostasic functions.

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Thermometabolic drive and peripheral chemoreception in the respiratory control according to sleep stages in the preterm neonate

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Energy expenditure (O2 consumption, VO2) and pulmonary ventilation (VE) are closely related. The nervous structures and processes connecting them are not yet understood. Peripheral chemoreceptors could be a potential candidate since their activity modifies VE when the O2 demand is high to hinder hypoxia. Peripheral chemoreceptor activity is influenced by both thermal and metabolic processes: it is greater whenever O2 demand was increased, i.e. in AS versus QS, in warm and cool environment versus thermoneutrality and with anti-apneic treatment of caffeine (hypermetabolic and hyperthermic) versus controls. Since VO2 and rectal temperature (Tre) are often associated, our goal was to dissociate the respective role of the thermal and the metabolic drives on the strength of peripheral chemoreceptor during active (AS) and quiet (QS) sleep in preterm neonates. Peripheral chemoreceptor activity, assessed by the immediate drop of VE during short-lasting hyperoxia (ΔVE), has been studied on 41 neonates at thermoneutrality, during cool (= thermometabolic

drive) and warm (= thermal drive) conditions. In AS, VO2 and Tre were significantly related (rho = +0.3;p = 0.01) whereas in QS, this relation was not significant. In an attempt to describe the respective influences of the metabolic and the thermal drive on the chemoreflex, multiple regressions have been made. The relationship during AS ($P<0.001$) was $\Delta VE = -1.3VO2 - 7.9Tre + 273.1$ (slope-values $P<0.05$). In contrast, during QS, Tre (but not VO2) was related to ΔVE decline. As a result, a simple regression can be drawn ($P = 0.001$; $\Delta VE = -12.2Tre + 428.2$). The results suggest that the difference between QS and AS could be viewed as a functional change of thermoregulatory influences, resulting in a decreased influence of thermal drive and an increased responsiveness to fulfil O2 demand by the tissues. This latter point is consistent with the general agreement that behaviour plays a major role on the control of respiration during AS. According to the hypothesis that great tonic activity of the peripheral chemoreceptors may impair their ability to respond adequately to a hypoxic challenge, our results suggest that during AS, increase energetic need associated with increased body temperature may be harmful, perhaps in a synergic way.

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Sleep related activation of the ventrolateral preoptic nucleus following the exposure to low ambient temperature

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Introduction: Cold exposure selectively reduce REM sleep occurrence and, at very low ambient temperature (Ta), it also decreases delta power density [1]. These changes are concomitant with a modification of cellular activity in the preoptic-anterior hypothalamic area [2]. In order to extend the map of cellular activity for a model of sleep deprivation based on cold exposure, we have investigated the expression of c-Fos and P-CREB in several brain regions. Here we present the results concerning the ventrolateral preoptic nucleus (VLPO), which is well known to be involved in sleep regulation [3].

Method: Twenty-four male albino rats were randomly assigned to one of the following experimental conditions: i) control: 5 h or 24 h at the normal laboratory (nl) Ta of 23.0 ± 1.0 °C; ii) exposure: 5 h, 24 h, or 48 h at Ta −10.0 ± 0.5 °C; iii) recovery: 5 h at nl-Ta after 24 h or 48 h of exposure. Brains were fixed with 4% p-formaldehyde and 40 μm coronal sections were alternately processed for c-Fos and P-CREB immunohistochemistry. Each fifth section was stained with cresyl violet for the anatomical identification. c-Fos positive nuclei and the extension of P-CREB stained area were counted within standardized grids on digital images of sections. The cluster, medial extended and dorsal extended nuclear subdivisions [4] were separately examined. Data were statistically assessed by means of ANOVA.

Results: In the whole VLPO, P-CREB but not c-Fos expression was higher in control 5 h than in control 24 h. In the three VLPO subdivisions, c-Fos expression was significantly higher during both exposure and recovery with respect to control levels. Interestingly, in the nuclear cluster c-Fos expression was significantly higher during recovery with respect to exposure. In the whole VLPO, P-CREB expression was significantly lower during recovery with respect to control levels.

Conclusion: These data appear to confirm a role of VLPO, in particular of the nuclear cluster, in wake-sleep regulation.

Reference: [1] Cerri et al. Sleep, 2005, 28: 694–705. [2] Zamboni et al. Brain Res., 2004, 1022: 62–70. [3] Sherin et al. Science, 1996, 271: 216–219. [4] Lu et al. J Neurosci., 2002, 22: 4568–76.

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Event-related P2 component during a psychomotor vigilance task indicates sleep pressure

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The presented study aimed to outline a possible relationship between event related potentials (ERPs) during a psychomotor vigilance task (PVT) and sleep pressure. 20 subjects (10 male; mean age ± SD: 23.45 ± 2.00) had to perform a PVT throughout a sleep deprivation night hourly (8 times at all). The task contained 120 stimuli and lasted about 12 min according to individual performance. Electroencephalography (EEG) was recorded simultaneously. ERPs were analyzed for P1, N1 and P2 components. P2 showed strongest sleep-pressure-related amplitude decrement throughout the night at occipital sites (Oz). We could demonstrate a gradual decrease in P2 amplitude-most significant ($t19 = 3.777$, $P = 0.001$) comparing P2 amplitude during the first PVT (11:30 pm) with that during the last PVT (6:30 am). Further we revealed a significant negative correlation ($R20 = -0.508$, $P = 0.022$) between P2 amplitude decrease and reaction time increase over the night. Taken together we found a sleep-pressure indicating ERP component peaking at 200 ms after stimulus onset, showing smaller amplitudes after prolonged wakefulness. Further we could demonstrate that there is a relationship between P2 amplitude decrease and PVT-reaction time increase. Therefore we suggest that P2 amplitude can be used as predictor for sleep pressure and-like the PVT-reflects the arousal and attentional state of an individual.

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Brain potentials over the visual area during REM sleep

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Dramatic and vivid visual imagery is one of the features of dreaming during rapid eye movement (REM) sleep. It is known that rapid eye movements during REM sleep were followed by a brain potential over the occipital visual area known as the lambda-like response that is similar to the lambda response observed when processing visual information after saccades during wakefulness. The lambda response is a positive brain potential. On the other hand, the lambda-like response has two positive peaks. In the present study, in order to investigate this form difference between the lambda and lambda-like responses, we examined the relationship between the type of visual stimuli and the lambda response form during wakefulness. Healthy students participated in the study. Saccades were recorded during visually-triggered saccade task during wakefulness. We used two types of visual stimuli, picture stimuli and LED stimuli. Electroencephalogram (EEG), horizontal and vertical electrooculograms (EOGs) ere recorded. The EEG from 400 ms before to 400 ms after the offset of saccade was averaged for lambda response. In the results, we found that the lambda response showed two positive peaks for picture stimuli but one peak for LED stimuli. This results indicated that the lambda-like response during REM sleep has similar form with the lambda response occurred after more complicated stimuli. The lambda-like response during rem sleep may suggeste that a kind of complicated visual information processing may occur during REM sleep.

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Low-density EEG study of dynamic properties of cortical sleep slow oscillation in humans: perspectives for clinical applications

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Aim: High-amplitude slow waves with long-range synchrony represent the hallmark of slow wave sleep (SWS) and anesthesia. Intracellular recordings in animals have revealed that during SWS the membrane potential of cortical neurons oscillates between a state of deep hyperpolarization and a state of wake-like depolarization. This cellular behavior, referred to as sleep slow oscillation (SSO), represents the fundamental cellular phenomenon underlying neural activity in SWS. SSO is also detectable in human EEGs and is characterized by typical frequencies less than 1 Hz. Aim of the study is to identify by 32 channels EEG dynamic and spatial features of cortical SSO.

Methods: EEG recordings were performed in 8 healthy right-handed male subjects (age 20–25 yrs) during the first sleep cycle of the night. All EOG, ECG and respiratory artifacts were removed by ICA algorithm. Following the approach used by Massimini et al. (J Neurosci, 24:6862–70, 2004), who employed a HiRes EEG (256 channels), each channel was scanned with a sliding window in order to identify all signal shapes with the following features: (a) a negative zero crossing and a subsequent positive zero crossing separated by 0.3–1.0 sec, (b) a negative peak between the two zero crossings with voltage less than -80 μV, (c) a negative-to-positive peak-to-peak amplitude >140 μV.

Results: Results indicate that each SSO originates more frequently in frontal scalp regions and propagates over the scalp in a fronto-occipital direction at an averaged speed of 5 m sec^{-1}.

Conclusion: The main findings of this work are 1) our data are consistent with those obtained by Massimini et al. (2004) by HiRes EEG, 2) the results obtained by 40 channels EEG open new possibilities to explore routes of research in different fields of applied neurophysiology and, particularly, of neurophysiopatology.

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Gestational hypertension and increased Mallampati grade during pregnancy

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Introduction: Increased Mallampati grade is associated with sleep-disordered breathing (SDB). SDB has been shown to be an independent predictor of hypertension in several epidemiological studies. None of these studies included pregnant women. We therefore sought to determine whether Mallampati grade as a proxy measure of SDBis associated with hypertension during pregnancy.

Methods: A retrospective review of both the Obstetrics and Obstetric Anesthesiology clinical databases was performed for all women presenting to the Labour and Delivery unit for an 18month period prior to November 2007. Mallampati grades I/II were considered low risk for SDB and grades III/IV were considered high risk for SDB. Gestational hypertension was considered present if systolic or diastolic blood pressures were above 140 and/or 90 mmHg respectively after 20 weeks of gestation.

Results: A total of 5389 obstetric charts were reviewed. Seven percent of women had a Mallampati grade III/IV. Such women were more likely to be older (30.2 ± 6.0 years versus 29.2 ± 5.9 years, $P \leq 0.001$) and have a higher pre-pregnancy body mass index (BMI; 25.1 ± 11.1 versus 22.8 ± 8.9, $P \leq 0.001$). Twelve percent of women had gestational hypertension. Mallampati grade III/IV independently predicted gestational hypertension, with an adjusted odds ratio of 1.7 (95% confidence interval 1.22.2, $P \leq 0.001$).

Conclusion: A Mallampati grade of III/IV, as a proxy measure of SDB risk, independently predicts adverse maternal outcome as defined as gestational hypertension. Use of a routine physical examination technique in the obstetric clinic to identify pregnant women at risk for SDB may have great cost-effective, clinical utility.

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First responses during sleep to hypertonic saline infusion differ between individuals and sleep stages

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Most experimental pain models used to investigate the relationship between pain and sleep are of short duration. Each study has tended to look at only one type of sleep interruption and selected sleep responses. The results from these studies have not been consistent. We have developed a new model using a ten-minute infusion of hypertonic saline which we used to assess a wider range of responses during sleep. Twelve healthy male subjects participated in two experimental nights for the study. They were exposed to either hypertonic or isotonic infusions, for a duration of ten minutes, both while awake and during all stages of sleep. The muscle pain intensity and quality during wakefulness were assessed using Visual Analogue Scales (VAS). Polysomnographic signals were recorded to score sleep changes and standard criteria were used to determine the presence of microarousals, alpha intrusion, sleep stage shifts and/or full arousals from sleep. The hypertonic saline infusions produced a significantly greater VAS score ($P<0.0001$) than the control infusions of isotonic saline. There was no significant difference between evening and morning hypertonic saline infusions indicating both a lack of circadian rhythm and a lack of hyperalgesia after the experimental night induced by the infusions during the night. Subjects were not consistent in their responses over multiple infusions. A full arousal was the most common first response during stage 2 sleep (75%). The responses to the infusions during stages 3 and 4 were equally split between full arousals and sleep stage shifts while in REM sleep full arousals and microarousals were the most common responses. The data suggests that pain during sleep triggers differing responses determined by both the sleep stage involved and the individual which may help explain contradictory results obtained in previous experimental pain and sleep studies.

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Morning blood pressure surges are greater when waking from stage 2 sleep compared to waking from REM sleep

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Introduction: The occurrence of cardiovascular events increases during the morning period. While the mechanism responsible is yet to be determined, possible contributors include surges in sympathetic activity and concurrent rises in blood pressure (BP) partly determined by arousal from sleep as well as postural changes. This study tested the hypothesis that the surge in sympathovagal balance and BP is greater when waking from stage 2 sleep compared to waking from REM sleep.

Methods: 26 healthy volunteers (10 males) had overnight polysomnography, including ECG measurements. Spectral analysis of heart rate variability (HRV) was conducted on 2 min blocks of stable data (free from state changes, movements and cardiac or respiratory disturbances) from the last 30 min of sleep and during 30 min of resting wakefulness (supine) immediately following sleep. Outputs included absolute low frequency (LF) and high frequency (HF) power, the LF/HF ratio, heart rate (HR) and average BP. 10 subjects woke from REM sleep and 16 woke from stage 2 sleep. To investigate the effect of waking from stage 2 or REM sleep on HRV and BP responses 2 way ANOVAs (stage 2 versus REM) with repeated measures (sleep versus wake) were performed.

Results: There was a significantly greater increase in BP when waking from stage 2 sleep compared to REM sleep ($P<0.05$) mainly as a consequence of higher systolic BP wake values during wake after stage 2 sleep compared to wake after REM sleep (131.2 ± 4.0 versus 119.0 ± 6.1 mmHg, $P<0.05$). Awakening was not associated with changes in HRV variables but it was associated with an increase in heart rate ($P<0.05$) independent of the sleep stage being awoken from.

Conclusion: Considering that the rate of BP rise was greater when waking from stage 2 sleep compared to REM sleep, we suggest that waking from stage 2 sleep may contribute to an increased risk of cardiovascular events during the morning period.

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Characteristics of micro-arousals in pregnant women's sleep at night: a comparison with non-pregnant women's sleep

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Introduction: To investigate pregnant women's sleep disturbance from fetal movement, we made polysomnographic and fetal movement recordings simultaneously. We succeeded in recording pregnant women's micro-arousals evoked by fetal movement thanks to a newly developed sensor (2007). In this study, we demonstrated characteristics of micro-arousals in pregnant women's sleep at night in comparison with non-pregnant women's sleep.

Methods: The subjects were seven pregnant women (mean 31.3 yrs) and twelve non-pregnant women (mean 32.5 yrs). All subjects gave written informed consent before participating in the study. The sensor was small with electrostatic capacity for clearly detecting acceleration of fetal movement. We recorded pregnant women's polysomnograms and fetal movement simultaneously during all-night sleep at home using a Medilog recorder during weeks 33 and 36 of gestation. Polysomnographic recordings in non-pregnant women were made during two nights. A micro-arousal was defined according to the criteria proposed by the American Sleep Disorders Association (1992). *T*-tests were used to compare the pregnant and non-pregnant women's groups.

Results: There were no differences in the length from sleep onset to final awakening between the groups. Wake time after sleep onset in pregnant women significantly increased compared to that in non-pregnant women. There was no significant difference in stage 3 and 4 between the groups, but REM sleep in pregnant women decreased significantly. The number of micro-arousals during night for pregnant women increased significantly compared with that for non-pregnant women (33 W:80.8, 36 W:70.7, Non pregnant:37.6). When we calculated the occurrence of micro-arousals per minute in each sleep stage, stage 1 was the highest, stage 2 and REM sleep showed a slight decrease, and stage 3 and 4 decreased much more in both groups.

Conclusion: Women in late pregnancy not only increased wake time after sleep onset, but also increased micro-arousals during the night. The occurrence of micro-arousals per minute in each stage was related to sleep depth.

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Prevalence, predictors and consequences of behaviorally induced insufficient sleep syndrome in adolescence

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Introduction: In the second edition of the International Classification of Sleep Disorders the diagnostic criteria for a new hypersomnia, "behaviorally induced insufficient sleep syndrome (BIISS)" were presented. BIISS is defined by three inclusion criteria: A) complaint about excessive daytime sleepiness, B) short habitual sleep episode and C) sleeping considerably longer than usual during weekends and vacations. To the best of our knowledge no previous prevalence study of BIISS has been conducted.

Methods: Population based cross sectional study. 1285 randomly selected high school students (668 boys and 610 girls, 16–19 years old; mean age 17.3, SD = 0.94) from the Hordaland county, Norway completed a web-based survey comprising questions about sleep habits, demography, alcohol use, smoking, mean school grade, body mass index, anxiety and depression. The response rate was 69.8%.

Results: In all 22.3% complained about excessive daytime sleepiness (criterion A), 39.2% normally slept less than 420 min on weekdays (criterion B) and 60.0% slept at least 120 min longer during weekends/vacations than during weekdays (criterion C). The overall prevalence of BIISS was 10.4% (95% CI = 8.7–12.1). BIISS was predicted by high levels of alcohol usage, smoking and living in an urban as opposed to a rural area. High education among mothers seemed to be a protective factor. BIISS was associated with elevated scores on anxiety and depression and poor grades.

Conclusion: BIISS seems to be a common hypersomnia in adolescence and is associated with several negative outcomes.

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REM-sleep sawtooth activity – spectral characteristics

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In spite of being the only typical EEG activity recognized in human Rapid Eye Movement sleep (REM) scalp EEG, sawtooth waves (STW) remain, to date, one of the least understood components of this sleep state. In this study, STW were quantitatively analyzed in a sample of whole-night sleep studies pertaining to eight healthy young subjects (T3-Cz channel). A total of 36 REM periods were reviewed for visual sawtooth activity scoring and data extraction (STW and background control segments). Mean frequency distribution on STW and control segments was analyzed by Fast Fourier Transform in 256-point windows (0.5 Hz resolution) corresponding to the central (2s) portion of each segment. There were 1070 STW segments, with an average of 133.75 ($\pm$ 38.84) STW bursts per subject, 29.72 ($\pm$ 20.51) STW bursts per REM period. Considering the first four sleep cycles (870 STW bursts),

mean STW prevalence was 11.63 (± 3.38)%, STW index was 1.39 (± 0.38)/min and median STW duration, 4.75s. Median STW voltage was 85 μv, whereas median REM sleep background activity voltage was 67.5 μv. An STW 2–2.5 Hz main peak was seen for all subjects, with a second peak between 4 Hz and 7 Hz present in 6 cases. Gabor spectrograms as well as visual STW inspection in 16s-windows allowed recognition of waxing and waning rhythmical faster theta activity often encompassing an STW burst. Some 5–7 Hz activity could be recognized on REM background canonograms for individual subjects, but it appeared to be more prominent in close proximity to, or embedded in STW bursts. STW bursts often appeared to be the sum of at least two basic rhythms, in a way similar to the theorectical construction of sawtooth waves (superposition of evenly-distanced frequency contributions with progressively smaller power). Investigation of REM sleep spectral composition variability over different time frames and topography should perhaps be attempted, as sawtooth wave activity might represent one critical step of a varying superposition of basic REM sleep EEG rhythms.

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Saporin-orexin-B lesion in the lateral hypothalamus and REM sleep homeostasis in the rat

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The lateral hypothalamic orexinergic system is involved in the control of the mammalian sleep-wake cycle. Lesions in the orexinergic system are causally related to narcolepsy in humans. Here we explore the REM sleep homeostatic process after selective REM sleep deprivation in rats lesioned with saporin-orexin-B in the lateral hypothalamus. Male Sprague-Dawley rats were bilaterally injected with 200 ng (0.5 uL) of saporin-orexin-B conjugate ($n = 13$) or saline solution ($n = 6$) in the lateral hypothalamus. After at least three weeks of recovery, rats were entrained to a skeleton phoperiod (SP) (20 min light pulses at local time 8:00–8:20 and 19:40–20:00 h). ''Rest phase'' and ''active phase'' correspond to the 8:00 to 19:59 and 19:00 to 7:59 h intervals respectivelly. After two baseline days, three hours of selective REM sleep deprivation protocols were performed during rest and active phases in non-consecutive days under SP. REM sleep recovery was evaluated as experimental minus baseline REM sleep accumulated in the five hours following deprivation. Lesions were evaluated by counting hypothalamic orexin-A immunoreactive neurons. Whereas saline treated and minor lesioned rats display an important recovery of REM sleep debt (74.9% after active phase and 77.3% after rest phase deprivation), rats with more than 30% damaged orexinergic neurons do not compensate REM sleep debt (− 65% after active phase and 2.9% after rest phase deprivation). The magnitude of REM sleep rebound and compensation efficiency of REM sleep debt correlate linearly with the number of remaining orexin-A immunoreactive neurons. Our results suggest that the hypothalamic orexinergic system is involved in the executive mechanisms of REM sleep homeostasis. Grant FONDECYT 1061089.

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Sleep alters the contribution of baroreflex and non-baroreflex mechanisms to the control of heart period in human subjects

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The pattern of coupling between heart period (HP) and systolic arterial pressure (SAP) reflects the integration of the baroreflex with central autonomic commands and positive-feedback reflexes. We investigated whether in human subjects, the contributions of baroreflex and non-baroreflex mechanisms to the control of HP differ among wake-sleep states. SAP (Portapres, FMS), HP, and the wake-sleep state were monitored for 48 hours in 15 non-obese adults (7 males) without obstructive sleep apnoea syndrome. The fractions of spontaneous SAP ramps associated with baroreflex (baroreflex effectiveness index, BEI) and positive-feedback (non-baroreflex effectiveness index, NBEI) changes of HP were computed with validated techniques. The time series of HP and SAP were then low-pass filtered (<0.15 Hz) and their cross-correlation function (CCF) was computed on 5-min windows. The results were analyzed with Friedman and Wilcoxon tests (significance at $P<0.05$). BEI was significantly higher in the deep (3 and 4) stages of non-rapid-eye-movement sleep (NREMS) than either in quiet wakefulness (QW) or rapid-eye-movement sleep (REMS). NBEI was significantly lower in deep NREMS than in the light (1 and 2) stages of NREMS, QW, and REMS. In each wake-sleep state, $>80\%$ of SAP ramps had a duration of 3 heart beats. At a longer time scale, a positive correlation between HP and the previous SBP values, which is consistent with baroreflex control, was evidenced by the CCF in all states but QW. The maximum CCF value was significantly higher in deep NREMS than in any other state, suggesting the greatest baroreflex contribution to HP control. The CCF also showed a negative correlation between HP and the subsequent SBP values in each state, consistent with central autonomic commands. The minimum CCF value was significantly lower in deep NREMS than either in light NREMS or QW, suggesting a lower contribution of central commands to HP control. These results indicate that in human subjects, the contributions of baroreflex and non-baroreflex autonomic drives to the control of HP vary consistently among wake-sleep states at different time scales. Deep NREMS entails the greatest baroreflex contribution to HP control and a low effectiveness of central commands and positive-feedback reflexes.

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Mobile phone battery affects EEG-determined sleep structure

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Increasing evidence from electroencephalogram (EEG) studies suggest that electromagnetic fields (EMFs) emitted from mobile phones alter sleep/waking neurophysiology. The EMF from a mobile phone combines: i) the radiofrequency (RF) fields transmitted via the antenna, and ii) the extremely low-frequency (ELF) magnetic fields stemming from the battery current drawn by the internal electronics. However, the contribution of each to affect the EEG is not known. Here, a GSM 900 MHz mobile phone was modified to separate the RF antenna from the phone's electronic components including the RF amplifier. This phone (thermally lagged) was then used for studying effects of the ELF magnetic field arising from the battery current supply (3.7 volts). The RF signal of the mobile phone was routed to a remote antenna situated 1.3 m away, pulse-modulated at 8 and 217 Hz by a base-station simulator. Ten healthy, right-handed men (age: 21.4 ± 0.9 y, range: 18–26 y), sleep restricted to 6 h, were exposed (blind) for 30 min to the ELF magnetic field and sham signal (nil-powered condition) separated by a week. Exposures commenced at 13:30, and given at the right ear. Continuous polysomnolographic (PSG) recordings were taken, with subjective sleepiness reports every 3 min only during exposure. Immediately after exposure, there was a 90-min sleep opportunity. The sleep structure (analyzed according to Rechtschaffen & Kales' criteria, 1968, EEG derivation C3-A2) was compared between two conditions using Wilcoxon signed-rank tests. After the ELF magnetic field exposure, there was a significant increase in stage 2 duration ($P = 0.02$), with no change in sleep latency ($P = 0.10$; defined as ''onset of first epoch of stage 2 sleep, continuous >3 min''), slow-wave sleep duration ($P = 0.39$), sleep efficiency ($P = 0.12$) or waking after sleep onset ($P = 0.68$). These findings imply that the mobile phone ELF magnetic field has a sleep maintaining effect. However, this outcome may be quite different when there is also a RF signal from the phone's antenna according to our previous findings.

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Sleep measures and motility trends in subjects who show ability to awake at preselected time

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Introduction: The ability to awake at a preselected time without the aid of external means has been ascertained by previous studies throughout subjective reports and objective recordings (Omwake and Loranz, 1933; Zung and Wilson, 1971; Lavie et al. 1979; Moorcroft et al. 1997). The aim of this study is to evaluate throughout the use of actimeter the sleep characteristics and motility time-course which could make a subject able to self-awaken at a preselected time.

Method: Seventeen young adults have been monitored by means of actigraphy for a baseline night and an experimental night during which subjects were asked to self-awake 1 h earlier than usual wake time. Sleep measures (sleep times, latency, duration and efficiency) and motility time-course of the baseline night sleep have been assessed and compared between subjects who successfully performed the task (successful subjects: $n = 9$) and subjects who did not (unsuccessful subjects: $n = 8$).

Results: Sleep measures do not differ between the two groups. As to motility time course, successful subjects display a linear increase throughout sleep ($y = 0.001\times \ -0.234$; $R^2 = 0.837$), whereas unsuccessful subjects do not ($y = -0.0001x + .035$; $R^2 = 0.024$).

Conclusions: A progressive increase of motility level throughout sleep is a prerequisite to allow subjects to correctly self-awake at a preselected time.

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Dawn and dusk: care home sleep routines and participation in activities

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This paper presents findings on sleep patterns and activity levels of older people living in care homes. Participating in activities not only increases positive mental wellbeing but also physical health and can even prevent falls. Care homes have specific routines related to resident's bedtimes and getting up times. This paper examines how the routines of the care home, in relation to the start and end of the day relate to the amount and nature of activities undertaken by the residents. Over a period of two weeks, 120 care home residents in 8 care homes completed 24 h diaries which recorded their sleep patterns and their day to day activities. Resident's activities were recorded on six separate occasions on each day; two simultaneous activities could be recorded. This produced 168 possible activities over the two week period ($6\times2\times14$). Activities were categorised as 'active' such as, organised by the home and going to the shops and 'passive' such as, napping, watching TV, reading and sitting. On average, residents undertook 80 'passive activities' over the two week period, but only 10 activities that were classified as 'active'. Time of going to bed influenced the number of activities undertaken; those going to bed later engaged in both more 'active' and 'passive' activities. However, residents getting up times, both early and late, had minimal effects on the amount of activities undertaken. Therefore later bedtimes were related to increase in activities, suggesting that activity may stimulate rather than tire care home residents. However, only 1% of evenings in the two week period across the 8 care homes offered evening organised activity. Our findings suggest care homes should provide more organized motivating activities during the evening period.

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Influence of presleep exercise on sleep is altered depending on both exercise intensity and exercise timing

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Presleep exercise is considered to have an effect on sleep via post-exercise physiological changes. Exercise intensity and exercise timing may thus be important factors for these effects. This study examined the effects of exercise intensity (Study 1) and exercise timing (Study 2) on sleep and on post-exercise physiological

changes. Subjects in studies 1 and 2 comprised 13 and 12 physically active male students (age range, 19–21 years), respectively. After an adaptation night, subjects completed experimental treatments. Study 1 consisted of baseline non-exercise (NE) and 2 exercise intensity conditions (ME, moderate intensity exercise day with 60% HRR (heart rate reserve); and VE, vigorous exercise with 80% HRR). Subjects completed 40 min of treadmill running 1 h before bedtime. Study 2 consisted of the NE and 2 exercise timing conditions, in which subjects completed 60% HRR running at 1 h (1HE) or 3 h (3HE) before bedtime. Subjects maintained a sedentary condition except for the exercise period, going to bed at 23:00 and getting up at 07:00. Sleep was assessed by standard polysomnographic (PSG) recordings and scoring procedures. In addition, subjects underwent 24-h recording of HR and rectal temperature (Tr). Bonferroni correction test was employed to compare scores. In Study 1, we observed a significant increase in sleep onset latency (SOL) (+14.8 min) and a decrease in REM sleep (-16.3 min) only after VE compared to NE ($P<0.05$). At bedtime on the VE night, we also observed significantly higher values both in Tr (+0.5 degrees C) and HR (+23.2 beats min^{-1}) compared to NE ($P<0.05$). In Study 2, PSG results showed significant decreases in SOL (-9.2 min) and increases in slow-wave sleep time (+10.6 min, particularly in the first half of the whole night) for 3HE compared to 1HE ($P<0.05$). HR variables were significantly lower for 3HE than for 1HE at bedtime (-6.6 beats min^{-1}) and during the first half of the night (-2.1 beats min^{-1}) ($P<0.05$). These results support the hypothesis that the influence of presleep exercise on sleep might be altered depending on both exercise intensity and exercise timing, and the physiological recovery process might play an important role in these effects.

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Music, a sound way to sleep?

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Music is one of the most used self-help strategies to promote sleep. The clinical and systematic use of music as a complementary treatment in various medical conditions has been subject of study in the last decades. We performed a systematic review and meta-analysis to evaluate the efficacy of music interventions for improving the sleep quality of adult and elderly patients with primary or secondary sleep complaints. We define music interventions as therapeutic interventions in which music is the single or key ingredient. The music can be accompanied by relaxation instructions or relaxation supporting measures. Music must have been intentionally applied for the promotion of sleep quality in a passive way. That is, listening to music while resting or relaxing. Two researchers conducted a search of trials in Embase, Medline, Cochrane, Psychinfo and Cinahl databases. Included were recently published (after 1990) randomized controlled trials (RCTs), reported in English, German, French and Dutch. Excluded were studies involving subjects suffering from neurological or severe cognitive disorders and studies performed under laboratory conditions. The researchers independently assessed the quality of RCTs using the Delphi list. Only studies with a score of 5 points or higher were included. We choose sleep quality as the primary outcome measure for the intervention. Four RCTs with a total of 140 participants in intervention groups and 109 controls met our inclusion criteria. A pooled analysis was performed based on a fixed effect model. Music interventions have a moderate effect on the sleep quality of patients with sleep complaints (standardized mean difference -0.63; 95% CI: -0.87, -0.39). Our results suggest that music interventions might offer significant benefits for the improvement of sleep quality. Since no adverse effects of music interventions are reported, and they can be applied without intensive investment in training and materials, they could contribute to the array of non-pharmacological treatment options for sleep problems.

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What is more important for the normal pregnancy: the total amount of sleep or sleep during the proper phase of the circadian rhythm?

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It was shown that neurons of cortical areas during the state of sleep are involved in analysis of information coming from the internal organs (Pigarev, 1994; 2005). This observation was used as an argument in favor of the idea that during sleep computational power of the cerebral cortex contribute to higher visceral control. Our previous experiments confirmed importance of deep sleep for normal pregnancy: even a short period of sleep deprivation (3 consecutive days, 3 h per day) before mating or during the first week of pregnancy significantly increase mortality of rat offsprings. It is known that circadian factors are very important for sleep regulation (Tobler, Borbély, 1990). The goal of this study was to investigate whether the impairment of pups vitality in our experiments was caused by reduction of total daily amount of sleep after sleep deprivation or by shift of sleep to uncommon phase of the circadian rhythm. Electrodes for standard polysomnogrphy to discriminate the states of SWS, REM and wakefulness were implanted in six 3 month-old female Wistar rats. Recordings were performed in freely moving animals during 3 days of baseline, 3 days of sleep deprivation (11:00–14:00, a period characterized by strong sleep pressure) and 3 days after the sleep deprivation. "Carusel device" (Rechtschaffen et al. 1989) was used to provide sleep deprivation. The room was kept on a 12 h/12 h light-dark cycle, light on at 8:00. It was found that inspite of sleep deprivation the total amount of both SWS and REM was the same during 3 days of sleep deprivation and in the next three days. It was connected with the increase of sleep duration in dark period (so called sleep rebound). These results let us conclude that not only the maintenance of daily quantity of sleep but also proper coincidence of the sleep with particular phase of circadian rhythm may be important for normal functioning of visceral systems during the pregnancy.

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Who is to blame if snoring becomes a problem?

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Objectives: To find out whether snoring becomes a problem because of the annoyance of the sound or the noise sensitivity of the bedpartner we applied psychoacoustic methods.

Methods: During an automatized hearing experiment 50 snoring sequences of 10 patients were randomly presented to 10 examiners for evaluation of their annoyance, making 500 scores. The mean annoyance score for each snoring sound and the covariance parameters for rater and snoring sounds (REML-method) were calculated.

Results: The average annoyance rating of all snoring sequences was 62.8 ± 22.1; the most acceptable snoring sequence rating was 49.2 ± 28.0, the most annoying rating was 77.7 ± 16.4. The

covariance parameters were estimated as 27% for the rater and 21% for the snoring sound.

Conclusion: Snoring sounds from different patients vary in their annoyance, which is not reflected in the snoring index. Therefore it seems useful to pursue the development of psychoacoustic methods for the measurement of snoring. The noise sensitivity of the bedpartner is at least equally responsible as the snoring sound itself in leading snoring to become a problem.

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Yawning and sleepiness in young and older adults

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Introduction: Yawning is linked with both sleep-wake and sleepiness rhythms (Provine, 2005; Zilli et al. 2007). Since aging modifies circadian rhythms, yawning frequency and its time course in elderly individuals should differ from young adults.

Method: Thirteen aged healthy subjects (77.15 ± 4.09 years) and 12 young adults (24.41 ± 3.31 years) were instructed to keep their habitual sleep schedules for 3 consecutive work-days, during which they were required to signal every yawning occurrence and to evaluate hourly their sleepiness level.

Results: Yawning frequency is reduced in aged subjects. As to the time course of yawning frequency, aged subjects showed earlier morning peak and evening rise compared with young adults, and they displayed two additional minor peaks in-between. Changes as a function of age in the time course of yawning correlated with changes in the time course of sleepiness. Nevertheless, yawning peak after the transition from sleep to wakefulness corresponds to low sleepiness level in aged subjects.

Conclusions: Aging modifies yawning frequency and its time course. Moreover, since in the elderly the relationship between sleepiness and yawning at the awakening differs from that observed in young adult, we suggest that sleepiness level and sleep-wake transitions could separately affect yawning.

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Investigation of sleep quality in subjects living close to mobile phone base stations–results from an experimental field study

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There is some evidence that sleep parameters are influenced by exposures to mobile phone fields, i.e. at field intensities below accepted limit values. For residents living close to mobile phone base stations, the subjective perception of a disturbed sleep is among the most often mentioned complaints attributed to the EMF exposure. The aim of the present study is to analyse the impact of electromagnetic fields of mobile phone base stations on sleep of residents in an experimental setting using a double-blind, sham-controlled, balanced randomized cross-over design. Altogether 397 subjects (>17 years) from 10 villages in various parts of Germany participated in the study. The mean age of participants was 45.0 ± 14.2 years, the range was 18 to 81 years. Twentyone subjects (5.3%) had to drop out of the study before the end due to illness (own or of relatives) or job-related reasons. Data acquisition comprised individual measurement of EMF-exposure, questionnaires to characterize the sample (LISST, PSQI, ESS, Zung scales of anxiety and depression (SAS and SDS), attitude towards mobile communication, and NEO-FFI), and subjective (morning and evening protocols) and objective (derived from frontal EEG and EOG recordings performed in an ambulant setting at home) sleep data. For each participant subjective and objective sleep data were recorded for twelve nights. Exposure was realized by an experimental base station working constantly with a well defined emission. The base station was manipulated to ensure blinding. Analysis of the questionnaires to characterize the sample showed that study participants are representative of general population based samples. The analysis of the subjective and objective sleep data in relation to exposure is under way and will be finalized by the end of March 2008. So it will be possible to present the data at the meeting.

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Determining the duration of sleep onset latency (SOL) in normal sleep: a cross-sectional comparison of SOL in normal and poor sleepers

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Introduction: Research typically focuses on the 'abnormal' and on therapies to decrease 'disease'. Ideally, however, the ultimate goal of therapy is not just to achieve symptom control but also to return the individual to normalcy. Without data on what latency constitutes SOL in normal sleep the element of stimulus control (Bootzin, 1972) 'get up and go to another room', found in every CBT for insomnia package, would be somewhat arbitrary. Interestingly, the amount of time permitted awake in bed prior to 'getting up and going to another room' varies from trial to trial: a few minutes to 25 min range. This cross sectional comparison examined the duration of subjective SOL that is typical of normal sleep so as to suggest what duration would be the best cut-off to include normal sleepers and to exclude poor sleepers (sensitivity/specificity).

Methods: Eighty volunteers (45 f, 34 m), aged 20 to 60 years, all self-reported as free from psychological or neurological disorders completed a sleep questionnaire (PSQI: Buysse et al. 1989) and a sleep diary every morning for a week. The mean PSQI score for the normal sleepers was 2.5 (SD 1.0) and for the poor sleepers was 10.0 (SD 1.9).

Results: Statistical analyses of the sleep diary data (SOL, WASO and total sleep time) confirmed the initial differentiation of the two groups on the basis of their PSQI scores (all ps = 0.0001). Analysis of sensitivity and specificity data, to establish the upper limit of normal sleep behaviour at sleep onset, indicated that a SOL of 15 min is the best cut-off to include normal sleepers and exclude poor sleepers (correctly identified 92% of normal sleepers and correctly excluded 86.7% of poor sleeper).

Conclusion: The present results indicated that a window of 15 min might provide the optimal cut-off when normalcy in sleep onset is considered desirable. It seems reasonable, therefore, to ask people complaining of insomnia to apply the stimulus control instruction 'get out of your bed and go into another room if not asleep within a quarter of an hour'. Bearing in mind that the ultimate goal of therapy is reinstating the person with insomnia as a normal sleeper, by setting a quarter of an hour limit, the goal of sleep normalcy in the treatment programme is reinforced.

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Evaluation of sleep disturbances due to environmental influences using a newly developed index

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This analysis aimed at the development of a sleep disturbance index (SDI) which allows a reliable estimate of physiological sleep quality and its alterations due to environmental influences such as noise. Seven variables, repeatedly reported to alter during noise exposure were derived from polysomnograms of a reference sample of 38 men and 28 women (19–34 yrs) as recorded in quiet conditions in the laboratory after at least one habituation night. The variables were then submitted to a principal component analysis. The scores of the first principal component that explained 35% of the variance were used for the calculation of the SDI. Reliability was ascertained by application of the SDI to a quiet night each of 82 persons of the same age range from two other laboratory studies where the index-value did not differ from that of the reference sample. Validity was verified by significantly lower index-values for quiet nights than for noisy nights of 50 persons (25 men, 25 women, 19–28 yrs) and for the first night in the laboratory of 62 persons (37 men, 25 women, 19–34 yrs). Moreover, the index-value increased with the age of the overall 261 participants in two laboratory studies and a field study whose age varied between 18 and 68 years. The SDI may facilitate the interpretation of sleep disturbances caused by environmental influences and its application would improve the comparability of studies performed in this area.

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Rhythmical theta activity in REM sleep: two atypical cases

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Most rhythmical theta activity appearing in human REM sleep scalp EEG corresponds to sawtooth waves (STW) or is regarded as non-specific. To date, STW origin and significance remain unclear. We describe two instances of prominent, atypical rhythmic theta activity in REM sleep EEG which may not be considered as normal STW activity. Case 1 is a 48-year-old female who underwent evaluation and treatment for mild sleep respiratory disturbance, headaches, depression and nightmares. Two standard PSG studies (one under amytriptiline and phenobarbital, another under carbamazepine and maprotiline) showed frequent trains of theta (5–6 Hz) rhythmic sharp-contoured activity during NREM S1, clearly present (although less frequent) also during REM sleep. Visual inspection of REM sleep did not show systematic association with arousals or obstructive respiratory events. There was no resemblance to REM-sleep STW, which were also present albeit infrequent. Full-coverage EEG showed the same pattern of waxing and waning, prolonged theta rhythmic activity, more prominent in temporal areas in early drowsiness, compatible with psychomotor variant. In this patient, headache and nightmare presence, medication changes and REM AHI reduction did not appear to affect the occurrence of psychomotor variant neither in NREM nor in REM sleep. The use of tricyclic drugs is not usually associated with this EEG pattern. To our knowledge, psychomotor variant has not been previously described in REM sleep. Case 2 is a 36-year-old female who undertook a standard sleep study in the context of multiple sclerosis, nocturnal headache and non-restorative sleep. Cranial MRI showed more than 2 white matter lesions. PSG was uneventful except for sleep spindle assynchrony in NREM sleep and bilateral, symmetrical, synchronic medium voltage, sharp prominent theta activity over anterior areas, often appearing as a varying superposition of two basic (4 Hz and 8 Hz) rhythms. Waking alpha had normal appearance. REM STW were not conspicuous. These findings are discussed in relation to REM sleep physiology.

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Facial muscle activation during slow wave sleep and REM sleep and its relation with rapid eye movements

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Muscular antigravitatory atonia is one of the main REM sleep features. During this stage, a wide limbic activation has been demonstrated. Facial musculature has both an antigravitatory and a mimic (emotional expression)function, and has an innervation from limbic structures. During W it has been shown an activation from zygomatic musculature with positive emotions, whereas corrugator musculature activates more with negative emotions. Yet, mimic facial musculature activity has not been analyzed during different sleep stages of the whole sleep cycle, neither its relation with Rapid Eye Movements (REMs) of REM sleep. We hypothesize that Facial Muscle Contractions (FMC) will be stronger during REM sleep and that will correlate with REMs. The aim of the present study was to analyze the FMC from 6 mimic facial muscles, during all sleep stages, and to analyze their relation with REMs of REM sleep.

Method: 12 healthy volunteer subjects were studied for two consecutive 8 hr. sleep recordings. Facial EMG recordings were obtained from left Occipito-Frontalis, Corrugator Supercili, Orbicularis Oculi, Levator Labi Superioris, Zygomaticus Major and Zygomaticus Minor. EEG, EOG and EMG were acquired and scored according to international criterion. FMC were quantified whenever amplitude exceeded by 50% the background EMG activity. FMC were quantified as: phasic and tonic. During REM sleep, REMs were quantified and correlated to facial muscle activity. The differences between all previous data were statistically evaluated by ANOVA and post hoc tests.

Results: A significant increase was observed during REM sleep's whole facial activation, whereas Delta Stage showed the least of FMC. Zygomaticus Major,Minor and Corrugator muscles were the most active among phases, REMs showed a significant correlation with the same muscles. Our results allowed us to conclude that Facial Muscles have a greater amount of activity during REM sleep than during SWS 1, 2 and Delta. The most active muscles during W showed a higher activation during sleep. REMs number correlated with the same muscles. These results allowed us to confirm that limbic activation during REM sleep is also manifested through facial muscle activation, and that REMs may play a critical role in this muscular activity.

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The effects of occupational low frequency noise and whole-body vibration exposure during daytime and nocturnal sleep architecture in helicopter pilots

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Objective: The purpose of the present study was to verify the effects of occupational low frequency noise (LFN) and whole-body

vibration daytime exposure related to impulsive noise produced by the helicopter blade slap upon nocturnal sleep architecture in military helicopter pilots.

Methods: Ten male active pilots, from the Portuguese Air Force (PAF), with ages between 35 and 55 years old, exposed to helicopter noise in 3500 h flight^{-1}, were studied. Thirteen workers from the PAF, not exposed to LFN in occupational environmental, in the same age range and equal physical characteristics, were used as controls. All the individuals agreed to participate in the study. None of them was exposed to LFN source in home residence during the night. All the subjects carried out a polysomnography and fulfilled the Pittsburg Sleep Quality Index (PSQI) and the Epworth Sleepiness Scale (EP). Statistical analysis was done by using the Student T test.

Results: The pilots had a significantly lower sleep efficiency ($P = 0.005$) and increased of sleep latency ($P = 0.045$), arousal index ($P = 0.019$), wakefulness after sleep onset ($P = 0.0019$), body movements ($P = 0.029$), body mass index ($P = 0.043$) and PSQI ($P = 0.001$) than the control group. There was no difference in the proportion of the different sleep stages, ESS scores and age.

Conclusions: Helicopter pilots exposed to occupational low frequency noise and whole-body vibration during daytime flight show significant changes in nocturnal sleep architecture, and have increased sleep com. This study aims to raise awareness of the damages caused by this kind of noise upon sleep architecture and sleep quality, taking into account the pilots sleep complaints. A larger study or different methodology is required to confirm these findings.

P493

Efficacy of mindfulness meditation practice on sleep architecture

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Introduction: Meditation practice helps to regulate the brain activity and intense meditation practice helps to attain the higher states of consciousness during sleep. The Present study is designed to evaluate the efficacy of Mindfulness meditation practice on age-associated changes in sleep architecture.

Methodology: The study was accomplished on two groups of Healthy Male volunteers-Meditation (Vipassana) group ($n = 38$, mean age 41.97 years) and Control group ($n = 34$, mean age 45.20 years). Whole night polysomnography was carried out during their habitual sleep time. Sleep architecture and EEG power spectra were analysed in subjects with sleep efficiency index more than 85%. EEG power spectra were obtained from artifact free epochs across all the sleep states in delta, theta, alpha and beta band.

Results: Controls subjects showed a temporal pattern of age-associated changes in sleep states. The NREM S2 was significantly enhanced with significant decrease in slow wave sleep (SWS). EEG power spectra showed an antero-posterior shift in NREM sleep. Vipassana practioneers showed a significant decrease in NREM S2 whereas the SWS and REM sleep state significantly increased. They did not show any age-associated antero-posterior shift of EEG power, however, showed a significantly higher frontal theta power during wake. During SWS theta and delta power was predominant in all the leads where as in control group it was found only in the occipital lead. Further during SWS, meditators showed less EMG activity with more theta-alpha power.

Conclusion: Mindfulness meditation practice helps to combat age associated changes in sleep architecture and can be considered as an intervention for sleep management in old age. Enhanced theta-alpha power with decreased EMG during SWS can be correlated with the higher states of consciousness.

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Optimal duration of power naps

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Power naps are helpful strategies to overcome increasing sleepiness and performance decrements in the early afternoon. Several studies have shown the positive impact of naps of different duration on performance after restricted night sleep or during night shifts. In the present study night sleep was not restricted in healthy young subjects and length of naps was varied between 10, 20 and 30 min bedtime and compared to resting periods of equal length. The study comprised 40 healthy subjects (20 female, 20 male), aged between 19 and 28 years (mean age 23.5+2.4 years) who underwent 3 different sleep and 3 different wake conditions in random order. Naps and resting wake conditions took place between 13:00 and 14:00 and were polygraphically recorded. All subjects performed three performance tasks (Psychomotor Vigilance Task = PVT, Simple Reaction Task = SRT, Flicker and Fusion Frequency = FFF) prior and after each nap or wake condition and filled in several subjective rating scales. During the observation period of two weeks, subjects wore an actigraph and kept a sleep log. All polysomnographies were visually scored according to the standard criteria of Rechtschaffen & Kales (1968). Mean sleep period time was 2.3 ± 1.6 min in nap condition 1 (time in bed: 10 min), 8.3 ± 4.6 min in nap condition 2 (time in bed: 20 min) and 15.5 ± 6.5 min in nap condition 3 (time in bed: 30 min). Performance in the PVT improved after the nap condition and deteriorated after the wake condition. The occurrence of sleep stage 2 led to significant reductions of reaction times in the PVT ($P < 0.01$). This effect was most prominent in the condition of 20 min time in bed. Subjects reacted slower after the resting period ($P < 0.05$). Performance in the SRT and FFF did not differ between sleep and wake conditions. Power naps of 20 min bedtime were most effective for improvement of reaction time.

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Sleep-wake patterns among college students during work days and days off

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Introduction: Previous studies among adolescents reported a longer sleep duration for females compared to males (Andrade et al. 1991; Levy et al. 1989; Teixeira et al. 2004). As female adolescents get older, this difference can increase due to new responsibilities, such as work, home duties and school activities.

Objectives: To evaluate sleep patterns among working College students, according to sex on work days and during days-off.

Methods: The study was conducted among College students working full-time jobs ($\geq$6 h per day) during week days (Monday-Friday) and attending evening classes (19:30–22:30 h) at

a public University in São Paulo, Brazil. The study group consisted of healthy males ($n = 23$) and females ($n = 23$), aged 21–26 yrs. Data collection took place in 2007. For seven consecutive days actigraphy measurements (Ambulatory Monitoring) were recorded. The students also recorded daily activities and sleep hours in a diary. Statistical analyses included ANOVA for repeated measures. In all analysis the level of significance were set to a 5%.

Results: The analysis showed that females obtained longer total sleeping time than males (Mean ± SD): males: 399 ± 59 min; females 436 ± 57 min ($P = 0.00$). Additionally, the mean total sleeping time during days-off (439 ± 71 min) was higher than during working days (396 ± 46 min) ($P = 0.00$). Also mean napping duration was longer during days-off (36 ± 49 min) than working days (7 ± 11 min) ($P = 0.01$).Other sleep-wake variables (sleep latency, number and duration of nocturnal awakenings and sleep efficiency) were not statistically significant comparing males and females, neither during work days and days-off.

Conclusions: The restricted time available to sleep during work days due to work and study can lead to increased sleep duration during days-off. Sleeping bouts were longer among females, which would suggest a greater recovery sleep period for females.

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Psychological characteristics and young drivers' risk of sleep-related car crashes

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Sleepiness is often a contributory factor in car crashes, especially in young drivers. Although young drivers as a group are more likely to be exposed to the risk of sleep-related accidents, this does not mean that all young drivers are equivalent. Individual differences in driving habits, in risk perception, and in susceptibility to sleepiness appear to contribute to sleep related crash risk. All these factors may be related to psychological characteristics. Thus, identifying psychological traits that are related to sleepiness episodes while driving would strengthen our understanding of factors that may contribute to elevated risks of sleep related accidents. To this aim, a questionnaire survey was administered to 1008 young drivers (56,8% Male; mean age = 18,33 ± 0,68). The questionnaire measured general personality traits [1], normlessness [2] driving anger [3], locus of control orientation in driving [4], circadian typology, night-time driving behavior and driver sleepiness episodes. Hierarchical cluster analysis was used to derive the number of subtypes within the novice driver sample. This number was then forced in the final analysis using k-means clustering. The Ward's cluster analysis suggested a three clusters solution. The distribution of cases provided by the k-means analysis indicated that Cluster 1 was a relative high-risk group. The individuals in this cluster reported the highest level of driving anger, sensation seeking and normlessness. They also reported an higher external locus of control and resulted evening-types. Finally, compared to individuals in the other two clusters, the cluster 1 individuals reported to have experienced sleepiness attack while driving more often. These results have implications for driving training programs designed to address the young drivers' risk of sleep-related car crashes.

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P497

Sleep and road traffic noise: day by day variability in actigraphic recordings and sleep diaries

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Sleep disturbances are regarded as one of the most deleterious effects of nocturnal noise exposure. But noise exposure not only affects the sleep period itself, it also compromizes daytime functioning, causing impairments in mood, performance and general well-being. In this field study, we assessed the objective and subjective sleep quality of people living in areas with a high density of road traffic noise in the Brussels Capital area. 20 volunteers completed a 7-day sleep log and were asked to wear an actigraph during the night. Sleep variables (Time in Bed (TIB), Total Sleep Time (TST), Sleep Latency (SL), Wake after sleep onset (WASO) and Sleep Quality (SQ) were assessed from both instruments and compared. Road traffic noise [LAeq (22 h–08 h)] was measured inside and outside the bedroom during 7 nights using Integrator Class 1 & 2 Sound Level Meter (Metravib). Significant day-by-day variability was found only for noise measurements outside the bedroom. Pearson correlational analysis shows a significant positive correlation between actigraphy and sleep logs for TST ($r = 0.64$) and SL ($r = 0.52$). TST as measured with the actigraphy was also negatively associated with the noise levels inside the bedroom. This analysis only partially confirm our hypotheses and the next step in our study, a test-retest situation in areas with high density of road traffic noise in the Brussels Capital, should provide a more elaborated view of the effects of road traffic noise on sleep.

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Subjective sleep latency and total sleep time compared to polysomnographic data: a possible link between perception of sleep onset and latency to slow wave sleep

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Background and Objectives: Insomniacs tend to perceive wake when asleep, underestimating sleep times compared to PSG (1, 2). When extreme this is termed sleep state misperception. We compared Objective and Subjective Sleep Latency (OSL & SSL) and Total Sleep Time (OTST & STST) in a heterogeneous group of patients who had undergone PSG.

Patients and Methods: OSL & SSL and OTST & STST were retrospectively compared using data from 55 patients (37 male, 43.7 ± 14.9 yrs). Diagnoses included respiratory (25) and non-respiratory cases (30–4 with insomnia). OSL to sleep onset (OSL-SO) was from lights out to 3 consecutive epochs of stage 1 sleep or 1 epoch of any other sleep stage. OSL to stage 2 sleep (OSL-S2), slow wave sleep (OSL-SWS) and REM sleep (OSL-REM) were from lights out to the first epoch of the respective sleep stage. OTST was defined as total time asleep from lights out to lights on excluding all wake. Subjective data were taken from a patient questionnaire completed the morning after PSG. Statistical analysis for all but TST used non-parametric tests and data are presented as median (IQR). TST met the assumptions for parametric analysis and therefore the dependent *t*-test was used.

Results: Eighty-four percent of patients overestimated latency to sleep onset and seventy-five percent underestimated TST. Significant differences were observed between SSL [30.0 (30.0) mins] and OSL-SO [13.5 (20.5) mins], OSL-S2 [15.0 (23.0) mins] and OSL-REM [144.0 (155.0) mins] ($P < 0.001$). SSL and OSL-SWS [37.0 (58.0) mins] were not significantly different ($P = 0.436$). There was a significant difference between OTST and STST [mean (SD) 427.8 (96.5) versus 348.5 (140.7) mins, $P < 0.001$].

Conclusion: Most patients were inaccurate in estimating SL and TST. Discordance between subjective and objective nocturnal sleep times is not confined to insomnia. The clinical significance of this discrepancy is not clear and requires more extensive study of diagnostic subgroups. Patients' subjective reports of latency to sleep onset approximated to SWS latency. This observation may have clinical utility but needs further study.

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P499

The contributing role of alcohol and sleepiness in vehicle accidents

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Study Objective: Both sleepiness and blood alcohol concentrations (BACs) can influence time distribution of vehicle accidents (VA). Alcohol can impair reflexes and vision. Sleepiness can worsen the alcohol intake effect. We studied the relationships between sleepiness and alcohol and their contribution to crash's risk.

Design: Data concerning car accidents occurred in Liguria (It) during the year 2005 were collected by police, including on-the-spot or in-hospital BAC test and self-administered questionnaires concerning sleep. 3016 VA out of 9321 (ISTAT) were available for the analysis. The hourly distribution of VA univocally ascribed to sleepiness by police (SA) were supplied by the Italian National Institute of Statistics (ISTAT) and by the Italian Automobile Club (ACI).

Measurements: We compared the hourly distribution of not-alcohol-influenced (NAI) and alcohol-influenced (AI) crashes by Kolmogorov-Smirnov test, also distinguishing between slightly-alcohol-influenced (SAI) and heavily-alcohol-influenced (HAI) drivers. The influence on accidents of two possible risk-factors: circadian sleep propensity and driver's BAC, was evaluated by polynomial regression.

Results: The hourly distribution of the ratio between the number of accidents and the traffic resulted similar in the alcohol-influenced (AI, SAI, HAI) and in the NAI accidents. All the distributions were similar to the SA one. Significant differences related to the presence of the alcohol risk-factor emerged between each alcohol influenced group (AI, SAI, HAI) and NAI accidents in a narrow daypart between 19 and 23, when the risk of alcohol-related accidents' was higher and associated with higher alcohol intoxication levels in presence of low levels of sleep propensity. During nighttime, we found an increased risk of accidents corresponding to high values of sleep-propensity, also sustained by SAI accidents, i.e. with alcohol intoxication levels lower than the legally sanctioned BAC threshold.

Conclusions: Driving impairment can be influenced both by alcohol and by sleepiness. The accident's risk associated to BAC involved higher alcohol intake in normally alert drivers while during periods characterized by higher sleep propensity lower BACs were associated to high crash's risk.

P500

The impact of a 10-week physical exercise program on sleep quality, cognitive and somatic pre-sleep arousal

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Introduction: Physical exercise has been promoted as part of the non-pharmacological treatment of insomnia, as it increases total sleep time and the amount of slow wave sleep. We examined whether a medium level of physical exercise during a 10-week running program, resulted in sleep quality changes in healthy sleepers. Also, we investigated the impact of the increase in physical exercise on pre-sleep arousal symptoms, as these can mediate the influence on sleep.

Method: The Pittsburgh Sleep Quality Inventory (PSQI), Epworth Sleepiness Scale (ESS) and Pre Sleep Arousal Scale (PSAS) were administered to participants of a Belgian 'Start-to-run' program, both at the start and at the end of the program (training group): 13 male and 23 female healthy adults, free of CNS medication, mean age of 40.58 years (SD = 9.7 y), not involved in physical exercise at the start of the program. The 10-week program consisted of three training sessions of 20 to 40 min a week. The participants who discontinued the program prematurely, were planned to be included as a control group (N = 7).

Results: The number of drop-outs was too low to allow a proper statistical comparison between the control group and the training group, so a comparison was made between pre and post scores only in the training group. PSQI scores were significantly lower at the end as compared to the beginning of the program ($F(1,35) = 19.21$; $P < 0.001$). Specifically, significant changes in sleep latency, total sleep time and daytime functioning were found (all $P < 0.05$), whereas no significant changes in medication use or in the presence of sleep disorder symptoms were reported. These effects were accompanied by significant decreases in daytime sleepiness (ESS) ($F(1,35) = 4.84$; $P < 0.05$) and in pre-sleep arousal symptoms (PSAS) ($F(1,35) = 9.30$; $P < 0.01$).

Conclusion: Participation in a 10-week running program had a positive impact on subjective sleep quality in healthy sleepers, who previously did not physically work out. This went together with lower levels of daytime sleepiness. Finally, a mediating role of a reduction in pre-sleep arousal symptoms can be hypothesized from the present findings. However, a proper control group remains to be established.

P501

Difference between going to bed and deciding to go to sleep: what can it tell us about adolescents' activities in bed

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Various electronic devices are commonly present in adolescents' bedrooms. In such living circumstances going to bed may not necessarily reflect wish to initiate sleep. In order to evaluate sleep patterns of adolescents living in such circumstances we constructed a sleep diary paying special attention to sleep onset behaviours, which included questions on time of going to bed, time of decision to go to sleep, time of falling asleep, as well as various activities performed in bed. A group of 16-year old secondary school students ($n = 97$) participated in the study. They kept sleep-wake diaries at bedtime and upon awaking for 14 consecutive days, one week when attending school in the morning and the other in the afternoon shift. The percentage of adolescents who performed some activity after going to bed ranged between 37% and 59% on different days. The most common activity in bed was watching TV. The group of adolescents who performed some activity in bed went to bed earlier than the group who went to bed only to sleep, on six days out of 14. However, performing activity in bed on those days did not affect their sleep time. On three days when both groups of adolescents went to bed at the same time, the adolescents performing some activity in bed subsequently decided to go to sleep and fell asleep later than adolescents going to bed only to sleep. Nevertheless, it did not affect their sleep time either. If difference is made between time of going to bed and time of decision to go to sleep, adolescents' activities in bed are related to

advanced bedtime on some days and delayed decision to go to sleep on other, with no consequent impact on sleep time.

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P502

The impact of traffic noise on the sleep quality of truck drivers

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Introduction: Sleepiness and disturbed sleep are important safety issues for truck drivers. We investigated whether the road traffic noise recorded at a motorway service area has a negative impact on restorative sleep and alertness of long-haul truck drivers.

Methods: 16 male professional truck drivers (age: 40.9 years, SD = 8.0; Body-Measure-Index: 25.9 $kg\,m^{-2}$, SD = 2.5) participated in a repeated, randomized measurement design consisting of 2 conditions (Noisy versus Quiet). As a "sleep lab on wheels" we used a Mercedes-Benz Truck (Actros II, Typ 1846), in which the drivers could be exposed to original recordings of motorway traffic noise (mean noise level: 41.6 dB_A). All subjects slept for three consecutive nights in the upper berth of the truck with the 2 experimental conditions following one adaptation night. To assess objective sleep quality we used standard PSG. Subjective sleep quality was evaluated by ratings and questionnaires. Daytime sleepiness was measured in the morning using sustained attention tests (PVT, Mackworth-Clock), pupillography and standardized subjective scales (SSS, TSS).

Results: All objective measures of sleepiness demonstrated no significant differences between both experimental conditions (all ps $>.150$). No increased subjective sleepiness or augmented symptoms of tiredness could be recorded after noisy nights. In contrast, subjective sleep quality was consistently rated poorer for nights with exposure to traffic noise. In the PSG, sleep stage 2 significantly increased during the noisy nights compared to the control condition (55.0% versus 51.2%; $P = 0.047$) accompanied by reduced REM sleep and slow wave sleep. For noisy nights the truck drivers even revealed shorter sleep latencies to sleep stage 2 than for quiet nights (14.8 min versus 27.9 min; $P = 0.033$).

Conclusion: Professional long-haul truck drivers seem to be quite habituated to increased levels of traffic sound. They revealed less noise sensitivity during the night and less impairment of daytime functioning in the morning than we expected. However, possible negative and cumulative effects of consecutive noisy nights-instead of one single night-should be taken into account and warrants further research.

P503

Moderate exercise two hours before bedtime significantly improves sleep

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Background: This study set out to contrast the effects of exercise taken either 2 h or immediately before bedtime on subjective and objective sleep measures as well as waking mood.

Methods: Twelve healthy participants (2 male, 10 female) with an average age of 25 years, who were normal sleepers (assessed by Pittsburgh Sleep Quality Index) participated in a repeated measures design with treatment order based on latin squares comparing the effects of following a 20 min exercise video either 2 h or immediately before bedtime, compared to a no exercise control. Each treatment was repeated for 2 consecutive nights at home with a minimum of 1 night recovery between conditions. Objective measures included actiwatches (CNT) to assess sleep and an ear thermometer (Omron) to record temperature. Subjective measures included a modified Leeds Sleep Evaluation Questionnaire (LSEQ) and a Bond & Lader Visual Analogue Scale (VAS) to assess waking mood.

Results: Ear temperature was lowest in the control condition and highest after exercise immediately before bedtime (+0.23C). Significant effects with actigraphy included reduced sleep onset latency following exercise at 2 h in comparison to immediately before bed, and improved sleep efficiency for exercise at 2 h compared to the control and marginally in comparison to immediate exercise, though sleep duration and waking were unaffected. Subjective sleep (LSEQ) indicated significantly improved sleep onset with exercise at 2 h, and marginally better for the control compared to exercise immediately before bed. Participants were significantly more relaxed in the control condition compared to exercise immediately before bed, which also produced trends for increased negative emotion both that night and the morning after. Post treatment reflections by participants rated exercise 2 h before bedtime as resulting in the quickest sleep onset, best quality sleep and feeling most refreshed and least tired next day, supporting the findings with LSEQ and VAS.

Conclusions: This study provided consistent findings that exercise earlier in the evening benefited sleep quality, whilst exercise at bedtime disturbed sleep.

P504

The impact of cold water immersion on recovery sleep in elite athletes

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Recovery from exercise is an important factor in elite athletic performance, especially in situations where the athletes must engage in successive days of strenuous competition. Cold water immersion (CWI) is commonly used as a post-exercise recovery strategy because it reduces muscle inflammation, oedema and pain and enhances subsequent exercise performance (1). There is also strong anecdotal support for improved sleep quality and quantity following CWI but this has not been objectively confirmed. Twelve nationally competitive cyclists completed two simulated race protocols over a two week period. Each race protocol consisted of three consecutive days of cycling training. At the completion of each training day, cyclists underwent a recovery intervention of either 10 min of CWI (11–12 °C) or placebo in a repeated measures, crossover design. Night-time sleep was assessed during each race protocol using wrist activity monitors and sleep diaries. Data were analysed using a repeated measures ANOVA. Similar bed times (~22:00 h), get-up times (~5:50 h) and time in bed (~7.8 h) were reported during each race protocol. For night-time sleeps, sleep latency and time spent awake were similar following CWI and PL, as was sleep efficiency (~81%). Total sleep time was not different across the conditions and averaged ~6.5 h on most nights. Subjective assessments of sleep quality and post-sleep fatigue were also similar. In the present study, night-time sleep parameters were not different between CWI or PL. Regardless of the recovery condition, low amounts of sleep were observed on most nights. This could reflect either the early wake-up times or the strenuous training loads imposed by the protocol. Anecdotal reports indicated that night-time sleep was being supplemented with afternoon naps, which were more prevalent after CWI. CWI may have an acute impact on sleep, however this can only be confirmed in studies that collect sleep information throughout

the day and night.

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P505

Non-pharmacological self-managements for sleep

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The present study was conducted to clarify the prevalence of the non-pharmacological self-managements as sleep aids, and association with excessive daytime sleepiness (EDS), in the general population in Japan. The survey was conducted in June 2000, using self-administered questionnaires, targeting a population that was selected randomly from among 300 communities throughout Japan. Among the respondents, data from 24,686 individuals aged 20 years or older were analyzed. The prevalence of the bathe as sleep aid was highest in both men and women (men: 59.0%, momen: 64.4%), and the prevalence of the having very regular habits as sleep aid, reading or listening to music, physical exercise and take refreshments was 49.0% (men) and 58.6% (women), 43.4% (man) and 49.4% (woman), 26.2% (man) and 29.4% (woman), and 36.1% (man) and 27.9% (woman), respectively. The prevalence of the having very regular habits as sleep aid increased gradually for men and women up to age 70 years. Multivariate analyses revealed that bathe and having very regular habits had significantly lower odds ratios for EDS, and that take refreshments had significantly higher odds ratio for EDS. The preferable non-pharmacological self-management that reduces EDS is bathe and having very regular habit. On the contrary, the not-preferable non-pharmacological self-management is take refreshments.

P506

Selective attention to sleep in heavy and light social drinkers

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Introduction: Espie et al. (2006) propose a route into primary psychophysiological insomnia (PI) along the attention-intention-effort pathway which focuses on the inhibition of sleep-wake automaticity. A contributing factor to this is selective attention to sleep (alongside explicit intention to sleep and effort in the sleep engagement process). Previous research has established selective attention to sleep in PI by demonstrating altered attentional processing of sleep stimuli in PI compared to normal sleepers. With alcohol dependent individuals, who have also developed insomnia, having a 60% relapse rate compared to 30% in those without insomnia (Brower et al. 2001), understanding sleep in this population is relevant to both alcohol dependence research as well as research into development and maintenance of insomnia.

Method: An ICB flicker paradigm was employed to investigate whether selective attention to sleep was present along the alcohol consumption spectrum. A between subjects design was used to analyse responses of heavy (more than 20 units per week) and light (less than 10 units per week) social drinkers obtained from a computer task presenting images of sleep salient, alcohol salient and neutral images.

Results: We found a significant effect of stimulus type (sleep, alcohol or neutral) but no main effect of alcohol consumption (heavy or light). A significant interaction was found between sleep (poor or normal) and alcohol consumption. On further analysis, it was found that those poor sleepers who consumed higher levels of alcohol were significantly faster at identifying the sleep salient stimulus compared to poor sleepers who consumed lower amounts of alcohol.

Conclusion: This study suggests that poor sleepers who consume higher amounts of alcohol show an attentional bias towards sleep compared to normal sleepers, irrespective of alcohol consumption level, and poor sleepers who consume lower levels of alcohol. Further research is called for to understand the underlying mechanism behind the selective attention in this particular group and whether this effect is mediated by the individuals' relationship with alcohol or sleep profile.

P507

Objective and subjective sleep quality of power naps with different duration

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Introduction: Several studies have shown the restorative effect of short naps on performance and wakefulness. To date, few analyses have investigated the effect of brief naps under regular sleep-wake conditions. The present examination determined the effect of power naps with different duration on objective and subjective sleep quality.

Methods: Forty healthy young subjects (20 men, 20 women; 23.5 ± 2.4 years) were assigned to three different sleep conditions and three different wake conditions. All subjects filled in a sleep log and were monitored by actigraphs to control regularly sleep-wake rhythm for two weeks. On six non-consecutive days subjects had the opportunity to take a power nap (bed time: 10-, 20- and 30-minutes) and to stay awake for the same time (10-, 20-, 30-minutes) between 13:00 and 14:00 h. Wakefulness, mood and well-being were measured before and after sleep-/wake-conditions as well as sleep quality was evaluated after the different sleep conditions. All polysomnographic recordings were visually scored according to the standard rules by Rechtschaffen & Kales (1968).

Results: In sleep condition 1 (time in bed: 10 min) mean total sleep time (TST) amounted 2.18 ± 1.48 min, in sleep condition 2 (time in bed: 20 min) 7.92 ± 4.20 min and in sleep condition 3 (time in bed: 30 min) 13.48 ± 6.05 min. Sleep architecture differed significantly between the three sleep conditions ($P < 0.01$). A total of 35% could fall asleep in sleep condition 1, 60% in sleep condition 2 and 65% in sleep condition 3. No significant differences were found between females and males. Subjective sleep quality was higher after actually falling asleep ($P < 0.05$) as well as in case of awakening out of sleep stage 2. In condition 1 awakening quality was significant better ($P < 0.05$) as compared to condition 3.

Conclusion: Power naps with shorter sleep time resulted in a better subjective awakening quality and well-being.

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P508

Auditory arousal thresholds as a function of sounds of different pitches and patterns

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Our previous research has tested various sounds (voice, fire cues and beeps) to determine which sound will wake people in slow wave sleep at the lowest decibel levels (auditory arousal threshold, AAT). Participants included children, sober and alcohol impaired young

adults, adults with mild/moderate hearing loss and adults over 65 years. Lowest AATs were yielded most consistently by beeps of a 520 Hz square wave signal. Square waves have one fundamental frequency followed by frequency peaks at the 3rd, 5th, 7th etc harmonics.

Aim: To measure AATs across signals with a range of pitches and patterns to determine the most effective waking signal.

Method: A sample of 29 young adults aged 18–26 years participated over three nights. Signals sounded for 30 seconds (at levels from 35–95 dBA), increasing every 30 sec by 5 dBA. In Part 1, nine signals with beeps of 0.5 sec duration were tested: (i)- (iv) four square waves (each one with a fundamental frequency of either 400, 520, 800 or 1600 Hz), (v) white noise, (vi) 400–1600 Hz whoop, (vii) 400–800 Hz whoop, (viii) three pure tones of 400, 800 and 1600 Hz, and (ix) 3 square waves of 520, 800 and 1200 Hz. Part 2 manipulated the temporal pattern of the Part 1 signal with the lowest AAT, inserting silences of 0, 10 and 21 seconds after each 12 second sequence of beeps (e.g. beeps ON for 12 sec, OFF for 10 sec, ON for 12 sec).

Results: Part 1: A One way ANOVA yielded a highly significant difference across the nine signals ($F\ (1,8) = 9.6$, $P = 0.000$). Analyses showed that the 520 Hz square wave yielded the lowest mean AAT, and this AAT was significantly different to any other signal presented in Part 1, with the exception of the 400 Hz square wave. No significant differences were found across the three temporal manipulations of Part 2.

Conclusions: The low frequency (400 and 520 Hz) square waves yielded lower AATs than white noise, pure tones and whoops. There was no advantage in presenting ongoing beeps with 12–21 sec of intervening silence. These findings support our earlier research showing that the best sound for awakening from deep sleep is a low frequency (e.g. 520 Hz) square wave. The results have implications for smoke alarm signals and other alarms sounding during the sleep period (e.g. to treat bedwetting).

P509

The *Philosophy of Sleep*; Glasgow's early contribution to sleep

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In 1830, Glaswegian doctor Robert MacNish completed the first British edition of his book 'The Philosophy of Sleep'. The book was intended to "to supply what had hitherto been a desideratum in English literature, viz. a complete account of Sleep". What 'The Philosophy of Sleep' and other early sleep books reminds us is that whilst we have indeed made many major advances concerning the 'science' of sleep, our basic practical understanding of the importance of sleep and our advice to the public has not really changed over the last 175 years. Below are a few quotes from this book, how could you as a modern day sleep expert say them better? "it (sleep) has a natural tendency to recur every twenty four hours and the periods of its accession coincide with the return of night" "The profoundness of sleep differs also during the same night. For the first four or five hours, the slumber is much heavier then towards morning. The cause of such difference is obvious, for we go to bed exhausted by previous fatigue, and consequently enjoy sound repose, but in the course of a few hours, the necessity for this gradually abates, and sleep becomes much lighter. From this circumstance, dreams are much more apt to occur in the morning than in the early part of the night" "Sleep, which shuns the light, embraces darkness, and they lie down together most lovingly under the spectre of midnight". "Sleep exists in two states- in the complete and incomplete" but where sleep is incomplete "as in dreaming, only certain of the mental functions are arrested, while others continue to act as usual". "There are two types of complete sleep- the light and the profound. So far as the extinction of the usual faculties goes, they are equally perfect, but the first is more easily broken then the other . . ." "The cure of almost any disease is favoured by sleep". "The strength given to the mind by slumber, is not less remarkable than that which it inspires in the body" "As a general rule, the person who eats nothing for two or three hours before going to rest, will sleep better then he who does". "Too little and too much sleep are equally injurious". "At what ever period we go to sleep, one thing is certain, we can never with impunity convert day into night".

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Effects of electromagnetic fields emitted by mobile phones on sleep in healthy young male subjects

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The present study investigated possible effects of electromagnetic fields (EMF) emitted by GSM900 and UMTS cell phones on the macro- and microstructure of sleep. In a double-blind cross-over design 30 healthy male subjects (mean age ± SD: 25.3 ± 2.6 years; range: 18–30 yrs) were exposed for 8 h during time in bed to three exposure conditions (Sham, GSM900 and UMTS) in random order by a cell phone at maximum radio frequency output power. The transmitted power was adjusted in order to approach, but not to exceed the specific absorption rate (SAR) limits of the law (localised SAR = 2.0 W kg^{-1}-averaged over 10 g). Analysis of the macrostructure of sleep revealed that various aspects of REM sleep duration under GSM900 exposure were significantly different from the sham condition. Furthermore a decrease of NREM1 sleep (3.2 min less than during the sham condition) and a reduced number of stage shifts from slow wave sleep to NREM1 sleep was observed. Duration of REM cycles increased (1.3 min), and duration of NREM cyles (2.5 min) and various NREM1 sleep parameters decreased under UMTS exposure. Analyses of power spectra of the sleep EEG revealed that with regard to sleep period time the only difference observed for GSM900 exposure was an increase for two frequencies out of the Beta-frequency range (21.0 Hz and 22.0 Hz). A stage specific approach showed that power spectra were significantly increased for frequency bands 6.5, 7.5 and 8.5 Hz during wake, and for 1.5–2.5 Hz and 6.5 Hz during NREM1 sleep. Effects seen during NREM2 sleep were restricted to the Beta-frequency range (18.0–24.0 Hz). With regard to UMTS exposure only nine out of 400 tested variables showed significant changes: for wake 8.5 to 9.5 Hz, five sporadic frequencies in NREM1 sleep (2.0, 6.0 6.5, 8.0, and 15.5 Hz), and one frequency (7.5 Hz) when NREM1 and NREM2 sleep were combined as light sleep. No effects were seen for REM and slow wave sleep. From the present results there is no evidence for a sleep disturbing effect of GSM900 or UMTS exposure, because most of the observed changes in the macrostructure of sleep are indicative of slight physiological adaptations.

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Mobile phone 'talk' and 'listen' modes have opposite effects on the sleep EEG

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Introduction: Mobile phone 'talk' and 'listen' mode signals are pulsed modulated microwaves, sharing the same pulse modulation frequencies at 8 and 217 Hz. However, listen mode has an extra 2 Hz modulation. Our previous study using EEG visual scoring and

spectral analysis showed talk-mode to delay sleep onset (Hung et al. 2007). Here, we examine the sleep EEG itself, especially during stage 2 (S2) and slow-wave sleep (SWS), in the first non-rapid eye movement sleep, to see if there are further differential effects of these phone signals.

Methods: Ninety-minuts sleep PSG recordings in the early afternoon were obtained from 10 right-handed healthy young men (sleep restricted to 6 h) after a 30-min exposure to standard GSM 900 MHz mobile phone separate emissions at talk, listen and sham (nil signal) modes during prior waking, given weekly. Mean S2 and SWS EEG power (log-transformed values) across 1–16 Hz range per recording were calculated in 1-Hz bins at bipolar derivations (F3-C3, C3-P3, P3-O1, F4-C4, C4-P4, P4-O2), by averaging individual time series, aligned with respect to the onset of S2 and SWS. Exposure effects on (i) accumulated EEG 1–4 Hz power throughout the sleep period, and (ii) S2 and SWS EEG power (as well as 'S2-SWS' power difference), under the two active modes, were each compared with sham mode.

Results: Only listen-mode had a significant effect on the accumulated 90-min EEG 1–4 Hz power, shown by increased power at the C4-P4 region compared with sham. Listen mode also increased SWS EEG spindle (11–15 Hz) power at frontal-central regions (C3-P3, F4-C4), suggesting an 'alpha-delta' sleep pattern. Talk mode, compared with sham mode, induced an obvious 'S2-SWS' EEG spectra difference at the spindle (12–15 Hz) range in all derivations, where spindle power was reduced during S2 but returned to baseline level in SWS.

Conclusion: The global S2 EEG spindle reduction produced by talk mode, and the alpha-delta sleep pattern during SWS of listen mode, suggest these two modes have opposite sleep effects: alerting (talk mode)-sleep maintaining (listen mode). As listen mode has an extra 2-Hz modulation, this could imply that the 2-Hz modulation has different sleep effects to those of 8 and 217-Hz modulations.

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Nocturnal aircraft noise exposure increases objectively assessed daytime sleepiness

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Question of the study: There is no doubt that noise in general and aircraft noise specifically disturb sleep. However, so far no study assessed the effects of traffic noise on daytime sleepiness objectively.

Patients and Methods: In a polysomnographic laboratory study, 24 subjects (mean $\pm$ SD age 33.9 ± 10.8 years, 12 male) were investigated between 7:30 am and 8:30 am with infrared pupillography after a noise-free baseline night and after 9 nights with varying degrees of aircraft noise exposure.

Results: The natural logarithm of the pupillary unrest index (lnPUI) differed significantly ($P = 0.006$) between noise (lnPUI = 1.61) and baseline (lnPUI = 1.48) nights. Objective sleepiness levels increased significantly with the number of noise events ($P = 0.021$), with the maximum sound pressure level of noise events ($P = 0.028$), and with the equivalent continuous noise level ($P = 0.013$) in exposure nights. However, these levels did not reach pathological levels observed in another study on untreated obstructive sleep apnea patients.

Conclusions: This is the first study to show that nocturnal aircraft noise exposure increases objectively assessed sleepiness in the next morning. These findings stress the relevance and the potential public health impact of sleep disturbances induced by environmental noise. Further studies are needed to investigate the association of nocturnal traffic noise exposure and objectively assessed sleepiness in the field.

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Sleeping with dogs – results of a pilot experiment

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According to Austrian censuses in 1998, there are pets in 25% of the households or in numbers 2.6 million units. In spite of the detailed information about where and how they live during the active phase of the dog day there are neither census data nor scientific studies about where and how they sleep. Dr. Shepard (Majo-Clinic California, USA) 2001 did report that every other patient in his clinic had a pet and that 60% of them slept in the same room as the patient, and 22% in the same bed. In light of the frequency of this sleeping arrangement we have decided to address the question of whether the presence of a pet in bed affects the sleep quality of the owner. Ten dog owners participated in the study, who regularly slept with their pets in bed. Over the course of four weeks the owners were instructed to sleep at least ten nights in bed with their pets and at least ten nights alone. The pet was allowed to be in the bedroom during the alone condition. Subjects were given a wrist worn actigraph and they completed a sleep diary every morning and evening. The following trends were seen in the data: Although the subject sleep- and awakening qualities did not differ between the two sleeping conditions, objective sleep efficiency (actigraph) was significantly lower and sleep fragmentation higher on nights with the pet in the bed. Oddly enough although the sleep of the owner appeared to be mildly disturbed, most subjects reported that they rather sleep with the dog than without. The common explanation here was that it was a matter of habit. The question is: Is it a healthy habit?

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Sleep quality in the psychiatric setting

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Introduction: The studies indicate a high frequency of sleep disorders in the psychiatric setting. In the majority of the cases, the sleep complaints are a part of the symptomatology of an anxiety disorder or depressive disorder. When such complications do exist, they are typically associated with decreased quality of life, increased morbidity and, in some cases, increased mortality rates. It is almost impossible to conduct polysomnographic recordings in large samples; therefore sleep disorders are to be detected by questionnaires. Few instruments have been especially developed to evaluate sleep quality in clinical populations. Buysse et al. (1989) designed the Pittsburgh Sleep Quality Index (PSQI) considered one of the most able instruments to establish the quality of the sleep.

Methods: The present study psychometrically assessed clinical profiles of subjective sleep quality in 50 control subjects (non clinical settings) and in 100 psychiatric patients (clinical settings) followed in hospitalization and general and addictive psychiatric consultation, using the Pittsburgh Sleep Quality Index. It is a self-rated questionnaire which assesses sleep quality and disturbances over a 1-month time interval and generates a global score and scores seven components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction.

Results: Acceptable measures of internal consistency (test-retest reliability) and validity were obtained. The Pittsburgh Sleep Quality Index global and component mean scores were significantly higher in psychiatric disordered subjects than control subjects.

Conclusions: This study shows the utility of the Pittsburgh Sleep Quality Index to measure sleep quality in psychiatric populations both in clinical practice and research activities.

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Perfectionism and sleep disturbance: a longitudinal study

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Aim: To examine whether perfectionists predict self-reported sleep disturbances over time.

Methods: The Hewitt and Flett Multidimensional Perfectionism Scale (1991) was used to measure total perfectionism, self-oriented perfectionism (SOP), socially-prescribed perfectionism (SPP) and other-oriented perfectionism (OOP). Sleep disturbance was assessed with two items: (1) I have difficulty in falling asleep and (2) I wake up many times during the night. Out of 870 students who completed those measures at baseline, 592 and 305 completed the same measures one year (T1) and two years later (T2) respectively.

Results: Subjects who reported insomnia (had difficulties initiating sleep/maintaining sleep often/very often and always) at baseline, T1 and T2 (persistent insomnia) had significantly higher scores of baseline SPP (T1 $M = 51.5$, SD = 15.8; T2 $M = 55.0$; SD = 19.0) than subjects that in all stages of the study reported that never/rarely had sleep problems (good sleepers group) (T1 $M = 41.9$, SD = 11.4; T2 $M = 42.2$, SD = 12.3, $P < 0.001$ in both cases). Regression analyses showed that baseline SPP at T1 and T2 was the only significant positive predictor of difficulties in falling asleep (T1 partial $R = 0.187$; T2 partial $R = 0.196$, $P < 0.001$) and difficulties maintaining sleep (T1 partial $R = 0.116$; T2 partial $R = 0.244$, $P < 0.001$).

Conclusion: A new finding is that SPP was found to be the most reliable predictor of sleep disturbances over time

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Executive functioning and sleep organization in patients with schizophrenia stabilized with atypical neuroleptics

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Introduction: Sleep loss is accompanied by impairment of executive functioning in healthy subjects. Persons with schizophrenia show sleep disorders as well as impairments on executive functioning tasks such as the Wisconsin Card Sorting Test (WCST). This study sought for relationships between sleep and performance on the WCST in persons with schizophrenia and control participants.

Method: Fifteen outpatients with schizophrenia (13 men, 2 women; age = 25.7 ± 3.1) stabilized on atypical neuroleptics and 14 controls (11 men, 3 women, age = 22.3 ± 4.2) matched for education were recorded in a sleep laboratory for two consecutive nights. Executive functioning was tested between 8:00 and 12:00 the next morning with the WCST. Groups were compared with *t*-tests. The correlation between sleep and performance was tested with Spearman's rho.

Results: Compared to controls, patients showed a longer sleep latency (11.6 ± 7.2 versus 42.8 ± 65.4; $P = 0.0.05$) but no other differences in sleep macrostructure. Patients were also impaired on the WCST compared to controls, with more total errors (21.6 ± 14.1 versus 35.9 ± 19.5; $P = 0.06$), more perseverative response (10.5 ± 6.7 versus 20.6 ± 12.2; $P = 0.02$) and more perseverative errors (9.6 ± 5.5 versus 19.0 ± 10.6; $P = 0.02$). In patients, these variables were found to correlate negatively with stage 2 duration (-0.61, $P < 0.03$; -0.69, $P < 0.009$; -0.69, $P < 0.009$, respectively) and sleep spindle activity during stage 2 (-0.48, $P < 0.09$; -0.62, $P < 0.03$; -0.62, $P < 0.03$, respectively) and to correlate positively with REM sleep duration (0.75, $P < 0.003$; 0.73, $P < 0.004$; 0.73, $P < 0.004$, respectively). No such correlation was found in the control group. Sleep latency did not correlate with these WCST variables neither.

Conclusion: First, these results confirm that normalization of sleep with atypical neuroleptics in persons with schizophrenia is not accompanied by normalization of performance on the WCST. Second, the result show a relationship between performance on the WCST and sleep structure as well as sleep spindle EEG activity in patients stabilized with atypical neuroleptics but not in healthy subjects. We conclude that there is a relationship between executive functioning and sleep in schizophrenia. The inverse relationship between nonREM and REM sleep deserves to be further investigated.

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Distinctive expression patterns of genes in basal forebrain in an animal model for sleep disturbance and depression

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Disturbances in sleep are encountered in the majority of patients with depressive disorder. In this study, we used microarrays to discover gene expression changes in a rodent model for sleep and depression. The animals were treated with daily injections of clomipramine or saline for 2 weeks in their early infancy, and the gene expression in basal forebrain was examined using the Affymetrix Rat 230.2 chip at the end of this period at the age of 3 weeks. In the data analysis we tested the levels of single transcripts, involved pathways, as well as searched for common nominators (i.e. transcription factors) behind these changes. Interestingly, many of the hereby revealed genes are known to be epigenetically regulated or involved in the maintenance and dynamics of epigenetic information, such as the gene encoding for DNA methyl transferase 2 (DNMT2). A promoter analysis showed a clear enrichment of some particular transcription factor binding sites amongst the differentially expressed genes. The strongest effect was seen for the site for CREB1, raising the possibility that this particular molecule may constitute one of the major links between disturbed sleep regulation and mood. Recognition of the binding site for CTF1, a constituent in complexes that mediate modifications of promoter chromatin structure, in a number of genes with deviated expression levels further supports the theory involving epigenetic regulatory mechanisms in sleep and mood regulation.

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Sleep spindle characteristics after augmentation treatment with clozapine in drug-resistant schizophrenia

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Aim: Clozapine is an atypical neuroleptic agent, effective in treating resistant schizophrenia. Clozapine increases neuronal activity, as shown by changes in the awake EEG. This increase may be achieved by either an increased dosage of the drug, or by repeated small doses. Polysomnographic studies performed during the treatment of schizophrenia patients have shown that it improves sleep efficiency, and that it increases stage 2 sleep. Sleep spindles, the characteristic EEG waveform of sleep stage 2, play an active role in inducing and maintaining sleep, and are generated by cortico-thalamo-cortical neural networks, possibly by the same mechanisms that produce epileptic spike-and-wave discharges. The aim of the present work was to investigate sleep spindle characteristics before and after augmentation treatment with clozapine, in patients with drug-resistant schizophrenia. Here we present preliminary data.

Methods and Results: Night sleep EEG data from 1 patient, GS (31 yrs, male), with drug-resistant schizophrenia were obtained twice. At the admittance recording (T1), GS was receiving 12 mg of risperidone. At the second recording (T2), GS was receiving 12 mg of risperidone plus 50 mg of clozapine for a month. At T1, GS's total PANSS score was 122, and at T2 it was 88 (which implies clinical improvement). Sleep EEG staging was similar at T1 and T2 (therefore, sleep efficiency was not affected by clozapine). Visually well-defined sleep spindles from sleep stage 2 were processed automatically for instantaneous envelope and instantaneous intra-spindle frequency estimation which defined 6 parameters. We compared sleep spindles from T1 and T2 in terms of these parameters. One of the parameters, which quantified the average instantaneous intra-spindle frequency, was significantly higher at T2.

Conclusions: After augmentation treatment with clozapine, GS showed clinical improvement. Although his overall sleep architecture remained the same, the average instantaneous frequency of sleep spindles increased after treatment. This may imply a change in thalamo-cortical neural dynamics reflecting the excitatory properties of clozapine.

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An investigation of delayed disengagement of attention, from 'negative' sleep-related stimuli, in psychophysiologic insomnia

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Recently researchers have focused on attention bias (AB) in PI and have outlined examples of the extensive research into human attention. We now know that stimuli that are salient are likely to attract attention. Support has been found implicating attention bias in the perpetuation of a wide range of anxiety-related psychological disorders (Clark, 1985, Barsky,1988). AB detected within these disorders have largely been attributed to perceived threat (Beck et al. 1997). When considering the implications of this theory with regard to insomnia, it is apparent that many characteristics if insomnia lie within Beck's anxiety framework, e.g. it has long been established that insomniacs experience excessive negative cognitive intrusions and the consequences of not sleeping. Consideration of this evidence in favour of a link between anxiety and insomnia has led us to consider the nature of the stimuli incorporated into the attention paradigms. Interestingly, none of the experimental stimuli utilized have been intrinsically commanding of attention, nor emotive or threatening. This experiemnt aims to extend the previous Posner Paradigm experiment (Marchetti et al. unpublished)) by manipulating the valence of the experimental sleep stimuli. By differentiating the+ive and -ive word types into separate groups, we hope to identify whether threatening (negative valence), craving (positive valence), or both, processes are accounting for the attentional biases detected in PI. PI, delayed sleep phase sufferes and good sleepers were included in the study. 4 of our 5 origninal hypotheses were confirmed. 1) PI took significantly longer to disengage from sleep-related cues than neutral cues.This effect was only detected at the -ive sleep word valence.2) PI were significantly slower to disengage from -ive sleep related words than both GS and DSPS.3) there were no significant differences in response times between, or within, GS and DSPS at any word valence.4) there were no speeded engagement effects on valid sleep-related trials.In conclusion, this experiment is the first to differentiate stimuli into+ive and -ive groups and show that intrinsically '-ive' sleep related stimuli are more successful in generating attention bias in PI than+ive sleep related stimuli.

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Sleep changes associated with mood improvement during acute deep brain stimulation of two different brain targets for treatment resistant depression

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Deep brain stimulation (DBS) has been used for many years in the alleviation of motor symptoms in Parkinson's disease, and more

recently for intractable psychiatric conditions. DBS for treatment resistant depression (TRD) is still in the early stages of evaluation. Results have been reported in fewer than 50 patients and although changes in HAMD (Hamilton Depression Rating Scale) sleep measures have been described, no objective sleep changes have been reported. We measured sleep before and during DBS treatment for depression in a 60 year old female patient with a 5 year history of sleep disturbance related to major depression. After baseline measurements, electrodes were implanted bilaterally in the subgenual cingulate (Cg25) and ventral anterior capsule (VAC). Following recovery the patient was admitted for stimulator parameter adjustment after which each site was individually stimulated. Measures of depression included the Hamilton depression rating scale 17 items (HAMD) and the Montgomery-Asberg depression rating scale (MADRS). Sleep recordings were performed at intervals throughout the treatment periods, and analysed according to R&K criteria. At baseline the patient's sleep was poor (sleep onset latency; (SOL) 53 mins, total sleep time (TST); 227 mins) and depression ratings high (HAMD; 34, MADRS; 51). In addition there was a complete suppression of REM (on MAOI). During the first week of stimulation targeting Cg25, remarkable REM restoration was observed (REM amount 105 min) despite continued isocarboxazid administration and this was accompanied by a reduction in sleep disturbance (SOL; 12 mins, TST; 439 mins) and depression scores (HAMD; 17, MADRS; 28). These improvements were not maintained during chronic stimulation, with recurrence of sleep disturbance and depression.Within the first week of VAC stimulation sleep disturbances and depression scores again improved (HAMD; 22, MADRS; 35, SOL 5 min; TST 359 min; REM 10 mins). Preliminary results suggest an association between sleep and depression score improvement with acute DBS. Effective acute DBS appears to exhibit powerful effects to restore sleep despite MAOI administration, although effects differed depending on stimulation target.

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Correlations between depressive symptom, daytime dysfunction and oxidative damage in healthy students

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Objective: The aim of the present research was to explore the relationship between depressive symptom, quality of sleep and oxidative stress.

Methods: We performed a cross-sectional study in Fifty four non-smoking and healthy students (24 males and 30 female, mean age 20.7 ± 0.9 years). We used the Beck Depression Inventory (BDI), Pittsburgh Sleep Quality Index (PSQI) and Insomnia Severity Index (ISI). Reactive oxygen metabolites (ROMs) and total antioxidant power (Bioantioxidant power; BAP) were evaluated using a spectrophotometric method, as oxidative stress state in the blood.

Results: We found a positive relationship between BDI scores and ROMs. Regarding antioxidant power, there was significant positive relationship between BDI scores and BAP in male subjects. The subcomponent of PSQI and ISI (Daytime dysfunction, Interference) positively correlated with ROMs significantly, although PSQI global score and ISI total score did not. Antioxidant power was not related to the quality of sleep.

Conclusion: Our findings in healthy participants indicate increased daytime dysfunction, and depressive symptom may tend to increase oxidative damage.

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NAPSAQ II; national patient sleep assessment questionnaire in depression; a survey for general practitioners

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Sleep disturbance is a common and distressing feature of depression. In a recent survey of a UK-based patient group we found that the vast majority of patients experienced sleep disturbance during depression. This often remained unresolved despite antidepressant treatment, and patients sought extra treatment in order to manage the problem. We have now asked GPs about their opinions of sleep disturbance in depression, and their strategies for treating them. 40794 GPs throughout the UK received a postal questionnaire: we received 5046 completed responses (12.4%). GPs estimated that 70% of the patients they diagnose with depression include sleep disturbance among their symptoms, with insomnia being more common than hypersomnia, and some 10% were thought to suffer from insomnia as a side effect of their antidepressant medication. When asked about treating symptoms of insomnia associated with depression, GPs reported that they 'frequently' or 'almost always' rely on watchful waiting or promotion of good sleep hygiene (72 and 87% respectively) and rely on switches in antidepressant medication or treatment of symptoms with medication less often (21 and 15% respectively). GPs estimated that 20% of depressed patients had their prescriptions altered as a direct result of insomnia, and that 10% suffer insomnia as a residual symptom once their depression is resolved. GPs were asked to what extent they agreed with statements about sleep problems in depression. Over 90% agreed that they are common, distressing, and should be managed in primary care. 67% agreed that they cause patients to visit more frequently. A significant proportion (42%) agreed that they were difficult to treat; many believed that they could be resolved by effective antidepressant medication (69%), or respond to add-on hypnotic medication (41%). 77% agreed that sleep problems can be reduced by good sleep hygiene, and 70% agreed that if left untreated they can lead to depressive relapse. Interestingly, GPs estimated that 50% of patients who present with sleep problems in primary care turn out to have depression. Our data suggest that GPs are aware of the problems of sleep disturbance in depression but that there is room for better management in order to minimise distress and improve long term outcome.

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Emotion regulation and sleep quality: the role of emotional inhibition and rumination

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Introduction: Although the association between emotion regulation strategies (rumination, cognitive reappraisal and emotional inhibition) and mood, coping and personality measures has been well studied, there is a lack of data relating those to sleep quality. The aim of this study was to establish the relationship between emotional inhibition, rumination, and sleep quality in a young adult sample.

Methods: The subjects included in this study were 196 young adults (147 females, 49 males; mean age 20.17 ± 0.996, range 19–28 years), who participated in an in-class survey to third year medical

students. The measures used evaluated: sleep quality (PSQI; Buysse et al. 1989), emotional inhibition (ERQ-S; Gross, 2003), rumination (ECQ-R; Roger et al.2001), coping stress strategies (CISS; Endler and Parker, 1990), and personality (NEO-FII; Costa and McCrae, 1993). The psychometric properties of all these questionnaires have been very well documented in their original version. First, bivariate relationships between all variables were examined with Spearman's Rho correlation coefficient. Second, a hierarchical regression analysis was carried out to study the independent contribution of all co-variables to PSQI scores.

Results: Mild to moderate positive correlations were found between poor sleep quality and emotional inhibition ($P = 0.014$) and rumination ($P = 0.002$). The items of the ERQ-S that significantly correlated with sleep quality were those related to expressive suppression of emotions ($P = 0.043$) and to hiding negative feelings ($P = 0.049$). Hierarchical regression analysis revealed that neuroticism ($\beta = 0.41$; $P = 0.0001$) and emotional inhibition ($\beta = 0.26$; $P = 0.023$) were the variables most significantly related to sleep quality, after controlling for sex, emotion-oriented coping, and rumination.

Conclusions: Our results confirmed that poor sleep quality in young adults is associated with rumination and emotional inhibition. Furthermore, regression analyses give further support to the hypothesis that emotional inhibition acts as a mediating factor between rumination and sleep quality, as proposed by Kales and Kales (1984) model of insomnia.

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Sleep/wake behavior in the stress reactivity mouse model – a new animal model to investigate sleep impairments in major depression

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Major depression is one of the most common affective disorders. It is accompanied amongst others by disturbances in psychomotor activity, a dysregulated hypothalamic-pituitary-adrenocortical axis and sleep alterations such as insomnia or hypersomnia, reduced slow-wave activity and altered REM sleep. In the present study we investigated the presence of impaired sleep behavior in an animal model for depression, recently established at our institute: the stress reactivity (SR) mouse model. This model was selectively bred upon differentiated plasma levels of corticosterone in response to stressors, namely the high reactivity (HR), the intermediate reactivity (IR) and the low reactivity (LR) mouse line. Electroencephalograms and electromyograms were recorded under baseline conditions in all three mouse lines. Additionally, orexin (OR) and corticotropin-releasing-hormone (CRH) were tested centrally to evaluate the effects of these two wake promoting neuropeptides on sleep/wake behavior. All animals also underwent a total sleep deprivation for the first six hours of the light period to investigate possibly differentiated reactions of the three breeding lines to this mild homeostatic pressure. Under baseline conditions, REM sleep was significantly elevated in HR animals, when compared with IR and LR mice. After the general wake promoting effect following CRH treatment observed in all three breeding lines, the HR line revealed the strongest REM sleep rebound, when compared to IR and LR mice. Neither OR-treatments nor sleep deprivation did yield any significant differences among the three lines. In summary, the significant changes in REM sleep together with the elevated amounts of basal corticosterone in the HR animals in comparison to the IR and LR breeding line support the attempt to establish the stress reactivity mouse model as a valid animal model for depression, especially when focussing on sleep impairments.

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Subjective sleep quality in workers with high and low burnout scores

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Burnout, i.e. acquired exhaustion and job dissatisfaction, is a growing problem in western Countries affecting both help professions and other employees. Sleep disruption could be a major link between work strain and the development of burn out; in fact Swedish employees in an ICT company with very high exhaustion scores in the Shiron Melamed Burn Out Questionnaire showed more polisomnographic arousals and absence of the reduced sleepiness during days off shown by their colleagues with very low burnout scores[1]. The present questionnaire study assessed subjective sleep quality, morning tiredness, and other sleep related measures in Italian samples of social workers and of employees in the sales and customer services of a major car company, who completed the Italian version of Maslach Burnout Inventory-General Survey [2] (MBOI-GS) and standardized sleep disorders and habits questionnaires. Subjective tiredness and sleep quality assessed with reference to workdays and days off by subgroups with very low (<10%), low (11–20%), high (81–90%), and very high (90–100%) standardized scores in the MBOI-GS scales were analyzed through different mixed ANOVAS 2×4 with days and subgroups as factors. The pattern of results was the same among social workers and employees. Concerning tiredness overall results show significant main effects for days, ($F1,136 = 17.59$), with higher tiredness on the weekdays, and for exhaustion groups ($F3,136 = 17.75$), with tiredness higher in the VH and lower in VL group, as well as an interaction ($F3,136 = 4.65$) showing less tiredness on the days off of the VH and H groups. Concerning sleep quality the ANOVA showed the same significant main effects with no interaction. With respect to the Swedish study, unless due to differences in the questionnaires or to other methodological factors, the present results suggest that an impairment of sleep in the days off might be a critical factor in the development of BO exhaustion only when strain in the workdays is very high.

1. Soderstrom et al. (2004). Sleep, 27 (7):1369–1377. 2. Borgogni et al. (2005). Bollettino di Psicologia.

P526

The effect of sleep deprivation on mood and on the processing of emotional information

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Introduction: It is well known that sleep deprivation (SD) impairs cognitive and psychomotor performance, but despite the commonly known effect on mood, only a few studies target mood and the processing of emotional cues after SD.

Methods: In a randomized crossover design 20 young healthy adults were tested after a night with sufficient sleep and in the morning after 24 h of wakefulness. Mood was assessed by Profile of Mood States (POMS, McNair et al. 1992). For the induction of mood changes, a sequence of positive, neutral and negative emotional pictures was presented (International Affective Picture System, Lang et al. 1988). The effect on mood was rated on a 9 step positive scale (Eigenschaftsliste). Cognitive and psychomotor functioning were tested by a sustained attention test (MacWorth clock, version of Quatember Maly, Nachreiner & Hänecke, 1992), Psychomotor Vigilance Task (PVT, Dinges & Powell, 1985) and Regensburg Word Fluency Test (RWT, Aschenbrenner et al. 2000).

Results: Performance in the sustained attention test (missed reactions and reaction time) and in the PVT declined sharply ($P<0.001$), but word fluency (RWT) was not significantly reduced. Mood was significantly impaired by sleep deprivation in 4 of 6 subscales of the POMS (tension, vigour, exhaustion, confusion, but not depression and anger). The mood rating at the presentation of positive, neutral and negative emotional pictures was significantly more negative in all conditions after sleep deprivation, but size and direction of change between conditions was not significantly different after well rested and SD nights.

Conclusion: As expected, a night of SD had a strong negative effect on mood and on tasks which require sustained attention. However, cognitive functioning in a non-monotonous task and the reaction to emotional stimuli are not impaired in size and direction.

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Disturbed sleep predicts disability pension due to depression

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Objective: The comorbidity of sleep disturbances and depression is well established. However, it is not clear whether disturbed sleep has an independent effect on development of depression. We investigated whether people with sleep disturbances but with no history of depression are at increased risk of permanent work disability due to depression.

Methods: Data were obtained from the Finnish Public Sector study. Survey questionnaires were sent the whole personnel of 10 towns and 21 hospitals in 2000–2004 (response rate 67%). 66,418 employees (80% women) responded to the survey and 53,706 were free of self-reported physician-diagnosed depression or recorded long-term sickness absence due to depression. Their sleep disturbances were defined as reported problems with sleep in 5–7 nights a week using 4-item Jenkins Sleep Problems Scale. Follow-up for disability pension began the year after the survey (mean follow-up 3.4 years). Cox proportional hazard models were used to estimate the association between sleep disturbances and disability pension. Analyses were adjusted for age, sex, socio-economical status, health risk behaviour, and psychological distress.

Results: During the follow-up, 93 participants were granted disability pension due to depression. Employees with sleep disturbances had 2.65 (95% confidence interval: 2.28, 3.16) times higher probability to be granted work disability pension than their colleagues with no sleep disturbances. Hazard ratio for work disability due to any cause was 2.68 (95% confidence interval: 2.28, 3.16). Sleep problems were not associated with disability pension due to mental disorders other than depression.

Conclusion: These findings suggest that impaired sleep without evidence of depression is an independent predictor for subsequent disability pension irrespective of cause and due to depression.

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A study exploring the prevalence of anxiety and depression in treated patients with obstructive sleep apnoea

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Background: There is a considerable overlap between the symptomatology of depression and Obstructive Sleep Apnoea (OSA). Surveys among OSA patients have shown high prevalence of anxiety and depression. However, trials of appropriate therapy i.e Continuous positive airway pressure (CPAP) therapy, has often failed to demonstrate consistent improvement. It is possible that endogenous depression is unrelated to OSA while anxiety associated with low mood may be a consequence of sleep deprivation.

Aim: We designed a study to explore the prevalence of anxiety and depression in OSA patients satisfactorily treated with CPAP.

Study Design and Methods: Patients with OSA based on domiciliary sleep studies with an apnoea hypopnoea index $>15\ h^{-1}$ on treatment with CPAP for at least 6 weeks, were invited to participate in a postal survey of concomitant anxiety and depression using the Hospital Anxiety & Depression scale (HADS) and Beck's Depression Inventory (BDI).

Results: Ninety six patients were included in the study with OSA (mild 4%, mod 26% & severe 70%), AHI 44 ± 20 hour-1 and baseline Epworth sleepiness scale (ESS) score 13 ± 5. Post-treatment ESS score reduced to 9 ± 5, $P<0.001$. The mean HADS anxiety score was 6.6 ± 4.7, HADS depression score was 5.1 ± 4.1 and BDI 11.6 ± 9.7. The prevalence of (HADS) anxiety was 17% mild and 26% severe, (HADS) depression was 20% mild and 8% severe. BDI depression was 18% mild, 23% moderate and 4% severe. HADS anxiety and depression scores were correlated with AHI; Pearson correlation coefficient HADS-A -0.2, $P=0.06$ and HADS-D -0.25, $P=0.02$. Unlike baseline ESS score the post-treatment ESS score was correlated with AHI Pearson correlation coefficient $=-0.265$, $P=0.013$. BDI scores showed no correlation with AHI or ESS scores.

Conclusion: Our study indicates a high prevalence of concomitant anxiety and depression among adequately treated patients with OSA. While HADS scores are related to nocturnal apnoea hypopnoea index the BDI depression scores were not. This suggests that unlike anxiety, depression may be unrelated to OSA and thus may not have been ameliorated by CPAP treatment.

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Depressive-like state and sleep in laboratory mice

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To induce the state of anhedonia, a key symptom of depression, a group of mice was subjected to a one month stress procedure comprising of various stressors. Several types of stressors were used, including immobilization, water immersion, rat-exposure and tail suspension. Employed chronic stress led to a state of anhedonia, which was defined by a decreased preference to sucrose solution over a tap water, only in some individuals (50–70%) defined as stressed-anhedonic; other stressed animals did not demonstrate such an effect and were assigned to the stressed-non-anhedonic group. This model let us to divide behavioral manifestations of anhedonia from those of stress per se. Conventional cortical and neck muscle electrodes were implanted to the control and stressed animals under chloral-hydrate anesthesia after the termination of stress procedure. After a 2-week recovery and habituation period mice from chronically stressed group were re-submitted to 5 day stress, and hedonic deficit was verified with a sucrose test. Seven-day continuous polygraphic recording was carried out in animals from both anhedonic and non-anhedonic stressed groups and a control group in recording chambers using a 12/12 h light/dark schedule. Visual scoring and analysis of the recorded polygrams revealed significantly advanced shift in circadian rhythm in anhedonic mice as compared to non-anhedonic animals, which was especially pronounced for paradoxical sleep (PS). Besides, in anhedonic group, a slight though significant decrease in total amount of slow

wave sleep in the dark period and sharply increased percentage of the PS during the light period, as compared to two other groups, were found. A latency of the PS did not change during the light period, while it was increased greatly during the dark phase of the nychthemeron. Taken together, the changes in a sleep structure, which were revealed in stressed mice with hedonic deficit, but not in ''resistant'' mice without anhedonia, are similar to those typical for human depression. Our data suggest that the changes in sleep structure documented in the applied model of anhedonia are similar to those known for human depression.

Learning, Memory and Cognition

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Sleep inertia following short naps lasts approximately 30 min

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The aim of this study was to investigate the effect of naps of different duration on the duration and magnitude of the subsequent sleep inertia (SI).

Methods: Twelve healthy male volunteers aged between 20 and 30 years (mean age 23.5) attended the sleep laboratory on 6 separate nights. For one night they remained awake throughout, whereas on the other five nights they were allowed to sleep for 10, 20, 30, 40 or 60 min and were woken at approximately 03:00. Performance was monitored at 30-minute intervals from midnight until the start of the nap, and then at 2, 10, 17 and 30 min after the nap (or at equivalent times in the no nap condition), and at 15-m intervals thereafter until 07:30. Each test session lasted approximately 6 min and included a test of short-term memory and a subjective assessment of alertness. The data from the 03:00 test session until the 07:30 session were investigated by fitting trends to the mean values from analysis of variance models.

Results: Initially on waking, response times from the memory test were slower and alertness was lower than before the nap by an amount dependent on the duration of the nap. Levels of performance and subjective alertness returned to pre-nap levels after approximately 30 min after waking. Beyond this point, levels of alertness and performance increased as a negative exponential function of time, where the extent of the improvement was dependent on the nap duration.

Conclusion: For naps of up to one hour, the impairment of performance and subjective alertness on waking is dependent on the nap duration. The return to pre-nap levels occurs within approximately half an hour of waking.

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Efficiency of the attentional networks following sleep reduction

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Aim of the present study is to evaluate the effect of sleep reduction on attention, using the Attention Network Test -ANT (Fan et al. J. Cog. Neurosci. 2002, 3: 340–347). ANT is a reaction time task designed to measure the efficiency of the three attentional networks which have been defined, in functional and anatomical terms, by Posner and Raichle (1994): Alerting, Orienting, and Executive Control. Alerting (achieving and maintaining an alert state) has been associated with the frontal and parietal regions of the right emisphere; Orienting (the selection of information from sensory input) with areas of the parietal and frontal lobes; Executive Control (resolving conflict among responses) with midline frontal areas (anterior cingulate) and the lateral prefrontal cortex.

Methods: 19 participants, university students, aged 19–24. Each of them completed ANT in two different conditions: (a) Baseline (BL) -testing in the sleep lab at 9 am after a regular night of sleep at home; and (b) Sleep Reduction (SR) -testing at the same time after one night (in the sleep lab under standard electropoligraphic control) during which they were allowed to sleep only 3 h from approximately midnight to 3 am Before testing their state of vigilance and mood was assessed by means of the Stanford Sleepiness Scale (SSS) and the Global Vigor-Affect Scale (GVA).

Results: No significant difference between BL and SR in the perceived sleepiness (SSL); a significant decrease ($P<0.05$) for the subscale Vigor of the GVA. As far as performance measure are concerned, after SR both mean Reaction Time and Accuracy are significantly worse than in BL ($P<0.01$ and $P<0.005$ respectively). When the three attentional networks are considered, only the efficiency of Executive Control significantly decreases after SR ($P<005$),while for both Alerting and Orienting no difference between BL and SR can be found. Results show a selective impairment of the three networks: Alerting and Orienting are virtually untouched, while Executive Control is severely affected. This result is coherent with the hypothesis of an impairment of the frontal lobe functions, when the normal architecture of sleep is disrupted (Jones & Harrison, Sleep Med Rev 2001, 5: 463–475).

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Effects of declarative and procedural learning on sleep stages and EEG power spectral analysis

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Aim: Previous data suggested that a cognitive function of sleep is to consolidate newly acquired memories for long-term usage. Other studies show there is no indication that sleep serves a unique role in the consolidation of declarative memory and procedural skills. In the present study we investigate effects of declarative and procedural learning on polysomnography recordings (PSG) in a repeated measures design.

Methods: A total of 84 all-night PSG records, acquired with Alice4 PSG system (Respironics, USA), were gathered from 21 healthy male subjects in four consecutive nights in the Sleep Laboratory at the University of Split School of Medicine. The first night was adaptation night in which subjects accommodated to the laboratory environment, whereas second night was a control or 'baseline' night. At the third and fourth nights participants learned declarative or procedural material just before sleep. In the declarative task, they learned new textual material about animals' characteristics for two hours before sleep. In the procedural task, subjects learned seven different Formula 1 races. Subjective sleepiness was assessed with a self-rating scale (Stanford Sleepiness Scale, SSS). Recall performance was tested in the morning after sleep. PSG records were aquired with Alice4 device and staged manually during post-acquisition data analysis with Alice4 software. The spectral analysis was carried out with the pwelch function in MATLAB.

Results: Total sleep time and time spent in each sleep stage did not differ among control nights, nights after declarative, and nights after procedural learning. There were no significant differences in the SSS score before ($P=0.83$), and after sleep ($P=0.62$) among three experimental nights. The subjects exhibited significantly greater knowledge compared with 21 control students who did not learn prior to sleep ($P<0.01$). Spectral analysis and power density spectra revealed no differences among experimental nights except in the theta frequencies band on central position of electrodes.

Conclusion: The results did not show significant difference in sleep architecture and EEG power distribution in NREM and REM sleep among polysomnographic records of control night, night after declarative, and night after procedural learning.

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Sleep and memory benefits from instrumental conditioning of human sensorimotor rhythm

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Early findings by Sterman, Howe and MacDonald (1970) as well as Amzica, Neckelmann and Steriade (1997) could demonstrate that instrumental conditioning of EEG oscillations in cats during wakefulness can be transferred into sleep. The present study sought to clarify the effects of instrumental conditioning of sensorimotor rhythm (SMR; 12–15 Hz) in humans on sleep quality and duration during a 90 min midday nap as well as on declarative memory performance. 27 subjects (13 male; mean age ± SD: 23.63 ± 2.69) were randomly assigned to either a SMR-conditioning protocol (experimental group; $N = 16$) or to a randomized-frequency-conditioning protocol (control group; $N = 11$). Whereas the experimental group was trained to enhance the amplitude of their SMR-frequency range during 10 instrumental conditioning sessions-each consisting of eight 3 min sequences of SMR-conditioning-over the course of 2 weeks, the control group participated in a randomized-frequency-conditioning program (i.e., every session a different 3 Hz frequency bin between 7 and 20 Hz). Before and after this instrumental conditioning period subjects had to attend the sleep laboratory to take a 90 min nap (2 pm–3:30 pm) including complete polysomnographic montage and additionally to perform a declarative memory task before and after sleep. The three major findings of the presented experiment are: (i) our experimental design was successful in conditioning an increase in relative 12–15 Hz amplitude within 10 sessions ($P = 0.014$, d = 0.7); (ii) the increased SMR activity is also expressed during subsequent sleep by eliciting positive changes in various sleep parameters (sleep spindle number [$P = 0.004$, d = 0.6], total sleep period [$P = 0.049$, d = 0.7], sleep onset latency [$P = 0.006$, d = 0.7]); and (iii) this increased 12–15 Hz amplitude is associated with enhancement in declarative memory performance ($P = 0.011$, d = 0.9). Results thus indicated that SMR amplitude constantly increased over the 10 training sessions (in the SMR group only) and that this "shaping of one's own brain activity" also facilitated the expression of 12–15 Hz oscillations during subsequent sleep. Most interestingly, these electrophysiological changes were accompanied by profound positive sleep as well as memory performance.

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Effect of post-learning sleep versus wakefulness on advantageous decision-making under uncertainty

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The role of sleep has been suggested in off-line reprocessing of memories acquired during wakefulness and in facilitation of adaptive behavior. One action for environmental adaptation is advantageous decision-making of individuals. However, the effect of sleep on decision-making remains unclear. This study examined the effect of post-learning sleep versus wakefulness on advantageous decision-making under uncertainty. Healthy subjects were allocated to a sleep group (N = 12; six women, mean age 22.8, 20–27 years old) or a wake group (N = 12; six women, mean age 22.1, 20–24 years old). A modified version of the Iowa Gambling Task was used to investigate the role of sleep in decision-making. The sleep group slept about 8 h in their homes between tasks (session 1, 9 PM; session 2, 9 AM). The wake group stayed awake between the tasks (session 1, 9 AM; session 2, 9 PM). In the tasks, participants made selections from four decks of cards with different schedules of rewards and losses. Two decks give an immediate small reward, but long-term overall gain (advantageous decks); the other two decks give an immediate large reward, but a long-term overall loss (disadvantageous decks). Subjects are told that the goal of the task is to maximize profits of points. The placement of decks does not change across experiments. Each session continued until the participants had drawn 60 cards. The net score (number of cards selected from advantageous minus disadvantageous decks) for session 1 was, respectively, −7.5 and −5.0 for the sleep group and wake group. This difference was not significant. After sleep or waking, the sleep group chose more frequently from the advantageous decks than the wake group in session 2. The net scores for session 2 were 30.2 and 11.3, respectively, for the sleep group and wake group. This difference was significant. Sleepiness and mood, as evaluated using the Visual Analog Scale and Profile of Mood States, did not differ between groups. These results clarify that the decision-making task performance after post-learning sleep is better than that after staying awake. Results of this study suggest that sleep facilitates and/or aids retention of advantageous decision-making ability under uncertainty.

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Changes in the human hippocampal very low frequencies after learning

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The exact neurophysiological and electrophysiological mechanisms underlying the involvement of sleep in the process of memory consolidation are still poorly understood. Recent findings point to the involvement of slow EEG rhythms in post-learning plasticity. However, little is known about the relationships between memory consolidation and hippocampal EEG features. The aim of the present study is to assess the effects of both procedural and declarative learning on qualitative and quantitative measures of sleep directly recorded from the hippocampus. Scalp EEG and intracerebral (hippocampal and neocortical) stereo-EEG was recorded in eight epileptic patients undergoing presurgical evaluations. After a baseline night, sleep was recorded after the counterbalanced administration of declarative (paired-associate word list learning task) and procedural (sequential finger tapping task) tasks. On morning retest, patients correctly recalled more word pairs than pre-sleep, and were tendentially faster on the motor task. Standard polysomnography showed an increase of slow wave sleep (SWS) amount only after procedural learning, accompanied by an increase of hippocampal SEEG power in the very low frequency range (0.5–1 Hz) during the first NREM sleep cycle. This is the first study reporting about the local effects of declarative and procedural learning on sleep recorded from both scalp and intracranial derivations. The increase of power in the very low frequency range can be interpreted, in the frame of the synaptic homeostasis hypothesis, as reflecting the need of the hippocampal neurons to regain the synaptic balance altered by presleep learning. Sleep-dependent plastic modifications of the hippocampal activation have been previously reported after learning the very same procedural task used here. Moreover, it has been recently shown that the hippocampus is not the main site of activity during either learning or recall of the same declarative task employed in the present study, maybe because used words are already well

represented in memory and pairs were already semantically related. In conclusion, our data support the idea that hippocampal slow oscillations during sleep may be associated to the local processes of post-learning synaptic downscaling.

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Sleep deprivation effect on auditory discrimination task: tonality versus lateralization

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Sleep deprivation affects cognitive performances, auditory reaction time was extensively explored in sleep deprivation but auditory discrimination was less studied. We designed a study in 4 different paradigms to explore the impact of sleep loss on auditory discrimination. Twenty nine young (age: $M = 22.8$ [S.D] = 1.3) volunteers were recruited. They were tested at beginning and end of 3 sessions: 13–19H, 19–02H, and 02–07H with 1 auditory simple reaction time task and 3 auditory discrimination tasks. Test A was an auditory simple reaction time task using the Target sound (T) of 500 Hz central sound. Test B1 was a discrimination task between T and a high pitched (550 Hz) distractor sound (D1). Test B2 was a lateralization discrimination task between T and a distractor sound (D2) (500 Hz left sound). In the Test C (C), Subjects had to discriminate T between D1 and D2. Order of tasks was randomized except for test A that initiated tests. Participants were instructed to selectively respond only to the Target (go/no go) that appeared in 50% of cases, and inhibit their response for the distractor sounds. Precision and response time were recorded. Subjects Correct Responses (CR) declined over night (CD: F (5,29) = 28.3, $P < 0.001$). Subjects performances to the B1 test were higher from those obtained to B2 and C (%CD: F (2,29) = 34.9, $P < 0.001$). B2 performances decreased most significantly over night compared to B1 and C tasks (%CD: F (10,29) = 1.9547, $P < 0.05$). Sleep deprivation impacts mainly orientation discrimination and less tonality perception. We hypothesize that orientation discrimination presents a more important attentional cost than tonality discrimination when exploring the discrepancy between results at the different tasks.

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The alerting effect of hitting a rumble strip – a simulator study

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In order to reduce sleep related crashes one countermeasure that has been increasingly applied by road authorities is the introduction of so called "rumble strips" on the road surface. However, there is no information available on what happens with sleepiness variables before and after a drowsy driver makes contact with the strip. The purpose of this study was to investigate this issue. A moving base driving simulator experiment was carried using simulated rumble strips both at the edge line and centre line. Four different physical types of milled rumble strips were used in the experiment. Sound and vibrations from real milled rumble strips were reproduced in the simulator. The road was a 2-lane, 9 meter wide rural road. In total 35 regular shift workers drove during morning hours after a full night shift. The main results showed an increase in lateral variability of the vehicle, eye closure duration, subjective sleepiness and EEG/EOG measures of sleepiness from start to before hitting the rumble strip and this was reversed for most parameters after hitting the strip. The effect, however, only remained for a few minutes after the hit. The increase in sleepiness before the hit was present for at least 5 min, suggesting no "last warning" before the hit. Essentially no effects were seen due to type of strip.

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Sleep inertia and alcohol impairment in young adults: neurocognitive effects and interactions

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This study investigated the combined decrements of alcohol consumption and sleep inertia in young adults. Cognitions investigated included those required in emergency situations; mental tracking, visual scanning, working memory, and sustained, selective, and divided attention. The study involved 24 subjects (18–26 yrs). During the alcohol administration night, 10-minute testing blocks occurred under (i) baseline sober and (ii) baseline .05 blood alcohol content (BAC) conditions. Subsequently, subjects were awoken from stage 4 and assessed in two consecutive 10-minute blocks (iii) and (iv). Subjective measures of sleepiness and clear-headedness were also taken. The same procedure was used during the sober night (with condition (ii) excluded). Mental tracking, visual scanning and attentional functions showed decrements between sober baseline (i) and conditions of alcohol (ii) and further decrements under conditions of sleep inertia (iii) and (iv). When the sober and alcohol nights were compared, no further decrements were found with combined alcohol impairment and sleep inertia. Performance speed on a complex working memory task showed a similar pattern, whilst performance accuracy on this task was adversely affected by alcohol only, with no further decrements with sleep inertia, or combined alcohol impairment and sleep inertia. Hence, conditions of sleep inertia caused a speed-accuracy trade-off on the working memory task. Subjective sleepiness increased whilst subjective clear-headedness decreased with alcohol only and sleep inertia only. However, only subjective sleepiness was further affected by the combination of alcohol and sleep inertia, revealing a synergistic effect. Moderate alcohol impairment and sleep inertia do not interact synergistically on neurocognitive functioning to produce further decrements in performance than those caused by the effects of alcohol or sleep inertia alone. Hence, when awoken abruptly in an emergency situation, prior alcohol consumption to .05 BAC will not further impede cognitive functioning that is already compromised by a state of sleep inertia. Alcohol impairment and sleep inertia in combination produce more subjective sleepiness than that reported under conditions of alcohol or sleep inertia alone.

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Investigating the relationship between subjective and objective sleepiness

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Introduction: Sleepiness impairs efficient functioning and contributes to domestic and workplace accidents and deaths. We rely on subjective feelings of sleepiness to warn us of impending sleep. However, research has shown variability in the correlation between subjective sleepiness and the objective PSG sleep latency measure. Recently it has been shown that if subjective judgments are elicited after a one minute period of quiet with eyes closed, correlations between subjective and objective measures can be increased substantially from about 0.3 to 0.6. (1) The aim of the present study was to investigate further this intriguing method.

Methods: Twelve young adult, good sleepers gave subjective judgments of sleepiness using the Stanford Sleepiness Scale and Visual Analogue Scale following three prior 1 min conditions (simple reaction time task, eyes open fixed gaze, and eyes closed) in balanced order just prior to a measure of PSG sleep latency. These

subjective and objective measures were obtained a total of 12 times from each participant half-hourly across the period 2000 h to 0130 h.

Results: The within-subjects correlations across this evening period of increasing sleepiness were generally high (means about 0.60) and significant ($P<0.05$). However, contrary to our expectation, there were no differences in correlations between the three conditions. If the correlations were calculated, instead, across subjects at each testing time separately, none of the correlations were significant with means in all cases close to zero for all judgment conditions.

Conclusions: In our carefully controlled laboratory study we found high correlations between subjective and objective measures of sleepiness only within subjects across a large range of sleepiness (2000 h to 0130 h). However, we failed to find an advantage with the eyes closed condition. When clock time was controlled there were no significant correlations across subjects. Our results suggest that the variability of findings in the past may be due, at least partly, to the way in which correlations are derived.

Reference: 1. Yang CM, Lin FW, Spielman AJ. A standard procedure enhances the correlation between subjective and objective measures of sleepiness. Sleep 2004; 27: 329–32.

P540

Support for "beauty sleep" by perceived attractiveness, health and tiredness

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The assumption that too little sleep leads to decreased attractiveness, as reflected in the expression 'beauty sleep', has not been scientifically confirmed. 23 participants (11 women) with an age range between 18–31 years were photographed at 14.00 h during two conditions, after normal sleep (7 h after normal sleep 23.00–07.00 h) and during sleep deprivation (after 31 h of wakefulness) in a balanced design. The photographs (two of each participant) were thereafter presented in a randomised order and judged on visual analogue scales with respect to attractiveness, health and tiredness by 65 naive observers (45 women) with a mean age of 30 years (range 18–61). The observers judged faces of sleep-deprived persons as less attractive (-4%, $P<0.001$) than after a normal night's rest. Sleep loss also entailed more negative impressions of health (-6%, $P<0.001$) and tiredness ($+19\%$, $P<0.001$) compared to after normal sleep. In addition, the attenuated attractiveness-due to sleep loss-was strongly associated with changes in the judged health and tiredness of the observed person (p's<0.01). Our findings do not only have bearing on the beauty-fixated society at large-showing that a good night's sleep indeed carries important benefits for tomorrow's date-but might also have implications on situations where correct judgements of others' health is crucial, as for example in doctor-patient interactions

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Motor skill and verbal learning during a week with cumulative sleep loss and recovery sleep

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Objective: Acute sleep deprivation is known to impair motor skill and verbal learning. Our aim was to elucidate to what extent these learning processes are affected by a five-day working week with restricted sleep and by the following weekend with normal sleep.

Methods: 22 healthy young men (19–29 years) participated in the study. 14 of them underwent two nights of baseline sleep (8 h in bed), then five nights of sleep deprivation (SD) (4 h in bed), followed by three recovery nights (8 h in bed). The other 8 participants were allowed to sleep 8 h per night throughout the study. The SD group performed training and recall sessions in the following conditions: 1) both training and recall following 8 h of sleep, 2) training following 8 h of sleep and recall following the 1st SD night, 3) training following the 3rd SD night and recall following the 4th SD night, 4) training following the 5th SD night and recall following the 1st recovery night and 5) training following the 2nd recovery night and recall following the 3rd recovery night. Training consisted of 12, 30-sec trials in a finger tapping task and a list of 16 Finnish words repeated four times. Different tapping sequences and word lists were used in the different conditions. Sleep was recorded with standard polysomnography.

Results: The SD group completed less motor sequences in the training phase after the 3rd and 5th SD night compared to the controls. In the retrieval phase, motor performance was impaired after the 1st and 4th SD night and 1st 8 h sleep compared to the control group. Eight hours of sleep improved motor skill learning by 19–20%, whereas only a 9–13% gain was found following 4 h of sleep. There were no significant differences in verbal learning between the groups. Amounts of stage 1 ($P<0.0001$), stage 2 ($P<0.0001$) and REM ($P<0.0001$) sleep decreased in the SD group during the SD nights compared with the controls and baseline. Amount of stage 1 sleep ($P=0.05$) was decreased and SWS ($P<0.01$) was increased in the SD group during recovery compared with the controls and baseline.

Conclusions: Five days with 4 h of sleep decreased rate of motor skill learning, but had no effect on verbal learning. Changes in sleep architecture may slower the rate of motor learning.

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Relationship between distinct cognitive abilities and self-estimated sleep duration in healthy adults

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Current concepts of sleep postulate an important role for sleep for higher cognitive processes. For example, a close relationship between synaptic potentiation occurring during wakefulness and homeostatic sleep regulation is the mainstay of the "synaptic homeostasis hypothesis" of sleep (Tononi and Cirelli, 2003 & 2006). According to this hypothesis, higher tolerance to elevated sleep propensity, such as in habitual short sleepers, may predict increased bandwith for cognitive processes and, thus, an inverse relationship between distinct cognitive abilities and sleep duration. In this ongoing study, various executive functions, attention and memory are quantified in a 2 h test session in 240 healthy subjects (age: 18–40 years) with variable educational background. All subjects also filled in detailed questionnaires about their sleep-wake habits, including the Munich Chronotype Questionnaire to estimate sleep duration, and donate a sample of blood for later genetic analyses. Consistent with our prediction, the first results in 139 right-handers (75 women; mean age: 25.7 years) suggest that measures of interference control ($P<0.04$, one-way ANOVA) and design fluency ($P<0.03$) are negatively associated with sleep duration (mean over work- and leisure-days). A comparable trend ($P<0.06$) was found for word fluency. In contrast, response suppression on a go/no-go task and a measure of sustained attention were not related to self-estimated sleep duration. Rather than looking at a measure of "intelligence", we aim to assess distinct neuropsychological parameters and to investigate their

relationship with sleep regulation. Our preliminary findings relying on questionnaires indicate that highly-functioning individuals-especially with respect to executive functions-have short habitual sleep. Prospective studies quantifying sleep duration by actimetry and investigating homeostatic sleep regulation with sleep- and waking-EEG recordings before and after sleep deprivation will have to confirm the robustness of the findings reported here. Such studies are currently under way.

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Cognitive and sleep EEG evolution after paramedian thalamic stroke – preliminary results

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Introduction: Paramedian thalamic stroke (PMTS) is characterized by hypersomnia, cognitive impairment and specific EEG changes (e.g. decreased or absent spindles, decreased NREM2 and REM sleep, increased NREM1). Functional recovery after stroke is dependent on the adaptive plasticity of the cerebral cortex. There is strong evidence that sleep contributes essentially to the processes of brain plasticity and learning. The exact link between sleep, EEG and cognition in stroke recovery remains unclear.

Aim: To investigate the relationship between sleep and stroke recovery by: 1) comparing EEG power in the slow wave and spindle frequency ranges in the acute phase after PMTS and 3 months later, 2) correlating these EEG parameters to behavioral changes during the recovery process.

Patients and Methods: Three patients, two men with bilateral PMTS and one woman with unilateral PMTS underwent high-density EEG (hd-EEG) examination with 128 electrodes (Electrical Geodesics Inc.) during sleep. Additionally executive functions, attention and memory were assessed. Both EEG and neuropsychological testing were performed in the acute phase after stroke and repeated 3 months later.

Results: Both patients with bilateral PMTS presented with hypersomnia, severe attention deficit and mild memory impairment in the verbal and figural domains. Verbal fluency, nonverbal mental flexibility and frontal executive functions were also impaired. In hd-EEG both slow waves and sleep spindles were recorded in typical locations without gross asymmetry; sleep spindle power was very low. After 3 months dramatic improvement of the hypersomnia and all behavioural tests but no difference in the sleep spindles were found in one of the patients. In the patient only slight improvement of the hypersomnia and the behavioural tests were observed, sleep spindles recovered. In the patient with unilateral PMTS no cognitive impairment was found, sleep spindles were preserved and no significant changes occurred 3 months after stroke.

Conclusion: Behavioural and EEG changes occurred only after bilateral PMTS. Sleep spindles were dramatically decreased in the acute phase after bilateral PMTS but not after a unilateral lesion. Sleep spindles recovery occurred only in the patient with slight clinical improvement.

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Delayed effects of sleep on declarative memory consolidation

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Chronic sleep deprivation, which is a common problem in today's life, has been repeatedly shown to impair neuronal functioning and learning. Particularly people with the need for high cognitive performance-like students, scientists or managers-often have a tendency to sleep less, which impairs their performance. However, daytime naps have been shown to improve memory consolidation and counteract the effects of sleep loss. We tested the effects of daytime naps on verbal learning of adolescent participants of a summer school for gifted students, who had experienced moderate to severe sleep loss for 10 days. 64 adolescent gifted students (age 17.5 ± 1.2 years) who had experienced 106 ± 68 min of nightly sleep loss for 10 nights were tested on two consecutive days after lunch with two verbal memory tests: Learning german short stories (25 information chunks in 2 min) and turkish words (20 words in 5 min). In a randomized design, on one of the two days the subjects were required to have a 45 min nap immediately after learning, while staying awake on the other day. The learned words and stories had to be recalled on a test session in the evening and on a retest session one week later. In the nap condition (naps of 39.0 ± 14.2 min), the subjects were able to remember 14.4 turkish words and 19.6 story information chunks in the evening recall, compared to 13.7 words and 18.1 chunks in the awake condition. While the difference between the two conditions was significant for story learning ($P<0.01$), it was not for word learning ($P>0.3$). However, at the retest session one week later, the difference between the nap and wake conditions also reached significance for word learning (10.7 versus 9.6, $P<0.01$) as well as becoming even larger for story learning (17.7 versus 15.9, $P<0.01$). In conclusion, daytime naps had a beneficial effect on verbal learning of gifted adolescents with sleep debt, which became more pronounced with time.

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Time-dependent impairment of memory consolidation induced by partial and chronic sleep deprivation in mice

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Numerous studies have demonstrated physiological alterations induced by sleep deprivation (SD) in humans as well as in laboratory animals. In this scene, a myriad of evidence has suggested that sleep plays an important role in the memory/learning processes and that SD induces behavioural alteration that could be related to memory deficits in animal models. While the most ordinary SD condition found in our round-to-clock society is partial and chronic sleep deprivation (PCSD), its effects on learning/memory remain overlooked. In this study, we aimed to verify the effects of PCSD for 3, 6, 9 or 15 days in mice tested in the plus-maze discriminative avoidance task (PM-DAT), which evaluates concomitantly learning/memory, anxiety and motor activity in rodents. Thus, 3-month-old Swiss male mice were submitted to control (CTRL-home cage), stress control (SC – 21 h in large platforms and 3 h in home cage) or to PCSD (21 h of SD and 3 h in home cage) procedures for 3, 6, 9 or 15 days. SD was set at 1 pm to 10 am and the multiple platform method was employed in this study. Immediately after the SD, the animals were submitted to a training session and 24 h later, to a test session. In addition, 30 days after the training session, animals were retested. Our results showed that in the training session, only PCSD for 15 days promoted learning impairments, followed by an increase in motor activity. Neither stress nor PCSD (irrespectively of duration) induced anxiety-like behaviour alterations in this session. Concerning memory (test session), only animals submitted to PCSD for 15 days presented an impairment in the intermediate-term memory of the discriminative avoidance task as well as habituation deficits. In the retest session (30 days after the training session), PCSD for 6, 9 or 15 days (and also SC for 15 days) impaired long-term memory of the task. Taken together, these

results suggest that partial and chronic sleep deprivation-a more translational condition of sleep restriction-impairs learning/memory in a time-dependent manner. In other words, the longer is the duration of PCSD, the more weakened seems to be memory consolidation ability. Additionally, these memory impairments do not seem to be promoted by anxiety-like or motor activity alterations.

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Four hours of sleep deprivation does not affect object recognition performance in the rat

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Several lines of evidence support the hypothesis that sleep is necessary for declarative and procedural memory processing in mammals. Object recognition task (ORT) is a hyppocampal-dependent learning process. Sleep deprivation performed immediately after ORT acquisition phase interferes with ORT performance in mice (Palchykova et al. 2006). Here we explore the effect of total and selective REM sleep deprivation on ORT performance in the rat. Male rats were EEG and EMG recorded under a 12:12 light-dark cycle in isolation chambers. During acquisition phase (AQP), animals were exposed during 5 min to a set of four objects in five sessions. AQP was performed during the last hour of the dark phase. Immediately after AQP, animals were subjected to three different delay phase conditions: (i) undisturbed sleep-wake (UD, $n = 5$); (ii) 4 h of total sleep deprivation (4TSD, $n = 6$); (iii) 4 h of selective REM sleep deprivation (4RSD; $n = 5$). Test phase (TEP) was applied 24 h later and consisted of two 10 min sessions. Two of the familiar objects were replaced by novel objects. Behavior was evaluated by infrared video records. Exploration time correspond to time spent at a distance of 2 cm or less of an object. Exploration ratio correspond to the sum of exploration time on novel objects divided by total exploration time in the interval. Total exploration time during AQP was similar for the three groups, and displayed a marked decay across exposition sessions (98.6 sec in first session to 28.2 in the fifth session). No differences were observed among groups for total exploration time during TEP. Novel object exploration ratio for UD, 4RSD and 4TSD were 0.58, 0.58 and 0.68 respectively ($P = 0.27$, one-way ANOVA). Four hours of TSD or RSD applied immediately after ORT acquisition phase does not affect object recognition performance in the rat. Grant FONDECYT 1061089

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Efficiency of working memory scanning and resolution of proactive interference are maintained during sleep deprivation in a modified Sternberg task

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Working memory (WM) functions, in particular resolution of proactive interference, are important for executive functioning. We examined the effects of total sleep deprivation (TSD) on WM in a validated, modified Sternberg task. Subjects were asked repeatedly to keep an item set in WM and decide whether a subsequently shown probe was present in the set. To examine WM scanning efficiency, half the sets contained two items, while half contained four. Furthermore, half the negative probes were found in the item set presented immediately beforehand. Inhibiting a positive (incorrect) response triggered by this recency effect requires resolution of proactive interference.

Methods: 24 healthy adults (22–40 y; 12f) spent 7 consecutive 24 h days in a laboratory with continuous behavioral monitoring. 12 subjects were randomized to 62 h TSD preceded and followed by two days with 10 h TIB; 12 controls had 10 h TIB each night. The modified Sternberg task was administered at 11:00 during baseline, 52 h TSD (or control), and recovery. During each test bout, subjects received one of three equivalent task versions in randomized, counterbalanced order. As a control task, the PVT was administered regularly throughout the study. Data were analyzed with mixed-effects ANOVA.

Results: PVT lapses (RTs >500 ms) showed the typical profile of impairment during TSD and no impairment in the control condition ($P<0.001$). Relative to controls, sleep-deprived subjects displayed decreased accuracy (85.1% versus 96.7%, $P<0.001$), and increased RTs for correct responses (864 ms versus 808 ms, $P<0.001$). The increase in RTs was independent of item set size ($F = 0.04$, $P = 0.84$). Additionally, the difference in RTs to negative probes with or without recency effect was unaffected by TSD ($F = 0.02$, $P = 0.89$).

Discussion: Overall performance on the PVT and on the modified Sternberg task was degraded by 52 h TSD. However, the effect on Sternberg task performance was the same regardless of set size, indicating that the efficiency of WM scanning was not impaired by TSD. Moreover, TSD did not affect the speed by which proactive interference from recent item sets was resolved. This suggests that executive functions may not be differentially vulnerable-perhaps even partially preserved-under conditions of sleep deprivation.

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Sleep modulates both spatial and contextual memory in virtual navigation

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Post-training sleep shapes the neural representations that subtend spatial memories acquired while navigating in a virtual environment [1]. However, navigation is not a pure process, as manifold cognitive processes including spatial and contextual memory contribute to performance [2]. In this context, it remains unclear whether post-training sleep globally promotes consolidation of all of the memory components embedded in virtual navigation, or rather favors the development of specific representations. We investigated the effect of post-training sleep on the neural substrates of the consolidation of spatial and contextual memories acquired while navigating in a complex 3D, ecological virtual town. Using fMRI, we mapped regional cerebral activity during various tasks designed to tap either the spatial or the contextual memory component, or both, 72 h after encoding with or without sleep deprivation during the first post-training night (12 subjects/group). fMRI data were analyzed using SPM2. Behavioral performance was not affected by post-training sleep deprivation, both in a natural setting or if looking more specifically at spatial or contextual memories. At the neuronal level however, variations in place-finding efficiency in a natural setting were associated with caudate activity, more in subjects allowed to sleep on the post-training night than in sleep-deprived subjects, suggesting that sleep had favored the automation of navigation. Furthermore, analyses focused on the contextual condition revealed correlations between performance and neuronal activity in frontal areas associated with recollection processes in subjects allowed to sleep, and in the parahippocampal gyrus associated with familiarity processes in sleep-deprived participants. Likewise, spatial memory was associated with posterior cortical activity in

sleep conditions and parahippocampal/medial temporal activity after sleep deprivation. Our data indicate that post-training sleep modulates the neural substrates of both spatial and contextual memory consolidation in virtual navigation. [1] Orban et al. 2006, Proc Natl Acad Sci U S A, 103:7124–9; [2] Rauchs et al. 2008, Hippocampus, Advance online publication 31 Jan.

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Prolonged spontaneous wheel running enables memory consolidation in mice

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There is compelling evidence that sleep is important for memory consolidation, whereas an interval of sleep deprivation following learning, leads to performance impairment both in animals and humans. Moreover, sleep should occur within a specific time window following upon learning, to facilitate consolidation. However, it is still unclear how sleep facilitates memory. Sleep might be essential to enable the processes leading to memory consolidation. Alternatively, sleep may provide favorable non-interference conditions, thereby allowing optimal consolidation. We investigated whether a specific interference occurring during waking affects memory consolidation in an object recognition task. Interference consisted of spontaneous, voluntary wheel running (RW) that was compared to the effect of either normal waking in the home cage, or the blocking of a RW immediately after learning. Mice of two strains (OF1 and C57BL/6) were either provided with a RW for several weeks or kept without a RW (controls). All animals were subjected to an acquisition phase at dark onset. Thereafter, the RW was blocked in half of the RW mice. The ability to discriminate between a novel and two familiar objects was assessed 24 h later during the test phase. Infra-red activity and RW revolutions were continuously recorded at 1-min intervals. Learning behavior was video taped. The RW groups of both strains ran vigorously for several hours during the first 7 h after acquisition and rested significantly less than the undisturbed controls or the mice with the blocked RW. At test, control mice and the mice with the blocked RW explored the novel object longer than the two familiar ones, indicating successful discrimination. Also the RW groups explored the novel object significantly longer than the familiar ones; therefore, they remembered the objects, despite obtaining little rest after acquisition. The results suggest that waking consisting of vigorous, monotonous activity occurring within the first 7 h after acquisition, enables object memory consolidation as sleep does. It is possible that the intense running either before or after acquisition had a direct facilitating effect on memory or provided favorable conditions for consolidation.

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Offline processing of memories induced by perceptual visual learning during subsequent wakefulness and sleep: a behavioural study

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To further characterize perceptual memory consolidation during sleep, we used a novel coarse orientation discrimination task in which participants had to discriminate the orientation of orthogonal gratings occluded by increasing levels of sinusoidal noise. In a first study ($N = 11$), we showed that the learning effect in this task is retinotopic (position-specific) and orientation-specific. In a second experiment, we assessed the effect of nocturnal sleep, as opposed to the effect of time, on perceptual learning. A first group of participants was trained in the morning, tested in the evening and retested the next morning (Morning-Evening-Morning, MEM, $N = 11$); a second group was trained in the evening, tested the next morning and retested in the evening (Evening-Morning-Evening; EME; $N = 12$). Between training and testing, EME subjects' performances improved significantly more (after a night of sleep) than MEM subjects (after 12 waking hours). Similarly, between test and retest, performance of MEM subjects (after a full night of sleep) improved significantly more than in EME subjects (after 12 further waking hours). These results suggest a beneficial effect of nocturnal sleep on coarse orientation discrimination, independent on circadian effects. Further studies are needed to characterize the neural correlates of this perceptual learning and the offline consolidation of perceptual memory.

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Making implicitly learned information explicitly available and the role of sleep herein

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In a previous study, we have demonstrated that post-learning sleep, selectively promotes the formation of explicit memory for a solely implicitly learned probabilistic sequence in a SRT-task (Fischer et al. 2006). These data indicated that sleep but not wakefulness is involved in an interaction of implicit and explicit memory systems during consolidation. We expand these data by further investigating this process. In this study two groups of 20 subjects either were allowed to sleep for two successive nights (sleep group) or were instructed to stay awake the first of two nights (wake group), after having performed a second-order probabilistic SRT-task. Afterwards, half of the subjects of each group additionally performed a Generation task, and thus became aware of the presence of a sequence. After the post-learning interval all subjects performed a Generation task. Results indicated that after training on the SRT-task subjects had acquired sufficient implicit knowledge of the sequence although the subjects that subsequently performed the Generation task did so at chance level. Analysis of the data for the Generation task performed after the retention interval showed that both sleep and being aware of the presence of a sequence, enhanced performance on the Generation task but these two factors did not seem to interact (significant main-effects for sleep and for awareness but not for their interaction, $F(1,36) = 4.43$, $P = 0.04$, $F(1,36) = 6.78$, $P = 0.01$ and $F(1,36) = 0.05$, $P = 0.82$ respectively. Hence, the data indicate that the sooner awareness about the presence of a sequence is acquired the more this information can be used explicitly and that sleep can further promote the process of transiting of implicit learning into explicit knowing.

Literature Cited: Fischer S, Drosopoulos S, Tsen J, Born J. 2006. Implicit learning – explicit knowing: a role for sleep in memory system interaction. J. Cogn Neurosci. 18 (3):311–9

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Decreases in stage 2 sleep, spindles and sigma power following acquisition of a declarative task

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A number of studies have reported increases in NREM sleep variables following acquisition of a declarative task. The present

study examined sleep state changes following acquisition of lists of two word pairs, separated by 12 h that included a night of sleep or a period of waking.

Method: Female adults were asked to learn a paired associate (PA) list (A-B) to 100% correct criterion. After 12 h, which included a night of sleep (SLP, $n = 10$) or an equal period of Awake (AW, $n = 10$), participants were given a second PA list (A-C). Then after a 15 min distractor task, participants were asked to recall both list A-B and A-C (Test 1). SLP subjects were recorded at central and frontal sites for 3 consecutive nights, an acclimatization night (discarded), a baseline, and post training night. A second retest was given 1 week later (Test 2).

Results: Behavioural: The SLP group had superior memory recall for the A-B list compared to the AW group at both Test 1 and Test 2 [$F\ (1,18) = 13.58$, $P < 0.002$]. Sleep Recording: There was a significant drop in number of minutes of Stage 2 sleep from baseline to post training night ($P < 0.05$). As well there was a drop in number of Stage 2 sleep spindles ($P < 0.02$) at frontal sites. Power spectral analyses revealed significant pre-post decreases in delta, alpha and sigma bands during NREM and REM sleep, especially in the right hemisphere ($P < 0.05$). The drop in number of spindles was highly correlated with correct performance ($r = -.823$, $P < 0.003$).

Conclusions: Post training sleep is beneficial to PA declarative memory. Results are unique in reporting reductions in a number of sleep state variables. The relationship of sleep to declarative memory is more complex than has been suspected.

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Dependence of planning efficiency on EEG slow-wave activity during sleep

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Introduction: Prefrontal cortex dependent cognitive functions such as planning appear to be particularly vulnerable to sleep deprivation, and may therefore depend strongly on the homeostatic recovery associated with the generation of slow-wave activity (SWA; EEG power density in the 0.75–4.5 Hz range) during sleep. Here we used an acoustic SWA suppression paradigm to test whether SWA is a determinant of planning efficiency during subsequent wakefulness. 20 healthy subjects participated in single-blind parallel-group protocol that included an adaptation and a baseline (BL) sleep episode, a 20 h sleep deprivation period, a 4 h experimental (EX) sleep episode with or without SWA suppression, and assessment of subjects' planning efficiency by means of the Tower of London (TOL) task on the day following EX. In 11 subjects (age 18–29 year; 7 F), SWA was suppressed with acoustic tones (45–100 dBA), and in 9 subjects (age 18–30 year; 6 F) no tones were administered (control). Subjects were presented de novo with 12 computerized TOL puzzles of increasing difficulty, and were asked to solve them with the minimum number of moves. Planning efficiency was quantified as the ratio (%) of the minimal number of moves to solve the puzzles divided by the actual number of moves made by a subject. During EX, SWA (derivation: F3/C3) was reduced to 71% in the suppression group compared to BL, but remained close to BL levels (95%) in the control group ($P = 0.015$ between groups, unpaired t-test). REM sleep amount did not differ between groups. Planning efficiency was lower ($P < 0.05$) in the suppression group (mean ± SEM: 71.2 ± 4.8%) than in the control group (84.4 ± 3.3%). Across individuals, SWA in EX sleep correlated with planning efficiency ($r = 0.61$, $P = 0.004$ for log/log-transformed values; $N = 20$). It is concluded that in contrast to neurobehavioral functions that depend to a lesser extent on the prefrontal cortex and that were found to be unaffected by SWA suppression, planning efficiency depends significantly on the sleep-homeostatic recovery associated with the generation of SWA. The results are consistent with the hypothesis that frontal brain regions have increased homeostatic sleep need.

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The role of kinase and phosphatase pathways in sleep-dependent consolidation of cortical plasticity

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We have shown that sleep consolidates a canonical form of in vivo synaptic remodeling in the visual cortex (V1), triggered by monocular deprivation (MD) during a critical developmental window (known as ocular dominance plasticity [ODP]). The effects of sleep on ODP are mediated by NMDA receptor (NMDAr)-dependent mechanisms, which may involve long-term synaptic potentiation (LTP) or long-term synaptic depression (LTD) within V1. Such long-term changes within V1 are mediated by NMDAr-activated kinase and phosphatase pathways, respectively. We investigated the role of LTP-like or LTD-like pathways in sleep-dependent consolidation of ODP by infusing specific kinase and phosphatase inhibitors into V1 during post-MD sleep. ODP was assessed by intrinsic signal imaging and single-unit recording of responses in V1 to stimuli presented to the deprived and non-deprived eyes (DE and NDE, respectively). A large shift in neuronal responses in favor of the open eye occurred when V1 was infused with vehicle during post-MD sleep. Further analyses revealed that V1 changes underlying consolidation of ODP in vehicle-infused cats involved both depression of DE responses and potentiation of NDE responses. MD alone (without subsequent sleep) induced depression of DE responses, but failed to potentiate NDE responses. Subsequent sleep resulted in NDE response potentiation and maintenance of prior DE response depression. Like NMDAr antagonism, cAMP-dependent protein kinase (PKA) inhibitor treatment during post-MD sleep blocked the consolidation of ODP, impaired sleep-dependent potentiation of NDE responses, and reversed the depression of DE responses. This result is consistent with roles for PKA in mediating LTP and LTD in V1. In contrast, inhibition of extracellular signal-regulated kinase (ERK) during post-MD sleep had no effect on consolidation of ODP. Inhibition of the protein phosphatase calcineurin during post-MD sleep resulted in an intermediate phenotype, with a moderate decrease in sleep-dependent ODP consolidation. These findings demonstrate that sleep consolidates synaptic remodeling via PKA- and calcineurin-dependent intracellular mechanisms, and suggest that both LTD-like and possibly LTP-like mechanisms are critical for sleep-dependent plasticity in V1.